Nos. 25A1207, 25A1208

In the Supreme Court of the United States

DANCO LABORATORIES, L.L.C.,
Applicant,

v.

LOUISIANA, ET AL.,
Respondents.

GENBIOPRO, INC.,
Applicant,

v.

LOUISIANA, ET AL.,
Respondents.

APPENDIX TO OPPOSITION TO DANCO LABORATORIES, L.L.C.'S AND GENBIOPRO, INC.'S APPLICATIONS FOR A STAY OR VACATUR

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Page	Parallel Citation	Description
APP00001	Dist.Ct.ECF.1	Complaint (Oct. 6, 2025)
APP00052	Dist.Ct.ECF.1-2	Society of Family Planning, #WeCount Report April 2022 to December 2024 (Jun. 23, 2025)
APP00120	Dist.Ct.ECF.1-3	2021 FDA Letter to ACOG and SMFM About Mifepristone REMS (Apr. 12, 2021)
APP00123	Dist.Ct.ECF.1-4	Dr. Margaret Carpenter indictment
APP00126	Dist.Ct.ECF.1-9	FDA-Approved Label for Mifepristone (Mifeprex) (Jan. 2023)
APP00146	Dist.Ct.ECF.1-10	FDA Letter to AAPLOG and Am. Coll. of Pediatricians denying in part and granting in part 2016 Citizen Petition, Docket No. FDA-2019-P-1534 (Dec. 16, 2021)
APP00187	Dist.Ct.ECF.1-11	Center for Drug Evaluation and Research, Application Number 020687Orig1s020 (Mar. 29, 2016)
APP00216	Dist.Ct.ECF.1-13	Jamie Bryan Hall & Ryan T. Anderson, *The Abortion Pill Harms Women: Insurance Data Reveals One in Ten Patients Experience a Serious Adverse Event* (Apr. 28, 2025)
APP00223	Dist.Ct.ECF.1-14	James Studnicki et al., *Comparative Acuity of Emergency Department Visits Following Pregnancy Outcomes Among Medicaid Eligible Women, 2004–2015*, Int'l J. Epidemiology & Pub. Health Rsch., Apr. 2024
APP00228	Dist.Ct.ECF.1-21	Citizen Petition of AAPLOG to FDA (Aug. 8, 2002)
APP00232	Dist.Ct.ECF.1-44	Exec. Order No. 14076, Protecting Access to Reproductive Healthcare Services, 87 Fed. Reg. 42053 (July 8, 2022)
APP00236	Dist.Ct.ECF.1-45	Exec. Order No. 14079, Securing Access to Reproductive and Other Healthcare Services, 87 Fed. Reg. 49505 (Aug. 3, 2022)
APP00240	Dist.Ct.ECF.1-47	White House, *FACT SHEET: President Biden Announces Actions in Light of Today's Supreme Court Decision on Dobbs v. Jackson Women's Health Organization* (June 24, 2022)
APP00243	Dist.Ct.ECF.1-48	Press Release, HHS, *HHS Secretary Becerra's Statement on Supreme Court Ruling in Dobbs v. Jackson Women's Health Organization* (June 24, 2022)
APP00245	Dist.Ct.ECF.1-49	Press Release, HHS, *Remarks by Secretary Xavier Becerra at the Press Conference in Response to President Biden's Directive following Overturning of Roe v. Wade* (June 28, 2022)
APP00249	Dist.Ct.ECF.1-50	Center for Drug Evaluation and Research, Application Number 020687Orig1s025 (Jan. 3, 2023)

APP00340	Dist.Ct.ECF.1-51	Center for Drug Evaluation and Research, Application Numbers 020687 and 91178 (Dec. 16, 2021)
APP00390	Dist.Ct.ECF.1-52	FDA Adverse Events Reporting System (FAERS) Public Dashboard
APP00408	Dist.Ct.ECF.1-59	Press Release, HHS, *HHS Releases Report Detailing Biden-Harris Administration Efforts to Protect Reproductive Health Care Since Dobbs* (Jan. 19, 2023)
APP00412	Dist.Ct.ECF.1-60	White House, *FACT SHEET: The Biden-Harris Administration's Record on Protecting Access to Medication Abortion* (Apr. 12, 2023)
APP00415	Dist.Ct.ECF.1-61	HHS, Secretary's Report, *Health Care Under Attack: An Action Plan to Protect and Strengthen Reproductive Care* (Aug. 2022)
APP00439	Dist.Ct.ECF.1-71	Aid Access, *Get Abortion Pill Online in Louisiana*
APP00444	Dist.Ct.ECF.1-84	Rosemary Westwood, *After Historic Indictment, Doctors Will Keep Mailing Abortion Pills Over State Lines*, NPR (Mar. 19, 2025)
APP00455	Dist.Ct.ECF.1-85	Katherine Donlevy, *Louisiana DA warns there's trove of evidence against NY doctor who allegedly mailed abortion pills to teen – who was planning gender reveal party* (Feb. 15, 2025)
APP00461	Dist.Ct.ECF.1-86	Lorena O'Neil, *Louisiana Mother Pleads Not Guilty Following Abortion Pill Indictment*, La. Illuminator (Mar. 11, 2025)
APP00465	Dist.Ct.ECF.1-90	Governor Kathy Hochul (GovKathyHochul), X (May 13, 2025, 4:28 PM)
APP00467	Dist.Ct.ECF.1-92	Declaration of Rosalie Markezich (Jul. 17, 2025)
APP00473	Dist.Ct.ECF.1-106	AP, *Texas Has A New Abortion Pill Law, But At Least One Provider Plans to Keep Shipping Them There*, Newsday, (Sept. 18, 2025)
APP00477	Dist.Ct.ECF.1-110	Letter from Robert F. Kennedy, Secretary of Health and Human Services, to Attorneys General (Sept. 19, 2025)
APP00480	Dist.Ct.ECF.20	Plaintiffs' Motion for Preliminary Relief (Dec. 17, 2025)
APP00485	Dist.Ct.ECF.20-2	Society of Family Planning, *#WeCount Report Summary Slides with National and 51 State-Level Findings April 2022 to June 2025* (Dec. 9. 2025)
APP00552	Dist.Ct.ECF.20-4	Robin Wallace et al., *P040 - Expanding Access to Abortion with Mifepristone and Misoprostol Through 84 Days Estimated Gestational Duration,* 151 Contraception 111117 (Nov. 2025)
APP00554	Dist.Ct.ECF.20-6	*US FDA has delayed abortion pill safety study, Bloomberg News Reports,* Reuters (Dec. 8, 2025)

APP00565	Dist.Ct.ECF.20-7	Elizabeth Troutman Mitchell, *EXCLUSIVE: Makary Responds to Report Saying He Slow-Walked Abortion Pill Safety Review,* Daily Signal (Dec. 9, 2025)
APP00579	Dist.Ct.ECF.20-16	FDA REMS Single Shared System for Mifepristone 200MG (May 2021)
APP00588	Dist.Ct.ECF.20-18	Declaration of John Voltz, M.D. (Nov. 17, 2025)
APP00592	Dist.Ct.ECF.20-19	Declaration of Kathleen Richard, LMSW (Nov. 12, 2025)
APP00596	Dist.Ct.ECF.20-20	Declaration of Kathleen Willis, M.D. (Dec. 15, 2025)
APP00601	Dist.Ct.ECF.20-21	Declaration of Dr. Christina Francis, M.D. (Dec. 12, 2025)
APP00618	Dist.Ct.ECF.20-22	Declaration of Michael J. New, Ph.D (Dec. 15, 2025)
APP00639	Dist.Ct.ECF.20-23	Declaration of Angela Parise, M.D. (Dec. 11, 2025)
APP00644	Dist.Ct.ECF.20-24	Declaration of Lindsey Sikes (Dec. 15, 2025)
APP00647	Dist.Ct.ECF.20-26	Plaintiffs' Memorandum of Law in Support of Their Motion for Preliminary Relief (Dec. 17, 2025)
APP00678	Dist.Ct.ECF.50	Federal Defendants' Motion to Stay the Case (Jan. 27, 2026)
APP00709	Dist.Ct.ECF.51	Federal Defendants' Memorandum in Support of Motion to Stay and in Response to Plaintiffs' Motion for Preliminary Relief (Jan. 27, 2026)
APP00735	Dist.Ct.ECF.111	Plaintiffs' Memorandum Reply ISO Motion for Preliminary Relief and in Opposition to Motion to Stay (Feb. 17, 2026)
APP00773	Dist.Ct.ECF.111-1	Declaration of E. Toner (Feb. 17, 2026)
APP00776	Dist.Ct.ECF.258	Memorandum Ruling Granting Motion to Stay and Denying Motion for Preliminary Relief (Apr. 7, 2026)
APP00813	CA5.ECF.12-1	Appellants' Motion for 705 Stay (Apr. 17, 2026)
APP00965	CA5.ECF.74	Federal Appellees' Response/Opposition to Motion for 705 Stay (Apr. 23, 2026)
APP00995	CA5.ECF.89	Plaintiff's reply in support of motion for 705 Stay pending appeal (Apr. 24, 2026)
APP01016	CA5.ECF.119-1	Fifth Circuit Order Granting 705 Stay (May 1, 2026)

UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF LOUISIANA
LAFAYETTE DIVISION

THE STATE OF LOUISIANA, by and through its Attorney General, LIZ MURRILL, and ROSALIE MARKEZICH, PLAINTIFFS, v. U.S. FOOD AND DRUG ADMINISTRATION; MARTIN A. MAKARY, M.D., M.P.H., in his official capacity as Commissioner of Food and Drugs, U.S. Food and Drug Administration; GEORGE FRANCIS TIDMARSH, M.D., PH.D., in his official capacity as Director, Center for Drug Evaluation and Research, U.S. Food and Drug Administration; U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; and ROBERT F. KENNEDY, JR., in his official capacity as Secretary, U.S. Department of Health and Human Services, DEFENDANTS.	Civ. No. 6:25-cv-01491 Judge _____ Mag. Judge _____

COMPLAINT

1. The fight for life is far from over.

2. In *Dobbs v. Jackson Women's Health Organization*, the United States Supreme Court "return[ed] the issue of abortion to the people's elected representatives." 597 U.S. 215, 232 (2022). That decision empowered each state to "evaluate the competing interests and decide how to address this consequential issue." *Id.* at 339 (Kavanaugh, J., concurring). And as a result, voters and their representatives may enact and enforce laws "based on their belief that abortion destroys an 'unborn human being.'" *Id.* at 256 (majority op.).

3. So it was in Louisiana. Before *Dobbs* overruled *Roe v. Wade*, 410 U.S. 113 (1973), Louisianans adopted a pro-life law—to become effective immediately upon *Roe*'s overruling—that would prohibit abortion with narrow exceptions. La. R.S. § 40:1061. After *Dobbs*, therefore, Louisiana's pro-life law took immediate effect, protecting the unborn in Louisiana.

4. Or so Louisiana thought. Shortly after *Dobbs*, pro-abortion activists and doctors launched a nationwide effort to effectuate abortions in pro-life states like Louisiana—all without setting foot in those states. How? By mail. Every year, doctors and activists in states like California and New York mail a U.S. Food and Drug Administration (FDA)-approved abortion drug called mifepristone to thousands of Louisiana residents for the express purpose of causing abortions in Louisiana that are blatantly unlawful.

5. The reality on the ground is striking. The pro-abortion Society of Family Planning's 2024 #WeCount report states that, from April to June 2024 alone, mail-order abortion drugs—sent into Louisiana from doctors and activists in other states—accounted for an average of 617 abortions in Louisiana *per month*.[1] And #WeCount data released in June 2025 describes that number as topping *800 abortions* in Louisiana in *December 2024 alone*.[2]

6. This extra-territorial mailing of abortion drugs is illegal under state law—and it is the direct result of the Biden Administration's 2023 agency action expressly facilitating this scheme. That action is the subject of this lawsuit.

7. For years, FDA required mifepristone to be dispensed in person. For good reason: As FDA continues to acknowledge today, mifepristone poses serious risks to women—so much so that the FDA-required label says that roughly 1 in 25 women who use mifepristone *as directed* will end up in the emergency room.

8. In 2023, however, the Biden Administration removed the in-person dispensing requirement from its Risk Evaluation and Mitigation Strategy (REMS) for mifepristone. The Biden

[1] Ex. 1, Society of Family Planning, #WeCount Report April 2022 to June 2024 at 10 (Oct. 22, 2024), perma.cc/WRW3-PMWK.

[2] Ex. 2, Society of Family Planning, #WeCount Report April 2022 to December 2024 at PowerPoint slide 35 (Jun. 23, 2025), perma.cc/RM6F-H2Q9.

Administration did so for avowedly political reasons. President Biden had ordered his Administration to "identify all ways" to make abortion available in those states that, after *Dobbs*, opted to protect the life of the unborn. And the 2023 REMS was a banner achievement in carrying out that directive for—as FDA freely noted—the 2023 REMS now allows the "dispensing of mifepristone through the mail ... or through a mail-order pharmacy."[3] In other words, but for the 2023 REMS, activists in New York and California could not blanket pro-life states like Louisiana with mifepristone by mail.

9. But some of the women who ingest the drugs do not want an abortion. Since FDA effectively allowed "blind" dispensing without the in-person care of a doctor, bad actors have been able to obtain FDA-approved abortion drugs from prescribers in other states and then secretly spike women's drinks without their knowledge or force women into taking these drugs against their will.

10. This is what happened to Rosalie Markezich. In October 2023, under immense pressure and fearing for her safety, Rosalie took abortion drugs that her boyfriend obtained via the U.S. Postal Service from a doctor in California. Rosalie did not want to have an abortion. But far from empowering Rosalie to make her own choice and preserving her autonomy, mail-order abortion drugs had Rosalie feeling trapped and terrified. She grieves the loss of her child and endures lasting emotional trauma. But for FDA's 2023 REMS, Rosalie would have received the protection of a private in-person medical appointment. And if she had been able to tell a doctor that she did not want an abortion, the drugs that took her baby's life would never have been provided.

11. There is no serious dispute that the 2023 REMS is unlawful on Administrative Procedure Act grounds—five Fifth Circuit judges already have recognized as much. So have Defendants.

12. *First*, the 2023 REMS is arbitrary and capricious, not least because it rests on FDA's unsupported determination that mifepristone is safe—a determination based on the absence of any adverse events reported *in a system FDA already gutted*. 5 U.S.C. § 706(2)(A). Said Judges Oldham and Engelhardt: The "ostrich's-head-in-the-sand approach" reflected in the reasoning adopted by the 2023

[3] Ex. 3, 2021 FDA Letter to ACOG and SMFM About Mifepristone REMS at 2 (Apr. 12, 2021).

REMS "suggests FDA's actions are well 'outside the zone of reasonableness.'" *All. for Hippocratic Med. v. FDA*, 2023 WL 2913725, at *17 (5th Cir. Apr. 12, 2023) (*Alliance I*). Chief Judge Elrod (for herself and Judges Ho and Wilson) echoed that sentiment, stating that the earlier panel "aptly" concluded that FDA's 2023 REMS is likely arbitrary and capricious. *All. for Hippocratic Med. v. FDA*, 78 F.4th 210, 249–51 (5th Cir. 2023) (*Alliance II*). The unanimous panel also determined that the 2023 REMS "was not reasonable" because the agency relied on published literature "despite FDA's admission that the literature did not affirmatively support its position." *Id.* at 250. So the Court here need only cite the Fifth Circuit's own conclusions to hold that the 2023 REMS is arbitrary and capricious.

13. Defendants recently admitted that there was a "lack of adequate consideration" of the safety risks "underlying the prior REMS approvals," including the decision to "remov[e] the in-person dispensing requirement."[4] Defendant Secretary Kennedy went so far as to concede that the "Biden administration removed mifepristone's in-person dispensing rule without studying the safety risks."[5]

14. *Second*, as Judge Ho recognized in *Alliance II*, the 2023 REMS also is contrary to law because it "violate[s] the Comstock Act, 18 U.S.C. §§ 1461–62, and [thus is] 'not in accordance with law' for that reason as well." *Id.* at 267 (Ho, J., concurring in part and dissenting in part) (quoting 5 U.S.C. § 706(2)(A)). Among other things, the Comstock Act prohibits the mailing of "[e]very article or thing designed, adapted, or intended for producing abortion." 18 U.S.C. § 1461. The Act also prohibits the use of "any express company or other common carrier or interactive computer service" for "any drug, medicine, article, or thing designed, adapted, or intended for producing abortion." *Id.* § 1462. Each one of these provisions covers, of course, precisely the mailing of mifepristone that the Biden Administration intentionally sought to facilitate through the 2023 REMS. So for that additional reason, the Court need only cite Judge Ho's concurrence to "set aside the [2023 REMS] because it

[4] Ex. 110, Letter from Robert F. Kennedy, Secretary of Health and Human Services, to Attorneys General at 1 (Sept. 19, 2025).

[5] Ex. 108, Secretary Kennedy (@SecKennedy), X (Oct. 2, 2025, 5:44 PM), perma.cc/Q2SA-BJKS.

violates the Comstock Act." *Alliance II*, 78 F.4th at 270 (Ho, J., concurring in part and dissenting in part).

15. Now, to be sure, the Supreme Court itself did not address these arguments because it ultimately disposed of the original *Alliance* plaintiffs on standing grounds. *See FDA v. All. for Hippocratic Med.*, 602 U.S. 367, 374 (2024). But this case supplies the standing piece that the Supreme Court found lacking in *Alliance*. Specifically, for example, Louisiana has incontrovertible evidence that, because of the 2023 REMS, doctors and others are (as the Biden Administration intended) sending streams of mifepristone by mail into Louisiana for the express purpose of causing thousands of abortions in Louisiana every year. That conduct directly violates Louisiana's abortion laws and prevents Louisiana from protecting the lives of unborn babies despite the promise of *Dobbs*. That conduct also has directly generated medical emergencies that harm Louisiana women and emergency room visits that harm the State. For these points, look no further than a pending indictment in Louisiana, which charges Dr. Margaret Carpenter of New York with mailing FDA-approved mifepristone into Louisiana that ultimately sent a teenage girl to a Louisiana emergency room.[6]

16. This is an extraordinarily serious case, but it is also an extraordinarily easy case: Through the 2023 REMS, the Biden Administration attempted to undermine *Dobbs* by facilitating the mailing of mifepristone into every pro-life state, thus harming Louisiana and causing women like Rosalie immense suffering. But the Fifth Circuit has twice recognized the likely illegality of the reasoning embraced by the 2023 REMS. Accordingly, the Court need only follow the Fifth Circuit's guidance in deeming unlawful, setting aside, vacating, and enjoining the enforcement of the 2023 REMS.

JURISDICTION AND VENUE

17. This Court has subject-matter jurisdiction under 28 U.S.C. §§ 1331, 1346(a), 1361 because this action against the United States' agencies and its officers in their official capacities raises

[6] Ex. 4, Dr. Margaret Carpenter indictment.

federal questions under the Administrative Procedure Act (APA), 5 U.S.C. §§ 553, 701–06, and the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. § 301 *et seq.*

18. This lawsuit seeks declaratory, injunctive, vacatur, and other appropriate relief under the Declaratory Judgment Act, 28 U.S.C. §§ 2201–02, 5 U.S.C. § 706, Fed. R. Civ. P. 57, and this Court's inherent equitable powers. *See Louisiana v. Biden*, 622 F. Supp. 3d 267, 288 (W.D. La. 2022); *Larson v. Domestic & Foreign Com. Corp.*, 337 U.S. 682, 689–91 (1949).

19. Venue is proper in this district under 28 U.S.C. § 1391(e)(1). Defendants are federal officers sued in their official capacities. Moreover, Plaintiff State of Louisiana is a resident of this District, and a substantial part of the events giving rise to the Complaint—including injuries to Louisiana caused by Defendants' actions—occurred and will continue to occur within this District.

PARTIES

Plaintiffs

20. Plaintiff State of Louisiana is a sovereign State of the United States of America. Liz Murrill is the Attorney General of the State of Louisiana. She is authorized by Louisiana law to sue on the State's behalf. La. Const. art. IV, § 8. Her offices are located at 1885 North Third Street, Baton Rouge, Louisiana 70802. Louisiana sues to vindicate its sovereign, quasi-sovereign, and proprietary interests.

21. Plaintiff Rosalie Markezich is a resident of Louisiana. She became a victim of FDA's mail-order abortion scheme in October 2023 when her boyfriend ordered FDA-approved abortion drugs from a California doctor, and, by her boyfriend's actions, she felt coerced to take them. The abortion drugs killed her child.

Defendants

22. Defendant FDA is an agency of the federal government within the U.S. Department of Health and Human Services (HHS). The Secretary of HHS has delegated to the FDA Commissioner the authority to administer the provisions of the FDCA for approving new drug

applications and authorizing a REMS for high-risk drugs. FDA's headquarters is located at 10903 New Hampshire Avenue, Silver Spring, Maryland 20993.

23. Defendant Martin A. Makary, M.D., M.P.H., named in his official capacity, is the Commissioner of Food and Drugs at FDA. Dr. Makary supervises the activities of FDA, including the approval of new drug applications, supplemental new drug applications, and the issuance, modification, waiver, suspension, or removal of a REMS. Dr. Makary's official address is 10903 New Hampshire Avenue, Silver Spring, Maryland 20993.

24. Defendant George Francis Tidmarsh, M.D., Ph.D., named in his official capacity, is the Director of FDA's Center for Drug Evaluation and Research. Dr. Tidmarsh is tasked with regulating drugs throughout their lifecycle, approving and evaluating new and existing drugs, monitoring post-marketing drug safety, and taking enforcement actions necessary to protect the public from harmful drugs. Dr. Tidmarsh's official address is 10903 New Hampshire Avenue, Silver Springs, Maryland 20993.

25. Defendant HHS is a federal agency within the executive branch of the United States government, including under 5 U.S.C. § 551 and 701(b)(1). Its address is 200 Independence Avenue SW, Washington, D.C. 20201.

26. Defendant Robert F. Kennedy, Jr., is the Secretary of HHS and is named in his official capacity. Secretary Kennedy is responsible for the overall operations of HHS, including the operations of FDA. His official address is 200 Independence Avenue SW, Washington, D.C. 20201.

27. Collectively and as applicable, all Defendants are referred to herein as "FDA" or "Defendants." Plaintiffs State of Louisiana and Rosalie also sue Defendants' employees, agents, and successors in office.

28. Defendants are subject to the APA. 5 U.S.C. § 701(b); 5 U.S.C. § 551(1).

FACTUAL ALLEGATIONS

29. *Dobbs* portended a sea change in America when, for the first time in a half century, the Supreme Court "return[ed] the issue of abortion to the people's elected representatives." 597 U.S. at

232. Indeed, for many pro-life states like Louisiana and others, *Dobbs* meant protecting unborn babies from abortion (with narrow exceptions) within their borders.

30. That promise, however, has not been realized in Louisiana and its sister pro-life states. That is because pro-abortion doctors and other activists across the nation are mailing the abortion drug mifepristone into Louisiana for the express purpose of causing abortions in Louisiana and circumventing Louisiana's pro-life laws. That mail-order abortion effort is possible only because of the Biden Administration's 2023 REMS, which attempts to thwart *Dobbs* by facilitating the mailing of FDA-approved mifepristone into pro-life states where abortions are prohibited or significantly curtailed. Such mailing is blatantly unlawful, not least because the 2023 REMS is arbitrary and capricious (as five Fifth Circuit judges have recognized) and the Comstock Act independently bans the mailing of abortion drugs. As a consequence, hundreds of unlawful abortions occur every month in Louisiana.

31. The allegations below (I) provide a brief explanation of mifepristone; (II) offer an overview of FDA's regulation of mifepristone; (III) describe the Biden Administration's 2023 REMS, which facilitated mail-ordered mifepristone as a response to *Dobbs* and as a means of circumventing pro-life states' laws; (IV) outline the nature of the resulting extra-territorial effort for mailing mifepristone into pro-life states; (V) identify data and examples of how that effort is playing out in Louisiana; and articulate the specific harms that give (VI) Louisiana and (VII) Rosalie standing to file this suit challenging the 2023 REMS.

I. A Brief Overview of Mifepristone.

32. A French pharmaceutical company called Roussel Uclaf S.A. first developed and tested mifepristone under the name RU-486 (also called "Mifeprex" today). In 1988, it was approved as an abortion drug in France.[7]

33. Mifepristone is a synthetic steroid and endocrine disruptor that blocks progesterone receptors in the uterus. Progesterone is necessary to maintain a pregnancy and support a growing

[7] Ex. 5, Center for Drug Evaluation and Research, Application Number: 20-687 Medical Review(s) at 1–2 (Jan. 27, 2000).

baby. By blocking progesterone receptors, mifepristone causes the uterine lining to deteriorate, starving the baby of oxygen and nutrition and eventually killing the baby.[8]

34. Today, mifepristone is generally administered as part of a two-drug regimen involving a second drug called misoprostol. Mifepristone is first introduced, killing the baby. And then misoprostol is introduced, which induces contractions to expel the baby from her mother's womb.[9]

35. The side effects from mifepristone are serious and undisputed. They include severe cramping and heavy bleeding.[10] In fact, FDA's own label states that roughly 1 in 25 women who take mifepristone will end up in the emergency room,[11] with up to 7% requiring a "surgical procedure because the pregnancy did not completely pass from the uterus or to stop bleeding."[12] The label also includes a black box warning that "serious and sometimes fatal infections or bleeding" may occur.[13]

36. The risks of complications and emergency surgeries increase with gestational age.[14] For example, FDA's label notes that the percentage of surgical interventions for ongoing pregnancies is ten times higher for women at 64–70 days' gestation than for women at less than or equal to 49 days' gestation.[15] And one study on which FDA previously relied[16] found that—as compared to those who take mifepristone before nine weeks' gestation—almost four times as many women who take it

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[8] Ex. 6, Blake M. Autry & Roopma Wadhwa, *Mifepristone*, StatPearls (Feb. 28, 2024), perma.cc/K2CL-CKP3; Ex. 7, *The Facts on Mifepristone*, Planned Parenthood, perma.cc/A7UB-P2DZ.

[9] Ex. 7, *The Facts on Mifepristone*; Ex. 8, *Medication Abortion: Your Questions Answered*, Yale Med. (Sept. 11, 2023), perma.cc/NA6N-GL2N.

[10] Ex. 9, FDA-Approved Label for Mifepristone (Mifeprex) at 7 (Jan. 2023), perma.cc/2UJ5-8WVF ("Mifeprex 2023 Label") ("Uterine bleeding and cramping are expected consequences of the action of MIFEPREX and misoprostol as used in the treatment procedure. Most patients can expect bleeding more heavily than they do during a heavy menstrual period.").

[11] *Id.* at 7, Table 2.

[12] *Id.* at 17.

[13] *Id.* at 1.

[14] Ex. 10, 2021 FDA Letter to AAPLOG and Am. Coll. of Pediatricians denying in part and granting in part 2016 Citizen Petition, Docket No. FDA-2019-P-1534 at 9 (Dec. 16, 2021) ("We agree that the failure rate of medical abortion regimens, including the currently approved regimen, generally increases with increasing gestational age."); Ex. 9, Mifeprex 2023 Label at 13, Table 4.

[15] Ex. 9, Mifeprex 2023 Label at 13, Table 4.

[16] Ex. 11, Center for Drug Evaluation and Research, Application Number: 020687Orig1s020 Summary Review at 19 (Mar. 29, 2016) ("FDA 2016 Summary Review").

after nine weeks' gestation experience an incomplete abortion, nearly twice as many suffer an infection, and over six times as many require surgical evacuation.[17]

37. Remotely dispensed abortion drugs present even greater risks to women because, without an in-person examination, prescribers cannot confirm and therefore are more likely to misdate the gestational age of a baby or fail to detect an ectopic pregnancy—with potentially fatal consequences.

38. A more recent review of large-scale insurance data concluded that the "real-world rate of serious adverse events following mifepristone abortions is at least 22 times as high as the summary figure of 'less than 0.5 percent' in clinical trials reported on the drug label."[18] Nearly 11% of women "experience sepsis, infection, hemorrhaging, or another serious adverse event within 45 days following a mifepristone abortion."[19]

39. Of the women who end up in the emergency room after taking abortion drugs, many suffer severe injuries. A study testing the severity of emergency department visits for Medicaid-eligible women following various pregnancy outcomes found that "an [emergency department (ED)] visit following a [mifepristone] abortion was significantly more likely to have a severe or critical acuity rating than a visit following surgical abortion, live birth, or an ED visit at any time by a woman who was never pregnant."[20] The study also found that ED visits coded severe or critical for women who underwent a chemical abortion increased by 4,041.1% between 2004 and 2015, compared to a 450.6% increase for surgical abortion subjects and 20.9% for live birth subjects.[21] (And all this assumes accurate reporting in the ED, notwithstanding that some abortion activists encourage women to tell

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[17] Ex. 12, Maarit Niinimaki et al., *Comparison of rates of adverse events in adolescent and adult women undergoing medical abortion: population register based study*, BMJ at 5 (April 20, 2011).

[18] Ex. 13, Jamie Bryan Hall & Ryan T. Anderson, *The Abortion Pill Harms Women: Insurance Data Reveals One in Ten Patients Experiences a Serious Adverse Event*, Ethics & Pub. Pol'y Ctr. at 1 (Apr. 28, 2025), perma.cc/YH5F-9R6C.

[19] *Id.*

[20] Ex. 14, James Studnicki et al., *Comparative Acuity of Emergency Department Visits Following Pregnancy Outcomes Among Medicaid Eligible Women, 2004–2015*, Int'l J. Epidemiology & Pub. Health Rsch., Apr. 2024, at 1.

[21] *Id.* at 2.

emergency room staff that they are having a miscarriage if they suffer abortion-drug complications requiring urgent care.[22])

40. That is not all. Without an in-person doctor visit, abortion drugs also present heightened risks for women with an Rh-negative blood type, which accounts for about 15% of North Americans.[23] If these women are not simultaneously administered Rhogam, they may experience isoimmunization, which threatens future pregnancies. If an Rh-negative woman is left untreated, her future baby will have a 14% chance of being stillborn and a 50% chance of suffering neonatal death or a brain injury.[24] In addition, beyond these physical risks, women have described their abortion-drug experiences as harming their mental health and leaving them feeling unprepared, silenced, regretful, or trapped.[25]

II. FDA's Regulation of Mifepristone.

41. After obtaining the American patent rights to mifepristone, the Population Council, "a nonprofit founded in 1952 by John D. Rockefeller III to address supposed world overpopulation,"[26] conducted clinical trials in the United States.[27] The Population Council granted Danco Laboratories, LLC ("Danco")—incorporated in the Cayman Islands in 1995—an exclusive license to manufacture, market, and distribute mifepristone under the brand name Mifeprex in the

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[22] *See, e.g.*, Ex. 15, *Will a doctor be able to tell if you've taken abortion pills?*, Women Help Women (Sept. 23, 2019), perma.cc/E89M-HUCG; Ex. 16, *How do you know if you have complications and what should you do?*, Aid Access, perma.cc/764Z-QBZQ.

[23] Ex. 17, *Am. Coll. of Obstetricians and Gynecologists Practice Bulletin No. 181: Prevention of Rh D Alloimmunization*, 130 Obstetrics & Gynecology 481, at e58 (Aug. 2017).

[24] *See id.*

[25] *See* Ex. 18, Katherine A. Rafferty & Tessa Longbons, *#AbortionChangesYou: A Case Study to Understand the Communicative Tensions in Women's Medication Abortion Narratives,* 36 Health Commc'n 1485 (2021).

[26] Ex. 19, Population Council, perma.cc/2YFW-FP5S.

[27] Ex. 5, Center for Drug Evaluation and Research, Application Number: 20-687 Medical Review(s) at 2.

United States.[28] Danco remains "one of the most enigmatic companies in the pharmaceutical industry,"[29] but its sole business of distributing abortion drugs has "been extremely profitable."[30]

42. FDA's regulation of mifepristone began with its handling of the Population Council's new drug application for "Mifepristone Tablets, 200 mg" filed on March 18, 1996.[31]

43. FDA approved mifepristone in 2000 "for the medical termination of intrauterine pregnancy through 49 days' pregnancy."[32] Because FDA had previously concluded that "restrictions ... on the distribution and use of mifepristone are needed to assure safe use of this product,"[33] FDA approved the Population Council's application with distribution restrictions "to assure safe use" under an accelerated approval program found at 21 C.F.R. § 314 Subpart H.[34]

44. FDA's 2000 approval contained a few requirements in addition to gestational age that are key here. *First*, FDA required at least three in-person doctor visits, including in-person dispensing of mifepristone: (1) the Day 1 dispensing and administration of mifepristone; (2) the Day 3 dispensing and administration of misoprostol; and (3) the Day 14 follow-up visit to confirm no fetal parts or tissue remain.[35] *Second*, FDA required that the dispensing be done by a certified physician.[36] And *third*, FDA stated that mifepristone's "labeling, Medication Guide, Patient Agreement, and Prescriber's

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[28] Ex. 20, 2002 Citizen Petition of AAPLOG to FDA at 9 (Aug. 8, 2002) ("2002 Citizen Petition").

[29] Ex. 21, Robert O'Harrow Jr., *Drug's U.S. Marketer Remains Elusive*, Wash. Post (Oct. 11, 2000), perma.cc/MY3N-83F8.

[30] Ex. 22, Hannah Levintova, *The Abortion Pill's Secret Money Men*, Mother Jones (March–April 2023), perma.cc/283E-UALT.

[31] Ex 23, Letter from Center for Drug Evaluation and Research to Ann Robbins, Ph.D. at 1 (Sept. 18, 1996), perma.cc/579K-KZ8B.

[32] Ex. 24, 2000 FDA Approval Letter for Mifeprex (mifepristone) Tablets at 1 (Sept. 28, 2000). In 2019, FDA approved GenBioPro, Inc.'s generic version of Mifeprex, and thus GioBioPro's generic mifepristone has the same labeling and is subject to the same regulation as Danco's mifepristone. Ex. 25, 2019 FDA ANDA Approval Letter to GenBioPro, Inc. at 1 (Apr. 11, 2019), perma.cc/QY87-UKNG.

[33] Ex. 26, FDA Center for Drug Evaluation & Research Letter to Population Council re: NDA at 5 (Feb. 18, 2000).

[34] Ex. 27, 2000 FDA Approval Memo. to Population Council re: NDA 20-687 Mifeprex (mifepristone) at 6 (Sept. 28, 2000); Ex. 26, FDA Center for Drug Evaluation & Research Letter to Population Council re: NDA at 5.

[35] Ex. 27, FDA 2000 Approval Memo. at 2–3.

[36] *Id.* at 6.

Agreement will together constitute the approved product labeling to ensure any future generic drug manufacturers will have the same risk management program."[37] To that end, FDA required mifepristone's label to include a "black box warning for special problems, particularly those that may lead to death or serious injury."[38]

45. Congress thereafter codified FDA's post-marketing regulations under Subpart H in the Food and Drug Administration Amendments Act of 2007 (FDAAA) and authorized FDA to require drug sponsors to submit and implement a REMS if the agency determines that one is "necessary to ensure that the benefits of the drug outweigh the risks of the drug." 21 U.S.C. § 355-1(a). In 2008, FDA followed Congress's mandate under the FDAAA to convert mifepristone's Subpart H post-marketing restrictions into a REMS under Section 909(b)(1).[39]

46. In 2011, FDA approved a REMS for mifepristone that included the previous Subpart H restrictions, noting that "a REMS is necessary for MIFEPREX (mifepristone) to ensure the benefits of the drug outweigh the risks of serious complications[.]"[40] The REMS consisted of a Medication Guide, elements to assure safe use, an implementation system, and a timetable for submission of assessments.[41] The REMS also required "prescribers to certify that they are qualified to prescribe MIFEPREX [mifepristone] and are able to assure patient access to appropriate medical facilities to manage any complications."[42] The 2011 REMS warned that women should not take mifepristone if they "cannot easily get emergency medical help [for] 2 weeks" after taking the drug.[43] The REMS required prescribers "to assure patient access to appropriate medical facilities"[44] that were

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[37] *Id.* at 2.

[38] *Id.*

[39] Ex. 28, Identification of Drug and Biological Products Deemed to Have Risk Evaluation and Mitigation Strategies for Purposes of the Food and Drug Administration Amendments Act of 2007, 73 Fed. Reg. 16313, 16314 (Mar. 27, 2008).

[40] Ex. 29, 2011 FDA Supplemental Approval Letter to Danco Laboratories, LLC at 1 (June 8, 2011) ("2011 Approval Letter").

[41] *Id.*; Ex. 30, 2011 REMS for NDA 20-687 Mifeprex (mifepristone) Tablets, 200mg (June 8, 2011) ("2011 REMS").

[42] Ex. 29, 2011 Approval Letter at 1; Ex. 30, 2011 REMS.

[43] Ex. 30, 2011 REMS at 5.

[44] *Id.* at 1.

"equipped to provide blood transfusions and resuscitation, if necessary."[45] And the agency instructed women to take the Medication Guide with them "[w]hen [they] visit an emergency room."[46] In 2016, FDA said it would continue to rely on emergency rooms as a backstop to "ensure that women have access to medical facilities for emergency care" to manage the expected complications.[47]

47. In 2016, FDA authorized "major changes" to the mifepristone REMS, including, as relevant here, extending the maximum gestational age from 49 days to 70 days, removing the requirement for in-person follow-up examinations on Day 3 and Day 14 after an abortion, and allowing "healthcare providers" other than physicians to dispense and administer abortion drugs.[48] FDA did not, however, eliminate the Day 1 in-person dispensing requirement for mifepristone.

48. In addition to these new changes to the conditions of use, FDA eliminated the requirement that prescribers report nonfatal, serious adverse events, asserting that "after 15 years of reporting serious adverse events, the safety profile for Mifeprex is essentially unchanged."[49] FDA acknowledged that "[i]t is important that the Agency be informed of any deaths with Mifeprex to monitor new safety signals or trends."[50]

49. During the COVID-19 pandemic, the American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine (SMFM) sent a joint letter to FDA asking the agency to abandon the in-person dispensing requirement for mifepristone and to allow remote dispensing for the duration of the pandemic.[51] One month later, ACOG and others sued to enjoin FDA's in-person dispensing requirement during the pandemic. *Am. Coll. of Obstetricians & Gynecologists v. FDA*, 472 F. Supp. 3d 183 (D. Md. 2020). The district court granted ACOG's request,

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[45] *Id.* at 7.

[46] *Id.* at 4.

[47] Ex. 31, 2016 FDA Letter to AAPLOG, Christian Medical & Dental Associations, and Concerned Women for America denying 2002 Citizen Petition, Docket No. FDA2002-P-0364 at 21 (Mar. 29, 2016) ("2016 Petition Denial").

[48] Ex. 11, FDA 2016 Summary Review at 5–10.

[49] *Id.* at 26.

[50] *Id.*

[51] Ex. 32, 2020 Letter from ACOG & SMFM to FDA about Mifepristone REMS (Apr. 20, 2020) ("2020 ACOG-SMFM Letter").

id. at 233, *order clarified*, 2020 WL 8167535 (D. Md. Aug. 19, 2020), and the Fourth Circuit denied FDA a stay of the injunction, Court Order Denying Mot. for Stay Pending Appeal, *Am. Coll. of Obstetricians & Gynecologists v. FDA*, No. 20-1824 (4th Cir. Aug. 13, 2020), ECF No. 116.

50. Under President Trump's first administration, FDA then requested an emergency stay from the U.S. Supreme Court. Appl. for Stay, *FDA v. Am. Coll. of Obstetricians & Gynecologists*, No. 20A34 (U.S. Aug. 26, 2020). In its filing, the agency affirmed that in-person dispensing was both "minimally burdensome" and "necessary" to preserve the safety of women who take abortion drugs. *Id.* at 4, 13. FDA added that it had reviewed "thousands of adverse events resulting from the use of Mifeprex," determined that abortion drugs continue to cause "serious risks for up to seven percent of patients," and concluded that in-person dispensing was "necessary to mitigate [those] serious risks." *Id.* at 4, 7, 21. The U.S. Supreme Court granted the requested stay in January 2021. *FDA v. Am. Coll. of Obstetricians & Gynecologists*, 141 S. Ct. 578 (2021).

51. After President Biden took office, however, FDA reversed course, stating that it "intends to exercise enforcement discretion" regarding the in-person dispensing requirement during the COVID-19 pandemic (2021 Non-Enforcement Decision).[52] By refusing to enforce that requirement, FDA authorized abortion drugs to be prescribed remotely and sent via mail. Indeed, FDA expressly recognized that its Non-Enforcement Decision would allow "dispensing of mifepristone through the mail ... or through a mail-order pharmacy."[53]

52. Later that year, in December 2021, FDA denied a 2019 citizen petition's request to preserve the in-person dispensing requirement and stated its intention to permanently remove that requirement.[54]

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[52] Ex. 3, 2021 FDA Letter to ACOG and SMFM About Mifepristone REMS at 2.

[53] *Id.*

[54] Ex. 10, 2021 FDA Letter to AAPLOG at 25. FDA likewise denied a similar petition filed in December 2022 by Students for Life of America that asked the agency to restore in-person dispensing. Ex. 33, Students for Life of America, Citizen Petition to FDA (Dec. 13, 2022). FDA rejected the petition on the grounds that it requested "the same or substantially the same" relief as the 2019 citizen petition. Ex. 34, 2023 FDA Letter to Students for Life of Am. denying 2022 SFLA Petition, Docket No. FDA-2022-P-3209, at 2 (Jan. 3, 2023).

53. In a separate December 2021 letter, FDA said it had "determined that the Mifepristone REMS Program continues to be necessary to ensure that the benefits of the drug outweigh the risks," but that "it must be modified to minimize the burden on the health care delivery system of complying with the REMS and to ensure that the benefits of the drug outweigh the risks."[55] The letter identified modifications to the REMS: "(1) removing the requirement that mifepristone be dispensed only in certain healthcare settings, specifically clinics, medical offices, and hospitals (i.e., the 'in-person dispensing requirement'); and (2) adding a requirement that pharmacies that dispense the drug be specially certified," signaling that FDA would soon allow pharmacies to dispense abortion drugs.[56]

III. The Biden Administration Responds to *Dobbs* with the 2023 REMS.

54. FDA's regulation of mifepristone (or lack thereof) took on a whole new life after *Dobbs* overruled *Roe* in 2022. The pro-abortion activists within FDA anticipated as much. As Ruth B. Merkatz (Director of FDA's Office of Women's Health (1994–1996) and later a director at the Population Council) explained, "[w]e knew [mifepristone] was going to be very important especially in states where surgical abortions are not permitted. And if they overturn *Roe v. Wade*, it's going to be really important."[57]

55. Following the U.S. Supreme Court's refusal to block a Texas pro-life bill in September 2021, President Biden directed HHS and the Department of Justice (DOJ) to explore steps to "ensure access to safe and legal abortion."[58] Officials were to "use every lever at their disposal to ensure … access" for "every woman … across the country."[59]

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[55] Ex. 35, 2021 FDA Center for Drug Evaluation & Research Director Patrizia Cavazzoni Letter to Dr. Graham Chelius (Dec. 16, 2021).

[56] *Id.*

[57] Ex. 36, FDA, Oral History Interview with Ruth B. Merkatz at 39 (Oct. 16, 2019), perma.cc/6JRY-DR92.

[58] Ex. 37, White House, Readout of White House Roundtable Meeting with Women's Rights and Reproductive Health Leaders (Sept. 3, 2021), perma.cc/CN85-AZM2.

[59] Ex. 38, White House, Press Briefing by Press Secretary Jen Psaki and Deputy National Security Advisor for Cyber and Emerging Technologies Anne Neuberger, September 2, 2021 (Sept. 2, 2021), perma.cc/6CVF-3MMQ.

56. FDA had planned its action in response to *Dobbs* for over a year. The *Dobbs* oral argument on December 1, 2021, indicated that *Roe v. Wade* was "doomed."[60] So just over two weeks later, on December 16, 2021, FDA announced sua sponte that it would permanently authorize a nationwide, mail-order abortion-drug regime and directed the drug sponsors to make the associated changes.

57. After *Dobbs*, the Biden Administration kicked its efforts into high gear. President Biden called *Dobbs* "an extreme decision"[61] by "not a normal Court"[62] and recommitted to "doing everything in his power" to "protect access" to abortion.[63] He noted: "Some states are saying that they'll try to ban or severely restrict access to these medications."[64]

58. To that end, President Biden issued multiple executive orders mandating access to abortion.[65]

59. The day *Dobbs* was issued, "[i]n the face of threats from state officials saying they will try to ban or severely restrict access to medication for reproductive health care, the President directed the Secretary of Health and Human Services to identify all ways to ensure that mifepristone is as widely

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[60] Ex. 39, Ian Millhiser, *It sure sounds like Roe v. Wade is doomed*, Vox (Dec. 1, 2021), perma.cc/M4EU-DSC2.

[61] Ex. 40, White House, Remarks by President Biden Before Meeting with His Task Force on Reproductive Healthcare Access (Jan. 22, 2024), perma.cc/N9KR-TKX9.

[62] Ex. 41, White House, Remarks by President Biden on the Supreme Court's Decision on Affirmative Action (June 29, 2023), perma.cc/7XU8-3KL4.

[63] Ex. 42, White House, FACT SHEET: President Biden to Sign Executive Order Protecting Access to Reproductive Health Care Services (July 8, 2022), perma.cc/F5ZZ-XGL8.

[64] Ex. 43, White House, Remarks by President Biden on the Supreme Court Decision to Overturn *Roe v. Wade* (June 24, 2022), perma.cc/B8Y3-EWUZ.

[65] Ex. 44, Exec. Order No. 14076, Protecting Access to Reproductive Healthcare Services, 87 Fed. Reg. 42053 (July 8, 2022); Ex. 45, Exec. Order No. 14079, Securing Access to Reproductive and Other Healthcare Services, 87 Fed. Reg. 49505 (Aug. 3, 2022); *see also* Ex. 46, Presidential Memorandum, Further Efforts To Protect Access to Reproductive Healthcare Services, 88 Fed. Reg. 4895 (Jan. 22, 2023) ("My Administration remains committed to supporting safe access to mifepristone...").

accessible as possible in light of FDA's determination that the drug is safe and effective—including when prescribed through telehealth and *sent by mail*."[66]

60. The same day, HHS Secretary Becerra announced HHS's "commitment to ensure every American has access to … medication abortion" and promised to "double down and use every lever we have to protect access to abortion care."[67] He noted a few days later that "HHS will take steps to increase access to medication abortion" and "will leave no stone unturned."[68]

61. President Biden then issued a follow-up executive order again directing HHS "to protect and expand access to abortion care, including medication abortion."[69]

62. These directives culminated in the permanent 2023 REMS, which made two key moves.

63. *First*, and perhaps most significant, the 2023 REMS permanently removed the in-person dispensing requirement, which had required that mifepristone must "be dispensed only in certain healthcare settings, specifically clinics, medical offices, and hospitals."[70] This move now allows doctors and other activists to dispense mifepristone *by mail*, and also expands the program to allow mifepristone to be dispensed by certified pharmacies, including retail pharmacies.[71]

64. FDA acknowledged in its 2023 Summary Review that it had "determined" on "12/16/2021" that "the REMS must be modified to remove the in-person dispensing requirement."[72] FDA added that the format of the REMS document would not be changed "[t]o avoid the

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[66] Ex. 47, White House, FACT SHEET: President Biden Announces Actions In Light of Today's Supreme Court Decision on *Dobbs v. Jackson Women's Health Organization* (June 24, 2022), perma.cc/66T6-BL87 (emphasis added).

[67] Ex. 48, Press Release, HHS, HHS Secretary Becerra's Statement on Supreme Court Ruling in *Dobbs v. Jackson Women's Health Organization* (June 24, 2022), perma.cc/89AZ-RFL4.

[68] Ex. 49, Press Release, HHS, Remarks by Secretary Xavier Becerra at the Press Conference in Response to President Biden's Directive following Overturning of *Roe v. Wade* (June 28, 2022), perma.cc/KW6H-KF7D.

[69] Ex. 44, Exec. Order No. 14076.

[70] Ex. 50, Center for Drug Evaluation and Research, Application Number: 020687Orig1s025 Summary Review at 3 (Jan. 3, 2023) ("FDA 2023 Summary Review").

[71] *Id.* at 3, 12–13.

[72] *Id.* at 6.

misperception that this REMS modification is making major changes to the REMS document that go beyond our December 16, 2021, determination that the REMS must be modified to remove the in-person dispensing requirement and add pharmacy certification," and that the "[c]hanges are in line with the REMS Modification Notification letters sent December 16, 2021."[73] FDA thus imported its 2021 rationale when it implemented the 2023 changes.

65. FDA's 2021 REMS Modification Rationale Review relied on the "small" number of adverse events voluntarily reported in the FDA Adverse Event Reporting System (FAERS) database, even though FDA had years before *abandoned* the requirement that abortion providers report nonfatal adverse events.[74]

66. FDA conceded elsewhere that: (1) "FAERS data does have limitations"; (2) the "FDA does not receive reports for every adverse event"; and thus (3) "FAERS data cannot be used to calculate the incidence of an adverse event ... in the U.S."[75]

67. Indeed, the FAERS database "is woefully inadequate to determine the post-marketing safety of mifepristone due to its inability to adequately assess the frequency or severity of adverse events," and the adverse events reported to FDA "represent a fraction of the actual adverse events occurring in American women."[76] Compounding the problem, the complicated FAERS electronic submission process itself erodes its reliability, since it takes FDA 48 pages of guidance to instruct users

[73] *Id.* at 9, 16.

[74] Ex. 51, Center for Drug Evaluation and Research, Application Numbers: 020687 and 91178 Rationale Review at 21 (Dec. 16, 2021) ("FDA 2021 Rationale Review").

[75] Ex. 52, FDA Adverse Events Reporting System (FAERS) Public Dashboard, perma.cc/CZ2G-4S75.

[76] Ex. 53, Kathi A. Aultman et al., *Deaths and Severe Adverse Events After the Use of Mifepristone as an Abortifacient from September 2000 to February 2019*, 26 Issues in L. & Med., no. 1, Nov. 1, 2021, at 25–26.

how to use it.[77] For all of these reasons, reporting "discrepancies render the FAERS inadequate to evaluate the safety of mifepristone abortions."[78]

68. In addition to FAERS data, FDA evaluated "assessment data" concerning healthcare provider certification, program utilization, and non-compliance. It noted that the eight reported cases of adverse events from this data set were also identified in the FAERS database.[79]

69. FDA also claimed support from published literature evaluating mail-order dispensing by pharmacies and clinics.[80] Yet the agency conceded that it was unable to "generalize" the results to the United States population and that "the usefulness of the studies is limited in some instances by small sample sizes and lack of follow-up information on outcomes."[81] FDA thus acknowledged that "[t]he studies [it] reviewed are *not adequate on their own* to establish the safety of the model of dispensing mifepristone by mail[.]"[82] Instead, the studies were merely "not inconsistent with" FDA's conclusion that removing the initial in-person visit would be safe.[83]

70. FDA reviewed three studies for "mail order pharmacy dispensing."[84] One (Hyland) alarmingly reported that 3% of the participants needed to be hospitalized—a 330% increase over the rate on the approved label.[85] FDA disregarded this dramatic increase, saying it could not make any "conclusions about [that study's] safety findings."[86] Another study (Upadhyay) had "numerous deviations" from abortion practices in the United States, "limited follow-up information, and small sample size"—all of which "limit[ed] [its] usefulness."[87] And a third study, an "interim analysis"

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[77] *See* Ex. 54, Specifications for Preparing and Submitting Electronic ICSRs and ICSR Attachments (Apr. 2021), perma.cc/CAD8-N4EM.

[78] Ex. 55, Christiana A. Cirucci et al., *Mifepristone Adverse Events Identified by Planned Parenthood in 2009 and 2010 Compared to Those in the FDA Adverse Event Reporting System and Those Obtained Through the Freedom of Information Act*, 8 Health Servs. Rsch & Managerial Epidemiology 1, 1 (2021).

[79] Ex. 51, FDA 2021 Rationale Review at 21–23, 38–39.

[80] *Id.* at 38.

[81] *Id.*

[82] *Id.* at 39 (emphasis added).

[83] *Id.*

[84] *Id.* at 28.

[85] *Id.* at 27–28.

[86] *Id.* at 28.

[87] *Id.* at 27.

(Grossman), was largely irrelevant because it evaluated outcomes for "dispens[ing] by mail-order pharmacy after in-person clinical assessment."[88]

71. FDA also cited five studies that "evaluated clinic dispensing by mail."[89] In one (Raymond), 7% of participants "had clinical encounters in [emergency department (ED)] and urgent care centers."[90] In another (Chong), "6[%] [of] participants had unplanned clinical encounters in ED/urgent care," and "[s]urgical interventions were required in 4.1[%] to complete abortion."[91] A third study (Anger) revealed that 12.5% "had an unplanned clinical encounter."[92] In the fourth study (Kerestes), 5.8% in the "telemedicine [plus] mail group" had "ED visits," a rate exceeding the range on the label (2.9% to 4.6%) and almost three times higher than the 2.1% for women who had an "in-person" visit.[93] The final study (Aiken) had "limitations" because "investigators were unable to verify the outcomes" and "the study's design did not capture all serious safety outcomes."[94]

72. FDA conceded that "the literature suggests there may be more frequent ED/urgent care visits related to the use of mifepristone when dispensed by mail from the clinic[.]"[95] The agency similarly acknowledged that the Anger study "suggests a pre-abortion examination may decrease the occurrence of procedural intervention and decrease the number of unplanned visits for postabortion care."[96]

73. Still, FDA concluded that, while the studies "suggest more frequent encounters with healthcare providers, they generally support a conclusion that dispensing by mail is safe"[97] and that mifepristone would "remain safe and effective for medical abortion if the in-person dispensing requirement is removed[.]"[98] And "[w]ith the removal of the in-person dispensing requirement,"

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[88] *Id.* at 26.
[89] *Id.* at 28.
[90] *Id.* at 29.
[91] *Id.* at 30.
[92] *Id.* at 31.
[93] *Id.* at 31–32.
[94] *Id.* at 33–34.
[95] *Id.* at 34.
[96] *Id.*
[97] *Id.* at 39.
[98] *Id.*

mifepristone is "no longer required to be dispensed only in a clinic, medical office or hospital. Under the REMS as modified, mifepristone can be dispensed through a pharmacy[.]"[99] (One year after the 2023 REMS took effect, Walgreens and CVS announced they had completed certification requirements and would begin dispensing mifepristone in their stores.[100])

74. *Second*, in addition to eliminating the in-person dispensing requirement, the 2023 REMS permanently "remove[d] the statement that the Medication Guide will be taken to an emergency room or provided to a healthcare provider who did not prescribe mifepristone so that it is known that the patient had a medical abortion with mifepristone."[101]

75. FDA formerly conditioned a mifepristone prescription on a patient's agreement to take the Medication Guide with her if she visits an emergency room or health care facility with complications "so that they will understand that [the patient is having] a medical abortion[.]"[102] This requirement ensured that a third-party physician will effectively diagnose and treat a woman's abortion-drug complication.[103]

76. Even so, the 2023 REMS jettisons the requirement that a woman "take the Medication Guide with [her if she] visit[s] an emergency room or [health care provider] who did not give [her] mifepristone so the emergency room or HCP will understand that the patient is having a medical abortion."[104] Despite the Guide's longstanding role in the administration of mifepristone, FDA "concluded"—without citing any literature or evidence—that "patients seeking emergency medical care are not likely to carry a Medication Guide with them, the Medication Guide is readily available

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[99] *Id.* at 40.

[100] Ex. 56, Pam Belluck, *CVS and Walgreens Will Begin Selling Abortion Pills this Month*, N.Y. Times (Mar. 1, 2024), perma.cc/AV5J-TTXF.

[101] Ex. 50, FDA 2023 Summary Review at 11.

[102] Ex. 57, 2019 REMS Single Shared System for Mifepristone 200MG at 8 (Apr. 2019).

[103] Ex. 30, 2011 REMS at 4–5 ("When you visit an emergency room or a provider who did not give you your Mifeprex, you should give them your MEDICATION GUIDE so that they understand that you are having a medical abortion with Mifeprex.").

[104] Ex. 50, FDA 2023 Summary Review at 20.

online, and information about medical conditions and previous treatments can be obtained at the point of care."[105]

77. FDA did not address the health risks associated with misdiagnosing an abortion-drug complication, or the common practice among abortion-drug dispensers of encouraging women to tell emergency staff that they are having a miscarriage when they present with complications.[106]

78. After the 2023 REMS, HHS issued a report called *Marking the 50th Anniversary of Roe: Biden-Harris Administration Efforts to Protect Reproductive Health Care*. HHS identified the 2023 REMS' removal of the in-person dispensing requirement as one of the critical actions it took since *Dobbs* to push abortion throughout the country.[107] In an accompanying press release, HHS highlighted FDA's REMS modification as one of the Department's "six core priorities" to "protect and expand access" to abortion post-*Dobbs*.[108]

79. The White House likewise identified FDA's 2023 permanent removal of the in-person dispensing requirement as a key response to President Biden's July 8, 2022, executive order directing HHS to "protect and expand access to abortion care, including medication abortion."[109]

IV. The Nationwide, Extra-Territorial Abortion Effort.

80. The Biden FDA's 2023 REMS has had its intended effect—facilitating a nationwide effort to mail FDA-approved mifepristone into states like Louisiana where abortion is prohibited (with narrow exceptions) and causing hundreds of unlawful abortions in those states every month.

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[105] *Id.* at 12.

[106] *See, e.g.,* Ex. 15, *Will a doctor be able to tell if you've taken abortion pills?*; Ex. 16, *How do you know if you have complications and what should you do?*

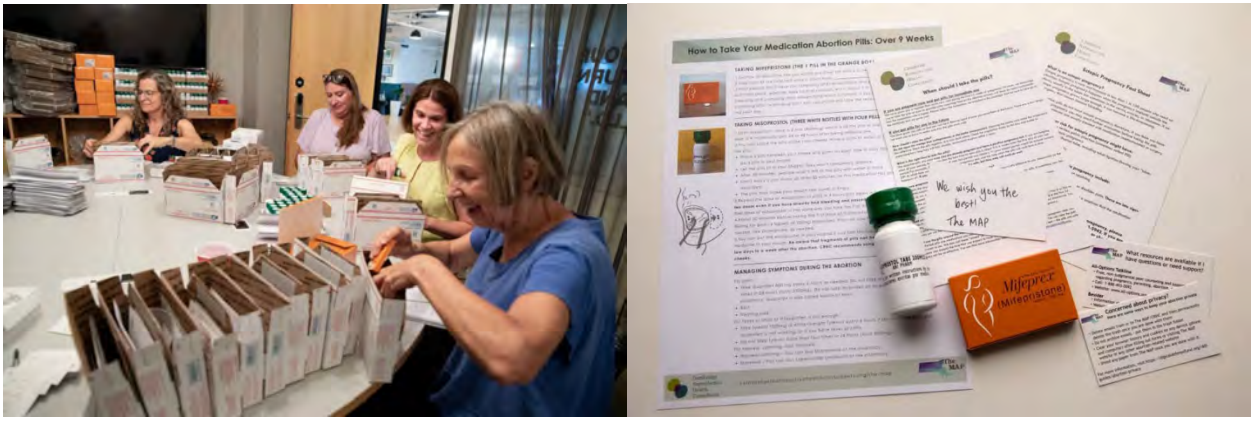
[107] Ex. 58, HHS, Marking the 50th Anniversary of *Roe*: Biden-Harris Administration Efforts to Protect Reproductive Health Care (Jan. 19, 2023), perma.cc/8EB4-P7US (HHS "continue[s] to activate all divisions of the Department in service to [its] commitment to ensuring" access to abortion).

[108] Ex. 59, Press Release, HHS, HHS Releases Report Detailing Biden-Harris Administration Efforts to Protect Reproductive Health Care Since *Dobbs* (Jan. 19, 2023), perma.cc/6CE3-J7DD.

[109] Ex. 60, White House, FACT SHEET: The Biden-Harris Administration's Record on Protecting Access to Medication Abortion (Apr. 12, 2023), perma.cc/78TT-3J2G (citing Exec. Order No. 14076, Protecting Access to Reproductive Healthcare Services, 87 Fed. Reg. 42053 (July 8, 2022)); Ex. 61, HHS, Secretary's Report, Health Care Under Attack: An Action Plan to Protect and Strengthen Reproductive Care (Aug. 2022), perma.cc/WWV5-CSFY.

81. The scheme is simple. Take one abortion facilitator, Abuzz, whose website tells Louisianans that they need only fill out a "short form" to obtain abortion drugs "discreetly packaged and delivered by mail."[110] "In most cases," Abuzz promises, "providers do not require a phone call or video visit."[111] Similarly, another abortion facilitator, A Safe Choice, promises mifepristone by mail after a person fills out a "quick" online form, "no phone call required."[112] Another facilitator, Choices Rising, assures Louisianans that "[t]here is no need to have a telehealth consultation" before receiving the "FDA-approved abortion pill" in "a few days."[113] And the Massachusetts Medication Abortion Access Project says their form can be completed in "less than 5 minutes," after which "[t]he pills [will] arrive in the mail and you take them at home or wherever is comfortable for you!"[114] Each of these facilitators states that it sends FDA-approved mifepristone into all fifty states, or to Louisiana specifically, through the mail to induce abortions.

82. And the scheme unfolds with activists hosting "pill-packing parties to help strangers in faraway states circumvent strict laws," preparing Danco's signature orange Mifeprex boxes for mailing while eating pizza and "sipp[ing] Chardonnay in red plastic cups":[115]



[110] Ex. 62, Abuzz, *Abortion Pill Access in Louisiana*, perma.cc/BDY4-5MX9.

[111] Ex. 63, Abuzz, *Need abortion care at home?*, perma.cc/ERK3-D97B.

[112] Ex. 64, A Safe Choice, *Home,* perma.cc/HCQ7-WYC6; Ex. 65, A Safe Choice, *Online Consultation Form*, perma.cc/NSA6-HGPQ.

[113] Ex. 66, Choices Rising, *Abortion Pill*, perma.cc/7NKQ-BYRU.

[114] Ex. 67, MAP, *Frequently asked questions*, perma.cc/3HNJ-ZFTC.

[115] Ex. 68, Scott Calvert, *The Parties Where Volunteers Pack Abortion Pills for Red-State Women*, Wall St. J. (Aug. 12, 2024), perma.cc/57KX-MD3V.

83. The sheer scale of this nationwide, extra-territorial abortion effort is striking. According to one report, in less than a month after *Dobbs* was decided, seven United States-based abortion-drug facilitators mailed approximately 3,500 doses of mifepristone and its generic equivalent to states that prohibit their use and distribution.[116]

84. Consider Aid Access, which has explained how FDA's removal of in-person dispensing has enabled its prescribers to frustrate state abortion restrictions and mail FDA-approved abortion drugs "to people in all 50 states, even those that have banned it."[117] When FDA imposed a temporary moratorium in 2021 on the "in-person dispensing requirement for mifepristone,"[118] Aid Access began sending FDA-approved abortion drugs by mail to certain states. "For the first time, legally prescribed medication abortion could be put in the mail."[119]

85. Then, after FDA permanently removed in-person dispensing in the 2023 REMS, Aid Access expanded its scope and began sending FDA-approved abortion drugs by mail to *all* states—including from states like New York that have adopted so-called "shield laws," which purport to protect from liability activists who use pro-abortion states as their home base to mail mifepristone into other states where abortion is prohibited.[120] All thanks to FDA, says Aid Access, women "feel more secure knowing that the pills are coming from licensed clinicians through an FDA-approved pipeline."[121] So today, because of FDA's removal of the in-person dispensing requirement, Aid Access has become the largest of the current abortion-drug facilitators.[122]

86. Dr. Linda Prine, a New York City-based abortion-drug prescriber for Aid Access, explained the scale of Aid Access's FDA-enabled operations by mid-2024. Within one month after

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[116] Ex. 69, Rachel Roubein, *'Shield' Laws Make it Easier to Send Abortion Pills to Banned State*s, Wash. Post. (July 20, 2023), perma.cc/A8MP-VXLJ.

[117] Ex. 70, Rebecca Grant, *Group Using 'Shield Laws' to Provide Abortion Care in States That Ban It*, The Guardian (July 23, 2023), perma.cc/49J6-3CZS; Ex. 71, Aid Access, *Get Abortion Pill Online in Louisiana*, perma.cc/J65J-M5LF.

[118] Ex. 70, Rebecca Grant.

[119] *Id.*

[120] *Id.*

[121] *Id.*

[122] Ex. 72, Elissa Nadworny, *Inside a medical practice sending abortion pills to states where they're banned*, NPR (Aug. 7, 2024), perma.cc/3XWU-PEXT.

New York's shield law passed, Aid Access "sent about 4,000 pills into restricted states, and now [as of April 2024] we're up to around 10,000 pills a month."[123]

87. Said Rachel Rebouché, the dean of Temple University Law School, to *The New York Times*: "Thousands and thousands of pills are being shipped everywhere across the United States from a handful of providers. That alone speaks to the nature of what mailed medication abortion can do."[124]

88. Finally, the dangerous disregard for women's health is undeniable. In another interview with the *Washington Post*, Dr. Prine said that when women call her for advice about complications, she tells them "that their experiences are nothing out of the ordinary, and that they almost certainly don't need to go to the emergency room."[125] Dr. Prine "said she's felt the need to send someone to the emergency room only once in nearly five years. 'Your uterus knows what to do,' Prine told a woman who called that January morning with reports of unexpectedly heavy bleeding. 'It's going to take care of itself.'"[126]

89. The *Washington Post* shared Dr. Prine's alarming comments with other doctors. It reported: "A woman in that situation could have hemorrhaged or become septic, according to five OB/GYNs interviewed for this article."[127] Keri Garel, an OB/GYN at Boston Medical Center, said, "Whenever there is something inside the uterus that is trying to come out and won't come out, the risk of bleeding and infection gets higher with every passing moment," and so she would advise someone in this woman's situation to go to the hospital immediately. "At that point, your life is the most important thing."[128]

90. Dr. Prine also described how a "quiet and scared" 15-year-old girl called her from "an area code in a state with an abortion ban" desperate for help after she "had taken pills and passed a

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[123] Ex. 73, Abigail Brooks & Dasha Burns, *How a network of abortion pill providers works together in the wake of new threats*, NBC News (April 7, 2024), perma.cc/B6B4-KWV2.

[124] Ex. 74, Pam Belluck, *Abortion Shield Laws: A New War Between the States,* N.Y. Times (Feb. 22, 2024), perma.cc/6YVK-5YCQ.

[125] Ex. 75, Caroline Kitchener, *Alone in a bathroom: The fear and uncertainty of a post-*Roe *medication abortion*, Wash. Post (April 11, 2024), perma.cc/N66P-FTWU.

[126] *Id.*

[127] *Id.*

[128] *Id.*

fetus larger than she'd expected." [129] The article states, "Unable to flush the fetus down the toilet, the girl asked about throwing it away."[130] Dr. Prine's main response: "There's nothing in there that's traceable back to you … As long as you don't tell anybody."[131]

91. Another Aid Access nurse practitioner also admitted to the *Washington Post* "that this system is far from perfect." [132] And she confessed that there are "occasions her patients in restricted states require in-person care" that she cannot provide.[133]

92. And these are not isolated instances. Prescribers and facilitators like Aid Access actively shroud their operations and disregard the serious risks women face when taking these drugs. Take Her Safe Harbor, for example.[134] Debra Lynch, the nurse practitioner who runs Her Safe Harbor, told *The New York Times* that she gives her patients who wish to obscure their abortions "additional 'plausible deniability'" by, for example, "send[ing] receipts with a medical code for a urinary tract infection consultation, one of the conditions the service treats, along with written information about U.T.I.s."[135] And "[s]he doesn't ask patients in states with abortion bans or restrictions to provide identification like a driver's license."[136] If women ask what they should do if they want or need to visit an emergency room, Lynch "counsels that there is no medical reason for women to tell hospitals they have taken abortion pills," and that they "can allow hospitals to assume they are miscarrying."[137]

93. Similarly, Abuzz tells women that they need not tell emergency room doctors that they have taken abortion drugs. In response to the question, "If I have to go to the hospital, what should I say?" Abuzz says, "The treatment for a miscarriage and abortion are the same, so you can just say something like 'I'm bleeding but it doesn't feel like my usual period. I'm afraid something is wrong'

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[129] *Id.*

[130] *Id.*

[131] *Id.*

[132] Ex. 107, Caroline Kitchener, *Blue-state doctors launch abortion pill pipeline into states with bans*, Wash. Post (July 19, 2023), perma.cc/85E8-RVML.

[133] *Id.*

[134] Ex. 76, Her Safe Harbor, *Abortion Pills Online*, perma.cc/8JCL-7DQU.

[135] Ex. 77, Pam Belluck, *A day with one abortion pill prescriber*, N.Y. Times (Jun. 9, 2025), perma.cc/8Y85-E7UJ.

[136] *Id.*

[137] *Id.*

or 'I'm pregnant and bleeding. I'm scared there's something wrong' and you should get the care you need."[138]

94. These abortion providers will not stop in response to state pro-life laws; only a change in federal regulation will stop them. As Angel Foster, who runs Massachusetts-based The MAP, which mails abortion drugs to "women in every state," said, "her organization will keep sending pills to women in Texas, as it has about 10,000 times in the past two years." "'We really don't change things unless we're legally required to,' she said."[139]

V. This Extra-Territorial Abortion Effort Is Playing Out in Louisiana.

95. Louisiana well knows the direct effects of this campaign—for it is living that reality every day.

96. Consider one recent high-profile example from Louisiana involving Dr. Margaret Carpenter. In 2022, Dr. Carpenter and Dr. Prine launched the Abortion Coalition for Telemedicine (ACT)—a group that "directly supports clinicians who" provide mail-order abortions to women "in all 50 states."[140] ACT works "directly with clinicians to launch shielded practices" so more women in pro-life states like Louisiana can receive mail-order abortions.[141] ACT is "committed" to enabling mail-order abortions "across state lines" and even helps "shielded practices" obtain "malpractice insurance."[142]

97. ACT promotes sending FDA-approved abortion drugs across state lines. Its website states that "[t]he two-step process of mifepristone and misoprostol is an FDA-approved method for terminating early pregnancies up to 12 weeks and can be done in the comfort of a patient's home with

[138] Ex. 78, Abuzz, FAQs, perma.cc/9LQ7-QZVL.

[137] Ex. 106, The Associated Press, *Texas Has a New Abortion Pill Law. But At Least One Provider Plans to Keep Shipping Them There*, Newsday (Sept. 18, 2025), perma.cc/84NU-BALB.

[140] Ex. 79, ACT, *Who We Are*, perma.cc/EX5M-RFUX.

[141] Ex. 80, ACT, *What We Do*, perma.cc/E3CM-SLYC.

[142] *Id.*

the support of a telemedicine provider."[143] ACT defines "medication abortion" as "FDA-approved mifepristone."[144]

98. ACT partners with several notorious out-of-state facilitators, including Aid Access.[145] As an abortion-drug prescriber, Dr. Carpenter has worked with Aid Access "to help facilitate access to abortion drugs in states where it's illegal."[146]

99. Dr. Carpenter's actions have revealed a dark consequence of remote dispensing: people other than pregnant women can order abortion drugs with ease. In April 2024, Dr. Carpenter allegedly prescribed and mailed abortion drugs to a woman in Louisiana who was not even pregnant.[147] The woman then allegedly forced her pregnant teenage daughter to take the drugs alone at home—even though the daughter reportedly wanted to keep the baby and even planned a gender reveal party.[148] After the daughter took the drugs, she experienced a medical emergency, called 911, and was taken to the hospital in an ambulance.[149]

100. On January 31, 2025, a Louisiana grand jury indicted Dr. Carpenter, her medical practice, and the girl's mother for knowingly causing an abortion by delivering, dispensing, distributing, or providing a pregnant woman with an abortion-inducing drug in violation of Louisiana law.[150] But not even criminal charges have deterred Dr. Carpenter's coalition or its allies. Despite the Louisiana indictment, New York Governor Kathy Hochul has refused to extradite Dr. Carpenter, citing New York's shield law: "I'm respecting the laws of New York. Am I supposed to make those

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[143] *Id.*

[144] Ex. 81, ACT, *FAQs,* perma.cc/55HW-PJ56.

[145] Ex. 82, ACT, *Resources*, perma.cc/A9ND-USQL.

[146] Ex. 83, Alaa Elassar, *New York Doctor Indicted in Louisiana Abortion Case Recognized as a Leader in Women's Reproductive Health*, CNN (Feb. 23, 2025), perma.cc/8F88-6BYA.

[147] Ex. 84, Rosemary Westwood, *After Historic Indictment, Doctors Will Keep Mailing Abortion Pills Over State Lines*, NPR (Mar. 19, 2025), perma.cc/CQ6Z-SVL7.

[148] *Id.*; Ex. 85, Katherine Donlevy, *Louisiana DA warns there's trove of evidence against NY doctor who allegedly mailed abortion pills to teen – who was planning gender reveal party: report*, N.Y. Post (Feb. 15, 2025), perma.cc/N6UV-2VF5.

[149] Ex. 86, Lorena O'Neil, *Louisiana Mother Pleads Not Guilty Following Abortion Pill Indictment*, La. Illuminator (Mar. 11, 2025), perma.cc/ TWX7-9FPS.

[150] Ex. 4, Dr. Carpenter indictment; Ex. 86, Lorena O'Neil.

subservient to laws of another state?"[151] For its part, ACT issued a press release conveying that the coalition "has and continues to stand behind New York and other shield laws across the country that enable the distribution" of mail-order abortion drugs.[152]

101. In response to Dr. Carpenter's indictment, New York enacted a law further shielding abortion-drug prescribers from liability by allowing them to list the name of their clinic instead of their own name on prescription labels—an attempt to make it more difficult to prosecute individual doctors in New York who illegally dispense abortion drugs to states that prohibit them.[153] Other states—including California, Colorado, Maine, Massachusetts, Rhode Island, Vermont, and Washington—have passed similar laws. In a troubling shift, California's newly enacted law (September 11, 2025) permits abortion drug prescriptions to be issued without identifying either the provider *or* the recipient. This is "to make it harder for states with abortion bans to develop evidence to make legal cases against doctors and others operating under shield laws."[154] But it also makes it harder, if not impossible, for women to build an evidentiary record to pursue providers and abusers for wrongdoing. These legal developments naturally and foreseeably follow the availability of mail-order abortion drugs.

102. Louisiana is also investigating a second case against Dr. Carpenter—this time for allegedly mailing mifepristone to a woman who was 20 weeks pregnant, who wrapped her aborted baby's remains in a towel and threw the baby in a garbage can.[155] Louisiana Attorney General Murrill

[151] Ex. 85, Katherine Donlevy.

[152] Ex. 87, Press Release, ACT, Statement on Governor Hochul's Response to Louisiana Extradition Order (Feb. 13, 2025), perma.cc/S7PG-NNAM.

[153] Ex 88, Press Release, Protecting Reproductive Freedom: Governor Hochul Signs Legislation Affirming New York's Status as a Safe Haven for Reproductive Health Care (Feb. 3, 2025), perma.cc/ZSH6-J6HW.

[154] Ex. 105, Pam Belluck, *California Passes Bill Allowing Omission of Patients' Names from Abortion Pill Bottles*, N.Y. Times (Sept. 11, 2025), perma.cc/U25B-S4M2.

[155] Ex. 89, Rosemary Westwood, *Louisiana Investigates Second Case Against New York Doctor Over Mailing Abortion Pills*, La. Illuminator (May 13, 2025), perma.cc/D4BR-RKFC.

cited the "problem" with "activists who are intent on sending these pills to people through the mail."[156] Governor Hochul doubled down on her defiance of Louisiana law on X[157]:

103. As these examples show, FDA's removal of the in-person dispensing requirement in the 2023 REMS has had its intended effect. Pro-abortion activists credit the 2023 REMS for their ability to blanket pro-life states with mifepristone—with impunity and without any fear of liability.

104. And the resulting numbers are shocking. A Society of Family Planning #WeCount report states that, "between July 2023 to June 2024," they observed a range of "from 310 to 620"

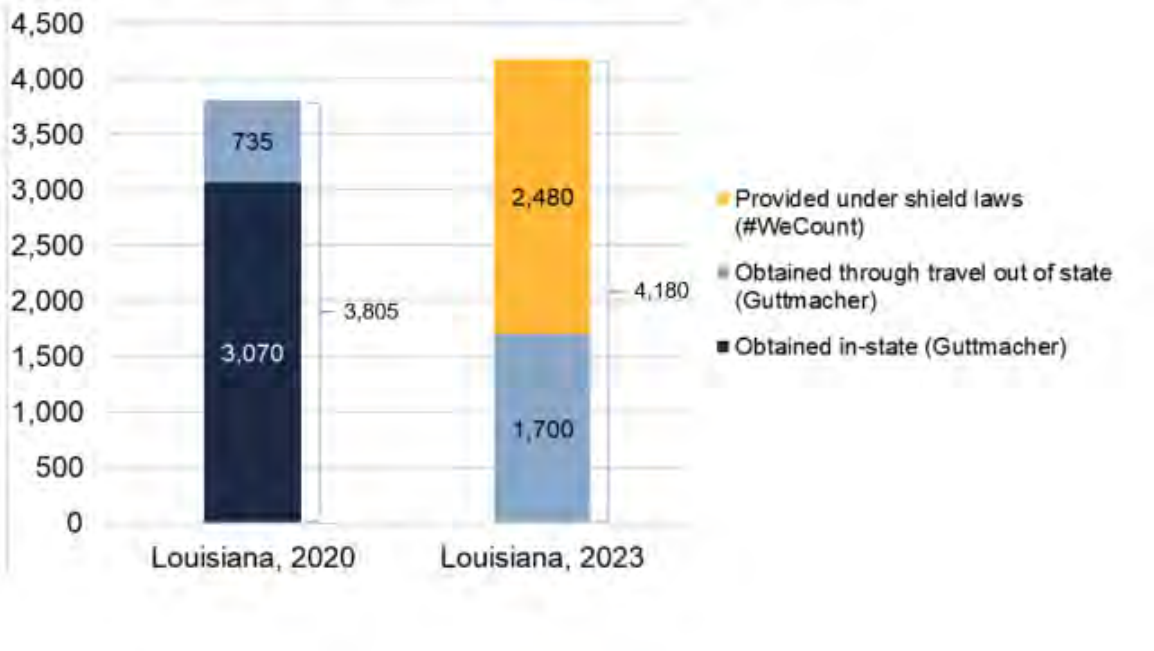
[156] *Id.*

[157] Ex. 90, Governor Kathy Hochul (@GovKathyHochul), X (May 13, 2025, 4:28 PM), perma.cc/ZA4U-G2CY.

mail-order abortions per month in Louisiana. From April to June 2024, the average number of mail-order abortions reached 617 per month in the State.[158] In December 2024 alone, it reached 800.[159]

105. In fact, FDA's approval of mifepristone-by-mail *increased* the number of abortions Louisiana residents obtained—even *after* Louisiana's abortion prohibition (with narrow exceptions) took effect.[160]

Figure 13. Louisiana, six months of 2020 and 2023, respectively



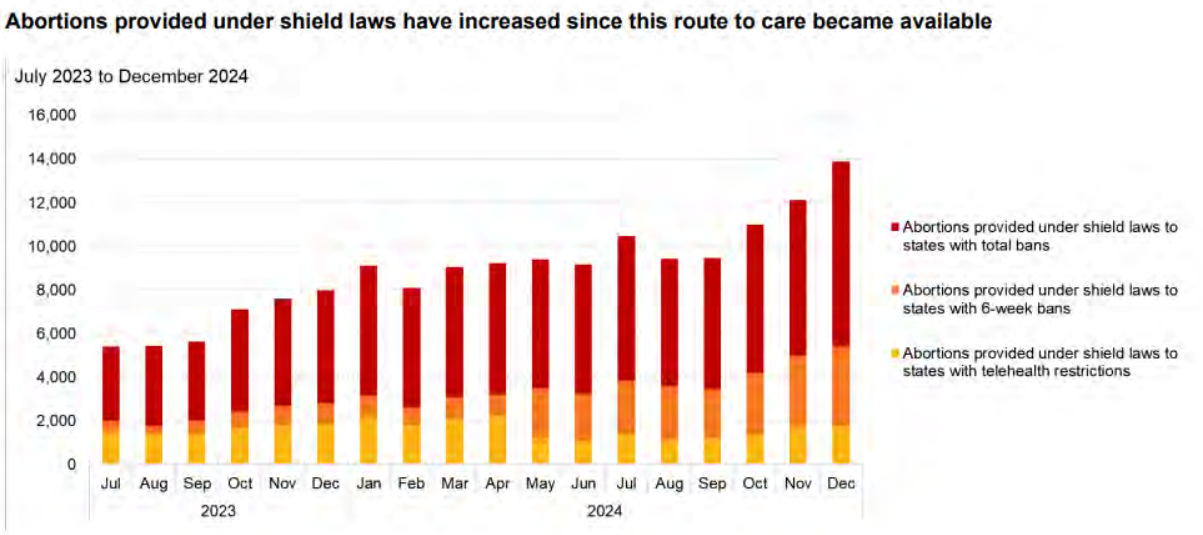
106. That trend coincides with national reported data, which shows that the mailing of mifepristone under the 2023 REMS accounts for *thousands* of abortions every month in pro-life states:[161]

[158] Ex. 1, Society of Family Planning, #WeCount Report April 2022 to June 2024 at 10.

[159] Ex. 2, Society of Family Planning, #WeCount Report April 2022 to December 2024 at PowerPoint slide 35.

[160] Ex. 1, Society of Family Planning, #WeCount Report April 2022 to June 2024 at 16.

[161] Ex. 91, Society of Family Planning, #WeCount Report April 2022 to December 2024 at 11. (Jun. 23, 2025), perma.cc/859P-G4FV.



107. And that trend will only get worse. Earlier this week, FDA approved a generic version of mifepristone for Evita Solutions, LLC.[162] This new purveyor of mifepristone touts that its mission is to make abortion "accessible to all"—"regardless of their ... age, . . . income, or where they live."[163]

VI. Louisiana Has Standing to Challenge the 2023 REMS.

108. As outlined above, the 2023 REMS is the direct cause of extensive harm that Louisiana suffers every day that the REMS is in effect. Indeed, this was the *intended* effect of the Biden Administration's 2023 REMS: to permit "dispensing of mifepristone through the mail ... or through a mail-order pharmacy"[164]—specifically to target those pro-life states like Louisiana where abortion is prohibited (with narrow exceptions) or narrowly circumscribed.

109. It is thus unsurprising that Louisiana has standing to sue in at least three separate respects: (A) the 2023 REMS harms Louisiana in its sovereign capacity because it predictably, and by design, enables third parties to violate Louisiana's pro-life laws, preventing Louisiana from effectively enforcing its prohibition on abortion and preventing the State from protecting the lives of unborn babies despite the promise of *Dobbs*; (B) the 2023 REMS harms Louisiana in its quasi-sovereign

[162] Ex. 109, Evita Solutions, *Making generic mifepristone available and accessible today,* perma.cc/BW83-MUE4.

[163] *Id.*

[164] Ex. 3, 2021 FDA Letter to ACOG and SMFM About Mifepristone REMS at 2.

capacity by subjecting untold numbers of Louisiana women to injuries and risks of injuries caused by mifepristone; and (C) the 2023 REMS causes Louisiana textbook pocketbook injuries through the Medicaid payments Louisiana must make to cover the predictable increase in mifepristone-induced harms and the ordinary costs that arise when uninsured or underinsured patients seek services at public hospitals. For any of these reasons, Louisiana has standing to sue.

A. The 2023 REMS Causes Sovereign Harms.

110. First and foremost is the direct sovereign harm inflicted by the 2023 REMS upon Louisiana.

111. This Court recently reaffirmed that "states [hold] a sovereign interest in creating and enforcing their own laws and public policy." *Louisiana v. EEOC*, 705 F. Supp. 3d 643, 654 (W.D. La. 2024). Put differently, they "have an interest in 'the exercise of sovereign power over individuals and entities within the relevant jurisdiction—this involves the power to create and enforce a legal code, both civil and criminal.'" *Id.* at 653 (quoting *Texas v. Cardona*, 2024 WL 2947022, at *11 (N.D. Tex. June 11, 2024) (quoting *Alfred L. Snapp & Son, Inc. v. Puerto Rico*, 458 U.S. 592, 601 (1982))). And central among the "direct stake[s] necessary to satisfy standing" is a state's objection to federal agency "interefere[nce] with the States' ability to enforce their laws and implement the chosen public policies of their citizens." *Id.* (citation omitted).

112. Case in point: If states "have unambiguously expressed their opposition to purely elective abortions by passing laws prohibiting the same," then "the principles of federalism" "clearly give the states Article III standing to challenge" a federal agency's intrusion upon that sovereign prerogative. *Id.* at 653–54.

113. That is the case here. Louisiana has enacted sovereign laws prohibiting (with narrow exceptions) abortion. *See, e.g.*, La. R.S. § 40:1061(C) ("No person may knowingly administer to, prescribe for, procure for, or sell to any pregnant woman any medicine, drug, or other substance with the specific intent of causing or abetting the termination of the life of an unborn human being."); *id.* § 14:87.9(A) ("Criminal abortion by means of an abortion-inducing drug is committed when a person knowingly causes an abortion to occur by means of delivering, dispensing, distributing, or providing

a pregnant woman with an abortion-inducing drug."); *id.* § 40:1061.11(A) ("When any drug or chemical is used for the purpose of inducing an abortion, the physician who prescribed the drug or chemical shall be in the same room and in the physical presence of the pregnant woman when the drug or chemical is initially administered, dispensed, or otherwise provided to the pregnant woman."). So each pill of mifepristone that is mailed directly to a person in Louisiana for the purpose of causing an abortion directly violates Louisiana's laws.

114. That *third parties* violate Louisiana's laws in doing so does not matter in the standing analysis—because their conduct is not just the "predictable" response to the 2023 REMS, *Dep't of Com. v. New York*, 588 U.S. 752, 768 (2019), but the *expressly intended* result of the 2023 REMS. But for the 2023 REMS, abortion facilitators like Aid Access could not mail mifepristone into Louisiana. But, by eliminating the in-person dispensing requirement, the 2023 REMS permits the "dispensing of mifepristone through the mail ... or through a mail-order pharmacy."[165] That direct affront to Louisiana's laws renders Defendants directly complicit in abridging Louisiana's sovereign prerogatives—and that "clearly [gives the states] Article III standing to challenge" the 2023 REMS. *Louisiana*, 705 F. Supp. 3d at 654.

115. In fact, the case for standing here on sovereignty grounds is even stronger than it was in cases like *Louisiana v. EEOC* because Plaintiff Louisiana already has been forced to expend time and resources prosecuting the violations of its laws. Take Dr. Carpenter's pending indictment—there is no question that the charged conduct violated Louisiana law. As a result, Louisiana spent significant time and money investigating the case, interviewing witnesses, drawing up filings, and pressing toward Dr. Carpenter's indictment. That whole-of-government effort transcended not just the local district attorney's office but also the Attorney General's office and other State law enforcement partners. A state's active defense and enforcement of its own laws—precipitated by the federal government's own unlawful action—plainly implicates the states' "sovereign interest in creating and enforcing their own laws and public policy." *Id.* This is a straightforward case for standing.

[165] Ex. 3, 2021 FDA Letter to ACOG and SMFM About Mifepristone REMS at 2.

116. But Louisiana's sovereign harms don't end there. Preemption of state law is itself an injury. *Deanda v. Becerra*, 96 F.4th 750, 760 (5th Cir. 2024). And more than one federal court has determined that state abortion-drug regulations are preempted by FDA's REMS.

117. For example, in a case brought by GenBioPro, Inc. (the generic manufacturer of mifepristone), the Southern District of West Virginia held that FDA's "2023 REMS reflects a determination by FDA that when mifepristone is prescribed, it may be prescribed via telemedicine." *GenBioPro, Inc. v. Sorsaia*, No. CV 3:23-0058, 2023 WL 5490179, at *10 (S.D. W. Va. Aug. 24, 2023). On that basis, and before the underlying claim was dropped, the court ruled that West Virginia's law prohibiting remote dispensing of abortion drugs was preempted. *Id.*

118. Similarly, the Middle District of North Carolina enjoined some of North Carolina's abortion-drug regulations because "[w]hen a state imposes a restriction on the sale or distribution of an FDA-approved drug that is designed to reduce the risks associated with the drug even though the FDA explicitly considered and rejected that restriction as unnecessary for safe use under the statutory regime imposed and required by Congress, then that state law is preempted." *Bryant v. Stein*, 732 F. Supp. 3d 485, at 505 (M.D.N.C. 2024), appeal filed, Nos. 24-1576, 1600, 1617 (4th Cir. 2024). According to the district court, "North Carolina cannot second-guess the FDA's explicit judgment on how to manage risks from and safely prescribe, dispense, and administer REMS drugs, including mifepristone." *Id.* at 508.

119. To be clear, Louisiana disagrees with these district court decisions and, instead, contends that FDA sets the "regulatory floor" for drug safety standards—while states are free to require more. *GenBioPro, Inc. v. Raynes*, 144 F.4th 258, 274 (4th Cir. 2025). But because both Defendant HHS[166] and GenBioPro argue otherwise, Louisiana maintains that its sovereign interests in creating and enforcing its laws are impeded, threatened, and potentially preempted.

[166] Ex. 61, HHS, Secretary's Report Health Care Under Attack: An Action Plan to Protect and Strengthen Reproductive Care 8 (stating in a section titled "Federal Preemption—Protecting Access to Medication Abortion" that "states may not ban mifepristone based on disagreement with FDA's expert judgment").

B. The 2023 REMS Causes Quasi-Sovereign Harms.

120. Not only that, but the 2023 REMS also causes Louisiana quasi-sovereign harms in the form of injuries to Louisiana women—and their unborn babies.

121. "[F]rom time immemorial," the states have been primarily responsible for regulating the medical field through their constitutionally reserved powers to protect their citizens' health and welfare. *Dent v. West Virginia*, 129 U.S. 114, 122 (1889). Each state "has a significant role to play in regulating the medical profession," *Gonzales v. Carhart*, 550 U.S. 124, 157 (2007), as well as "an interest in protecting the integrity and ethics of the medical profession," *Washington v. Glucksberg*, 521 U.S. 702, 731 (1997). This includes "maintaining high standards of professional conduct" in the practice of medicine. *Barsky v. Bd. of Regents of Univ. of N.Y.*, 347 U.S. 442, 451 (1954).

122. In fact, *Dobbs* itself recognized these basic principles, crediting states' ability to regulate abortion with an eye toward "legitimate interests" such as: "respect for and preservation of prenatal life at all stages of development; the protection of maternal health and safety; the elimination of particularly gruesome or barbaric medical procedures; the preservation of the integrity of the medical profession; the mitigation of fetal pain; and the prevention of discrimination on the basis of race, sex, or disability." *Dobbs*, 597 U.S. at 301 (citation omitted).

123. Louisiana has enacted the laws detailed above and others like them—yet the State faces unquestionable quasi-sovereign harm each time a woman or her unborn child endures an unlawful abortion.

124. Consider not only Rosalie Markezich,[167] but also stories of Louisiana women who have faced complications from unlawful abortions induced by mifepristone that was mailed into Louisiana. One Lafayette OB/GYN treated a woman suffering complications after taking remotely dispensed mifepristone this year. He performed a dilation and curettage (D&C) procedure to resolve an incomplete abortion and bleeding at five weeks' gestation. Another teenage woman and her mother requested from the Lafayette doctor an ultrasound to confirm the teen's uterus was empty following

[167] *See infra* Sec. VII.

an elective abortion and brought with them the envelope that had contained the abortion drugs they received in the mail from New York.

125. Another New Orleans OB/GYN and ACOG fellow has personally treated at least fourteen patients for abortion-drug complications—including roughly eleven for incomplete abortions and three for infection and sepsis—since Louisiana's pro-life law went into effect in 2022. One patient took the drugs at 19 weeks' gestation. Roughly half of the patients this doctor treats are Medicaid recipients. This doctor's staff saw roughly 30 serious abortion-drug complications, including bleeding, hemorrhaging, suction D&C, blood transfusions, and hospital stays, in just a two-month span (from April through May 2025). She estimates that the total number of abortion-drug complications treated by her hospital system is roughly 30 per month.

126. In addition to women who suffer from and are treated for complications, many more call local hospitals concerned about heavy bleeding or taking multiple doses without knowing how far along they are in their pregnancies or whether they have an ectopic or molar pregnancy.

127. The State is also aware of many women who have sought the assistance and support of pregnancy care centers after taking abortion drugs received through the mail, including from out-of-state prescribers and facilitators of FDA-approved mifepristone like Dr. Margaret Carpenter and Aid Access.

128. For example, one pregnancy center in North Central Louisiana receives at least one call per week asking for a follow-up ultrasound after taking abortion drugs. The pregnancy center has also encountered several women on Louisiana Medicaid who have suffered abortion-drug complications, including a woman who sought emergency medical care to treat excessive bleeding after passing out.

129. And these are just direct injuries to pregnant Louisiana women that Louisiana law would prevent but the 2023 REMS now enables. Consider also the fatal injuries to the unborn babies that are the subject of hundreds of unlawful mifepristone abortions every month in Louisiana. By Louisiana law, an unborn child is "considered [] a natural person for whatever relates to its interests from the moment of conception." La. Civ. Code art. 26.

130. In seeking to protect such natural persons by generally prohibiting all abortions, including mifepristone-induced abortions, Louisiana has precisely sought to regulate the "legitimate" interest *Dobbs* credited: "respect for and preservation of prenatal life at all stages of development." *Dobbs*, 597 U.S. at 301. And by directly overriding Louisiana's sovereign prerogative in that respect by facilitating the deaths of thousands of unborn Louisiana children every year, the 2023 REMS directly and irreparably harm the State itself. *See, e.g.*, *Kansas v. United States*, 249 F.3d 1213, 1227 (10th Cir. 2001) (holding that Kansas suffered an irreparable harm where a federal agency's decision "places [Kansas'] sovereign interests and public policies at stake[.]"); *see also State of Ohio ex rel. Celebrezze v. U.S. Dep't of Transp.*, 766 F.2d 228, 233 (6th Cir. 1985) ("The threatened injury to a State's enforcement of its safety laws is within the zone of interests of the Administrative Procedure Act[.]").

131. To be clear, this quasi-sovereign theory of harm is not a *parens patriae* theory because Louisiana is not asserting the rights of its citizens. *Cf. Murthy v. Missouri*, 603 U.S. 43, 76 (2024). Instead, Louisiana is invoking its *own* sovereign right to regulate for the protection of its citizens, which is directly harmed by the 2023 REMS.

C. The 2023 REMS Causes Economic Harms.

132. Last but not least are the economic harms caused by the 2023 REMS. As recounted above, FDA itself has long recognized the serious risks that mifepristone poses to women. Relevant here is FDA's recognition—on the required label itself—that approximately 1 in 25 women who use mifepristone *as directed* will end up in the emergency room.[168] Also relevant is FDA's recognition—reflected in the black box warning—that mifepristone can cause "[s]erious and sometimes fatal infections and bleeding" warranting emergency attention.[169] And these warnings appeared on FDA's label for mifepristone before the 2023 REMS action when the agency acknowledged that "the literature suggests that there may be more frequent ED/urgent care visits related to the use of mifepristone when dispensed by mail."[170]

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[168] Ex. 9, Mifeprex 2023 Label at 8, 17.
[169] *Id.* at 1.
[170] Ex. 50, FDA 2023 Summary Review at PDF 75.

133. It is thus no surprise that, as reflected in the various Louisiana accounts above, women who use mifepristone mailed into Louisiana—facilitated by the 2023 REMS—are being treated in emergency settings for serious complications resulting from such use. Indeed, as the number of mifepristone-induced abortions continues to increase in states like Louisiana, the overall number of women seeking emergency care in Louisiana hospitals will also increase. That reality reveals basic pocketbook injuries to Louisiana.

134. *First*, Louisiana is on the hook for any Medicaid-related expenses arising from these emergency room and other hospital visits. Louisiana Medicaid historically swallows 44.4% of the State's total budget—dwarfing other budget items like secondary education (16.8%) and higher education (8.6%).[171] The State is set to spend about $19 billion on Medicaid next year, with the help of $14.2 billion in federal funding.[172]

135. As of January 1, 2023, 534,294 women from ages 15–44 were enrolled in Louisiana Medicaid and 538,139 women from ages 15–44 were recipients of Louisiana Medicaid.[173] The State has reason to believe that it has already expended Medicaid dollars on treating abortion-drug complications. And the State ultimately covers medical expenses for treating abortion drug-related complications.

136. HHS estimates that the average cost of a Medicaid-covered ER visit in 2021 was $600—and that has likely since increased from inflation and increasing medical costs.[174] A Medicaid "covered charge" may only be a fraction of total costs for that visit.

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[171] Ex. 93, *Exhibit 5: Medicaid as a Share of States' Total Budgets and State-Funded Budgets, SFY 2021*, Medicaid and CHIP Payment and Access Commission (MACPAC) (2023), perma.cc/KUQ2-9ZAY. The Medicaid and CHIP Payment and Access Commission (MACPAC) is a non-partisan federal legislative branch agency that provides data analysis on Medicaid to Congress, HHS, and the States. *See* 42 U.S.C. § 1396(b)(3).

[172] Ex. 94, Julie O'Donoghue, *Louisiana Medicaid Set to Grow Under Landry, Even as D.C. May Force Cuts*, La. Illuminator (Mar. 26, 2025), perma.cc/S2Y8-B8JE.

[173] Ex. 95, Louisiana Department of Health, Medicaid Annual Report 2022/2023 at 26.

[174] Ex. 96, Marc Roemer, HHS, Agency for Healthcare Research and Quality, *Costs of Treat-and-Release Emergency Department Visits in the United States, 2021* (September 2024), perma.cc/WDE2-CV77.

137. For example, one common method of treating abortion-drug complications is a D&C (dilation and curettage) to evacuate the contents of the uterus. Louisiana Medicaid covers D&Cs in an inpatient setting for incomplete or missed abortions, provided that the unborn child is not alive at the time of the D&C and the documentation indicates that the D&C procedure is not itself an abortion or pregnancy termination.[175] D&C costs vary slightly by practice setting. Louisiana Medicaid reimburses up to $552.64 for an outpatient D&C at a state hospital,[176] up to $535.50 for an outpatient D&C at a rural hospital,[177] and up to $550.32 for an outpatient D&C at a non-rural and non-state hospital.[178]

138. Louisiana Medicaid also covers both inpatient and outpatient emergency room services.[179] Louisiana Medicaid reimburses all outpatient emergency room services at a cost-to-charge ratio (CCR) that divides the provider's total costs by its total charges.[180]

139. Louisiana Medicaid also covers blood transfusions.[181] And Medicaid covers some vaginal hysterectomies at rates ranging from $1,405.95 to $1,450.94[182] and other vaginal hysterectomies at a CCR rate.[183]

140. Louisiana Medicaid likewise covers miscarriage treatment. Patients often present their abortion-drug complications as miscarriages for several reasons, including mistaken fear of legal

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[175] Ex. 97, Hospital Services Provider Manual: Chapter Twenty-Five of the Medicaid Services Manual, State of Louisiana Bureau of Health Services Financing, § 25.2 at PDF 16 (July 1, 2011).

[176] Ex. 98, Louisiana Medicaid Hospital Ambulatory Surgery Fee Schedule: State Hospitals (Effective Jan. 1, 2025), at PDF 58.

[177] Ex. 99, Louisiana Medicaid Hospital Ambulatory Surgery Fee Schedule: Rural Hospitals (Effective Jan. 1, 2025), at PDF 57.

[178] Ex. 100, Louisiana Medicaid Hospital Ambulatory Surgery Fee Schedule: Non-Rural and Non-State Hospitals (Effective Jan. 1, 2025), at PDF 58.

[179] Ex. 101, Medicaid Services, Louisiana Department of Health, perma.cc/T8L3-FGGP.

[180] Ex. 102, State Hospitals Outpatient Services Fee Schedule (Effective Jan. 1, 2025), at PDF 5; Ex. 103, Small Rural Hospital Outpatient Services Fee Schedule (Effective Jan. 1, 2025), at PDF 5.

[181] Ex. 102, State Hospitals Outpatient Services Fee Schedule at PDF 30.

[182] Ex. 100, Louisiana Medicaid Hospital Ambulatory Surgery Fee Schedule: Non-Rural and Non-State Hospitals at PDF 57; Ex. 99, Louisiana Medicaid Hospital Ambulatory Surgery Fee Schedule: Rural Hospitals at PDF 56; Ex. 98, Louisiana Medicaid Hospital Ambulatory Surgery Fee Schedule: State Hospitals at PDF 57.

[183] Ex. 103, Small Rural Hospital Outpatient Services Fee Schedule at PDF 37; Ex. 102, State Hospitals Outpatient Services Fee Schedule at PDF 37.

reprisal and (as discussed above) prescribers' advice that patients do not disclose the fact that they took abortion drugs and rather let emergency-room doctors assume they are treating a miscarriage.[184] Medicaid reimburses miscarriage treatment and care at rates ranging from $752.85 to $776.94.[185]

141. These figures do not include the standard per diem rate for hospital stays, if needed. Per diem rates for Louisiana Medicaid providers range from $213.60 to $4,382.07.[186]

142. As detailed above, Louisiana has experienced actual emergency-room visits by patients who took mifepristone received by mail and whose care costs will likely ultimately fall to Medicaid and the State.

143. This "effect on the states' fiscs" is a concrete, economic injury. *Texas v. United States*, 809 F.3d 134, 152 (5th Cir. 2015), *as revised* (Nov. 25, 2015) (cleaned up); *see also, e.g.*, *Biden v. Nebraska*, 600 U.S. 477, 490 (2023) ("financial harm is an injury in fact"); *TransUnion LLC v. Ramirez*, 594 U.S. 413, 425 (2021) ("[C]ertain harms readily qualify as concrete injuries under Article III. The most obvious are traditional tangible harms, such as physical harms and monetary harms."). Indeed, "[f]or standing purposes, a loss of even a small amount of money is ordinarily an 'injury,'" *Czyzewski v. Jevic Holding Corp.*, 580 U.S. 451, 464 (2017); *U.S. v. Texas*, 599 U.S. 670, 687–88 (2023) (Gorsuch, J., concurring in the judgment) (acknowledging that the same principle of concrete, monetary injury applies to states challenging the federal government under the APA).

144. Louisiana thus satisfies Article III in this way as well. *See California v. Azar*, 911 F.3d 558, 571–73 (9th Cir. 2018) (finding that the state had standing based on an injury to its economic interests where the state was responsible for reimbursing women who seek contraception through state-run programs).

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[184] *See supra* sec. IV.

[185] Ex. 100, Louisiana Medicaid Hospital Ambulatory Surgery Fee Schedule: Non-Rural and Non-State Hospitals at PDF 58; Ex. 99, Louisiana Medicaid Hospital Ambulatory Surgery Fee Schedule: Rural Hospitals at PDF 57; Ex. 98, Louisiana Medicaid Hospital Ambulatory Surgery Fee Schedule: State Hospitals at PDF 58.

[186] Ex. 104, Louisiana Medicaid Hospital Provider Inpatient Per Diem Rates (Effective 7/1/2024).

145. *Second*, Louisiana and other states with pro-life laws, though not "directly regulated parties," are effectively the objects of the regulations here because the Biden Administration "explicitly" used FDA's 2023 REMS to "target" pro-life states and "impede" the enforcement of their laws in response to the *Dobbs* decision. *See Diamond Alternative Energy LLC v. EPA*, 145 S. Ct. 2121, 2135–36 (2025). The 2023 REMS "pose[s] a legal barrier" to meaningful pro-life state laws and "den[ies] [states like Louisiana] the opportunity to [enforce abortion prohibitions] without government interference." *Id.* at 2136.

146. Indeed, this case can be viewed as "a typical APA suit" where "[a]n unregulated plaintiff ... will sue under the APA to challenge an allegedly unlawful agency rule that regulates others but also has adverse downstream effects on the plaintiff." *Corner Post, Inc. v. Bd. of Governors of Fed. Rsrv. Sys.*, 603 U.S. 799, 826 (2024) (Kavanaugh, J., concurring). "One example" is *Motor Vehicle Manufacturers Association of United States, Inc. v. State Farm Mutual Automobile Insurance Co.*, 463 U.S. 29, 103 (1983), where "several insurance companies challenged a federal agency's rescission of safety standards for new motor vehicles." *Id.* (emphasis added).

147. That is also the case here. Louisiana has standing to seek redress from a deregulatory action—*i.e.*, the 2023 REMS' elimination of the in-person dispensing requirement—which has resulted, and continues to result, in more expenses paid through public insurance claims and at state-run hospitals. Because even if FDA does not directly regulate the State itself, the State can "obtain relief from the downstream effects of the agency's rescission of the safety standards only if" the State can "obtain vacatur of that rescission." *Corner Post*, 603 U.S. at 834–35 (Kavanaugh, J., concurring). And here, vacating the 2023 REMS would disable out-of-state actors from sending FDA-approved abortion drugs into Louisiana against state law, thereby forestalling the presently existing harms to women in Louisiana and the state resources needed to address them.

148. *Third*, and last, separate and in addition to the regular payments public hospitals receive for providing inpatient care to Medicaid beneficiaries, Louisiana Medicaid also pays a determined rate to public hospitals that serve a disproportionate share of uninsured or indigent patients. In some cases,

these payments may be lower than the hospital's costs. Those public hospitals agree to accept the payment as payment in full, even if it is less than their actual cost.

149. If the State pays only a portion of a medical bill related to a mifepristone-induced abortion, the public hospital will incur as an expense the difference between the full amount of the medical bill and what was paid. In that way, too, the State suffers a monetary injury every time a public hospital foots the remainder of a bill that Medicaid does not cover.

VII. Rosalie Has Standing to Challenge the 2023 REMS.

150. In October 2023 Rosalie Markezich felt coerced by her boyfriend to take FDA-approved abortion drugs that he ordered from an out-of-state prescriber in her name and had delivered to her home through the U.S. Postal Service.[187]

151. Rosalie told her boyfriend that she wanted to keep her baby. But he had other plans.[188]

152. When Rosalie refused the drugs, her boyfriend became angry and shouted at her. Rosalie had suffered domestic abuse before, and she knew the signs of a dangerous man.[189] Her boyfriend had a criminal record.[190] Yet she was alone with him in a car, and her friends were unaware of her whereabouts.[191] She was terrified.[192] To pacify him, Rosalie agreed to take the drugs.[193] And he watched her swallow them.[194] Although she intended to throw them up as soon as she could get away from him, she was unsuccessful, and she lost her baby.[195]

153. Rosalie did not want to have an abortion.[196] Had she received the drugs in person, she would have told the doctor that she did not want to take the drugs—she would have sought help and

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[187] *See* Ex. 92, Rosalie Markezich Decl. ¶¶ 10–13.
[188] *Id.* ¶¶ 5, 11.
[189] *Id.* ¶ 12.
[190] *Id.*
[191] *Id.*
[192] *Id.*
[193] *Id.* ¶¶ 12–13.
[194] *Id.* ¶ 13.
[195] *Id.* ¶¶ 12–14.
[196] *Id.* ¶ 16.

support.[197] Rosalie now faces prolonged emotional trauma and mourns the loss of her child.[198] No woman should have to experience that heartbreak and devastating loss.

154. Rosalie suffered and continues to suffer concrete, particularized injuries. She lost her unborn child. She endured physical pain and heavy bleeding from ingesting unwanted abortion drugs. And she continues to suffer mental-health effects from the trauma she experienced for which she seeks counseling and receives medication.

155. Rosalie is also at risk of future injury. Without a requirement for an in-person office visit to prevent coercion, Rosalie could be placed in the same position for future pregnancies. Under FDA's current regime, anyone can obtain mifepristone and pressure or trick a woman into taking it. Rosalie has a strong interest in reinstating the in-person dispensing requirement to prevent future coercion.

156. The 2023 REMS caused Rosalie's injuries, and her injuries are traceable to the 2023 REMS. If FDA had required an in-person office visit, a medical professional would have screened Rosalie for coercion and abuse. But the 2023 REMS allowed abortion drugs to be provided through the mail—enabling abusers to order them in others' names and coerce pregnant women like Rosalie to take them. Had FDA required in-person dispensing, Rosalie's boyfriend would not have been able to access the drugs and compel Rosalie to take them.[199] She could have told a doctor that she did not want them.

157. Rosalie's injuries are redressable. It is not just speculation that the Court can remedy her situation by removing the risk of future abortion-drug coercion: if the 2023 REMS is rolled back and FDA's actions ruled unlawful, the in-person dispensing requirement will be reinstated. This legally vindicates Rosalie, who has an interest in FDA following lawful procedure to ensure high-risk drugs do not harm her.

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[197] *Id.* ¶ 19.
[198] *Id.* ¶ 18.
[199] *Id.* ¶ 19.

158. Rosalie was hurt by government agencies who turned a blind eye to the risks that mail-order abortion drugs pose to women like her. A judicial acknowledgment that FDA unlawfully failed her would mitigate the ongoing pain and suffering that she experiences as she attempts to heal. Most importantly, a final judgment reduces the risk that she will be subject to the same coercion and bodily injury in the future by removing the means by which others could order these drugs without her full and free consent during a future pregnancy. Rosalie has an interest, as a matter of bodily autonomy, in not being subjected to abortion-drug coercion again—coercion that is only possible because of the 2023 REMS. Rosalie has a right to protect her future unborn children.

159. The State found out about Rosalie's circumstances in 2024, and it has issued a warrant for the arrest of the California-based doctor from whom Rosalie's boyfriend ordered the abortion drugs. That warrant is still outstanding. Rosalie learned about this case and the opportunity to seek relief against FDA in 2025.

CLAIMS FOR RELIEF

COUNT ONE
The 2023 REMS Is Arbitrary and Capricious and an Abuse of Discretion (5 U.S.C. § 706)

160. Louisiana and Rosalie re-allege and incorporate, as though fully set forth, paragraphs 1 to 157 of this complaint.

161. As five Fifth Circuit judges have already indicated, the 2023 REMS is arbitrary and capricious and an abuse of discretion. 5 U.S.C. § 706(2)(A).

162. That is principally so because the 2023 REMS eliminated the in-person dispensing requirement—based on sources that the agency conceded did not independently support its decision. For example, it was arbitrary and capricious for FDA to conclude that adverse event reports supported the 2023 REMS. The agency acknowledges that voluntary FAERS data *cannot be used* to indicate drug safety or calculate the incidence of adverse events. Yet FDA used mifepristone FAERS data for expressly those purposes.

163. It was also arbitrary and capricious for FDA to conclude that scientific literature supported the 2023 REMS. FDA conceded that the studies it relied on were "not adequate on their own to establish the safety of ... dispensing mifepristone by mail." The studies the agency relied on could not be generalized to the United States population because of small sample sizes, lack of information about safety outcomes, and the inclusion of pre-abortion safeguards like in-person examinations and ultrasounds. The studies also uniformly showed that emergency room visits would go up without in-person dispensing. And one study found that hospitalizations would likewise increase.

164. Not only that, but prior to its 2021 Non-Enforcement Decision, the agency asserted and repeatedly reaffirmed over two decades that in-person dispensing was "minimally burdensome" and "necessary" to preserve safety.

165. FDA's unlawful and unreasonable rationales for the 2023 REMS—particularly in light of the *Dobbs* decision that the Biden Administration was actively trying to undermine—illustrate that the supposed justifications for the 2023 REMS were all just pretext.

166. Again, this should not be controversial, since five Fifth Circuit judges have written along the same lines. Judges Oldham and Engelhardt expressed disbelief that, "[a]fter eliminating th[e] adverse-event reporting requirement [in 2016], FDA turned around in 2021 and declared the absence of non-fatal adverse-event reports means mifepristone is 'safe.'" *Alliance I*, 2023 WL 2913725, at *17. "This ostrich's-head-in-the-sand approach is deeply troubling," they said, "especially on a record that, according to applicants' own documents, necessitates a REMS program, a 'Patient Agreement Form,' and a 'Black Box' warning." *Id.* "And it suggests FDA's actions are well 'outside the zone of reasonableness.'" *Id.* (citation omitted). For those reasons, Judges Oldham and Engelhardt emphasized that "[i]t's unreasonable for an agency to eliminate a reporting requirement for a thing and then use the resulting absence of data to support its decision"—and thus "it [is] unlikely that plaintiffs' arbitrary-and-capricious challenges will fail on the merits." *Id.* at *17–18.

167. Chief Judge Elrod (writing for herself and Judges Ho and Wilson) agreed: "FDA's decision to rely so heavily on data from FAERS 'runs counter to' the critical limitations associated

with that data." *Alliance II*, 78 F.4th at 250. And that says nothing of "[t]he second defect ... [which] is that [FDA] relied on various literature relating to remote prescription of mifepristone—despite FDA's admission that the literature did not affirmatively support its position." *Id.* "Especially in light of the unreliability of the adverse-event data, it was not reasonable for FDA to depend on the published literature to support its decision." *Id.*

168. "Courts must set aside agency action where there are 'shortcomings in the agency's explanations' or where '[n]o record evidence affirmatively makes' the agency's case." *Id.* "That is the case here. In the face of concededly limited data, and lacking more probative information from prescribers, FDA fell back on studies that were merely 'not inconsistent' with its intended conclusion." *Id.* at 250–51. But FDA "did not refer to any literature that affirmatively supported the notion that mifepristone would remain safe and effective even without the in-person dispensing requirement." *Id.* at 251. Thus, Chief Judge Elrod had no trouble "conclud[ing] that the [plaintiffs] are likely to succeed in showing that this action violated the APA."[200] *Id.* All the same here.

169. That fatal defect arising from the 2023 REMS' elimination of the in-person dispensing requirement goes hand-in-glove with two related defects. *First*, as FDA recognized, its handling of the in-person dispensing requirement was directly related to FDA's simultaneous decision to allow certified pharmacies—including retail pharmacies—to dispense abortion drugs. For all the reasons why the elimination of the in-person dispensing requirement was arbitrary and capricious, therefore, the certification decision was likewise arbitrary and capricious. *Second*, and in the same vein, FDA contemporaneously removed the Medication Guide Protection from the Patient Agreement—an independently arbitrary-and-capricious action because FDA relied solely on a subjective view of whether a woman would be likely to follow the Agreement's directive and failed to address serious safety concerns. Indeed, FDA did not base its conclusion on any reasoned explanation or data, nor

[200] "This action" technically referred to the 2021 Non-Enforcement Decision in *Alliance II*; however, as Chief Judge Elrod explained, the 2023 REMS "formaliz[ed] [] the policy" and, in fact, that formalization kept the case alive since "[t]he decision that FDA made in 2021—to permanently not enforce in-person prescription and dispensing requirements—remains in force." 78 F.4th at 248. Because "the effect is the same," her reasoning directly applies to the 2023 REMS as well. *Id.*

did it attempt to address the health risks associated with (1) complication misdiagnosis or (2) the common practice of conflating abortion-drug adverse events with miscarriage.

170. For these reasons, the 2023 REMS—in its entirety—must be held unlawful, stayed, set aside, vacated, and preliminarily and permanently enjoined under the APA.

COUNT TWO
The 2023 REMS Is Contrary to Law
(5 U.S.C. § 706)

171. Louisiana and Rosalie re-allege and incorporate as though fully set forth, paragraphs 1 to 157 of this complaint.

172. The 2023 REMS is "otherwise not in accordance with law." 5 U.S.C. § 706(2)(A).

173. That is because the "[t]he text of the Comstock Act prohibits the mailing of abortifacient drugs." *See Alliance II*, 78 F.4th at 267 (Ho, J., concurring part and dissenting in part); *see* 18 U.S.C. § 1461 ("Every article or thing designed, adapted, or intended for producing abortion ... [and every] drug ... calculated to lead another to use it or apply it for producing abortion ... [i]s declared to be nonmailable matter and shall not be conveyed in the mails or delivered from any post office or by any letter carrier.").[201] "Congress later extended the mailing prohibition to cover common carriers as well," and then included "interactive computer service[s]." *Alliance II*, 78 F.4th at 267 (Ho, J., concurring part and dissenting in part); *see* 18 U.S.C. § 1462 (prohibiting the use of "any express company or other common carrier or interactive computer service" for "any drug, medicine, article, or thing designed, adapted, or intended for producing abortion"). "So it's also illegal to use the internet to ship or receive abortifacients." *Alliance II*, 78 F.4th at 267 (Ho, J., concurring part and dissenting in part).

174. The 2023 REMS "violates the Comstock Act" because it expressly "authorizes the dispensing of mifepristone 'through the mail ... or through a mail-order pharmacy.'" *Id.* "But 'us[ing] the mails for the mailing of a 'drug ... for producing abortion' is precisely what the Comstock Act

[201] Because Chief Judge Elrod resolved the case on arbitrary-and-capricious grounds, she did "not consider" the alternative Comstock Act argument. *Alliance II*, 78 F.4th at 251 n.8.

prohibits." *Id.* at 267–68. To be clear, the 2023 REMS "doubles down on this violation by permanently eliminating the in-person dispensing requirement" so that "pharmacies [can] ship mifepristone to its users" and "distributors [like] Danco and GenBioPro [can] '[s]hip mifepristone ... to certified pharmacies.'" *Id.* at 268. This is exactly what "violates the Comstock Act." *Id.*

175. Because a federal agency cannot permit what federal law expressly prohibits, FDA lacked legal authority to permanently remove the in-person dispensing requirement through the 2023 REMS. *See FCC v. Next Wave Pers. Commc'ns Inc.*, 537 U.S. 293, 300 (2003) ("The Administrative Procedure Act requires federal courts to set aside federal agency action that is 'not in accordance with law,' 5 U.S.C. § 706(2)(A)—which means, of course, any law, and not merely those laws that the agency itself is charged with administering.") (citation omitted). The 2023 REMS thus must be held unlawful, stayed, set aside, vacated, and preliminarily and permanently enjoined under the APA.

PRAYER FOR RELIEF

For these reasons, Louisiana and Rosalie respectfully request that the Court enter an order and judgment against Defendants, including their employees, agents, successors, and all persons in active concert or participation with them, in which it:

A. Holds unlawful, stays, sets aside, and vacates the 2023 REMS.

B. Issues a preliminary and permanent injunction ordering Defendants to withdraw the 2023 REMS.

C. Retains jurisdiction of this matter to enforce this Court's order.

D. Awards Plaintiffs costs, attorneys' fees, and other disbursements for this action.

E. Grants any other relief this Court considers equitable, just, and appropriate.

Dated: October 6, 2025

Respectfully submitted,

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EXHIBIT 2

Society of Family Planning, #WeCount
Report April 2022 to December 2024
(Jun. 23, 2025)

National findings

Summary of findings

- Abortion volume is **higher in 2024** than it was in 2023 or 2022.
- The majority of abortions occur **in-person**.
- The number of abortions delivered via **telehealth continued to increase**.
  - By the end of 2024, 1 in 4 abortions was delivered via telehealth.
- **Shield laws** continue to facilitate abortion access, with an average of 12,330 abortions per month in the final quarter of 2024.
- Implications of these trends are unclear in the context of multiple changes in the service delivery environment:
  - Shifting price of abortion
  - Decreases in abortion funds to cover patient costs
  - Election-related spikes in demand
  - Ongoing financial pressure on brick-and-mortar clinics

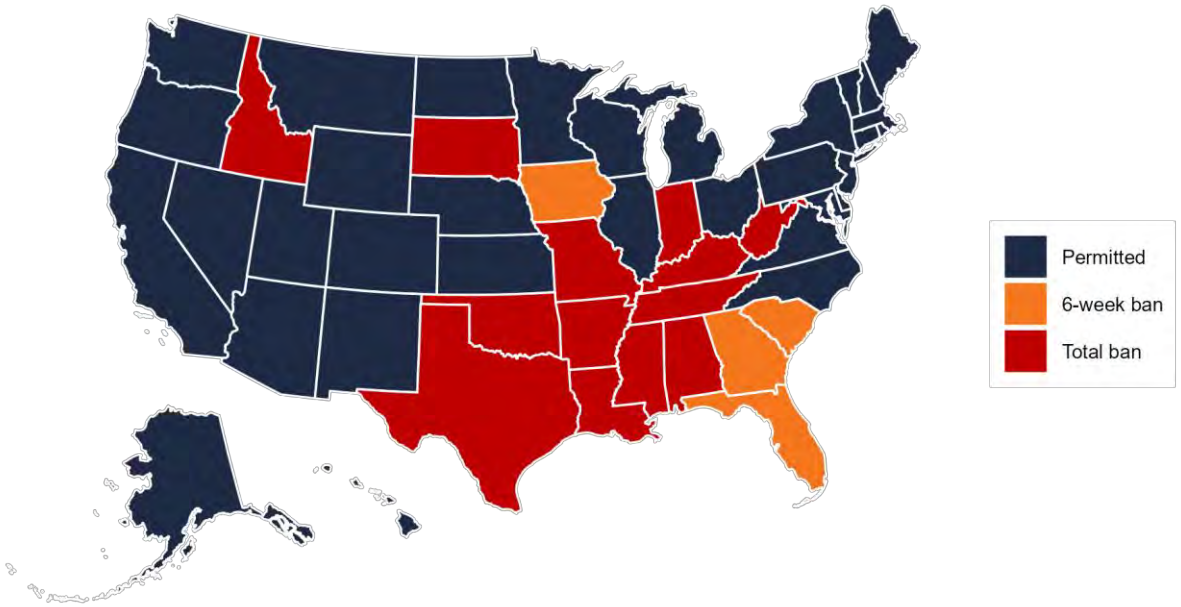
Changes in legal status since January 2024

- In **Florida**, a 6-week ban went into effect in May 2024
- In **Iowa**, a 6-week ban went into effect in August 2024
- In **North Dakota**, a total ban was ruled unconstitutional in October 2024

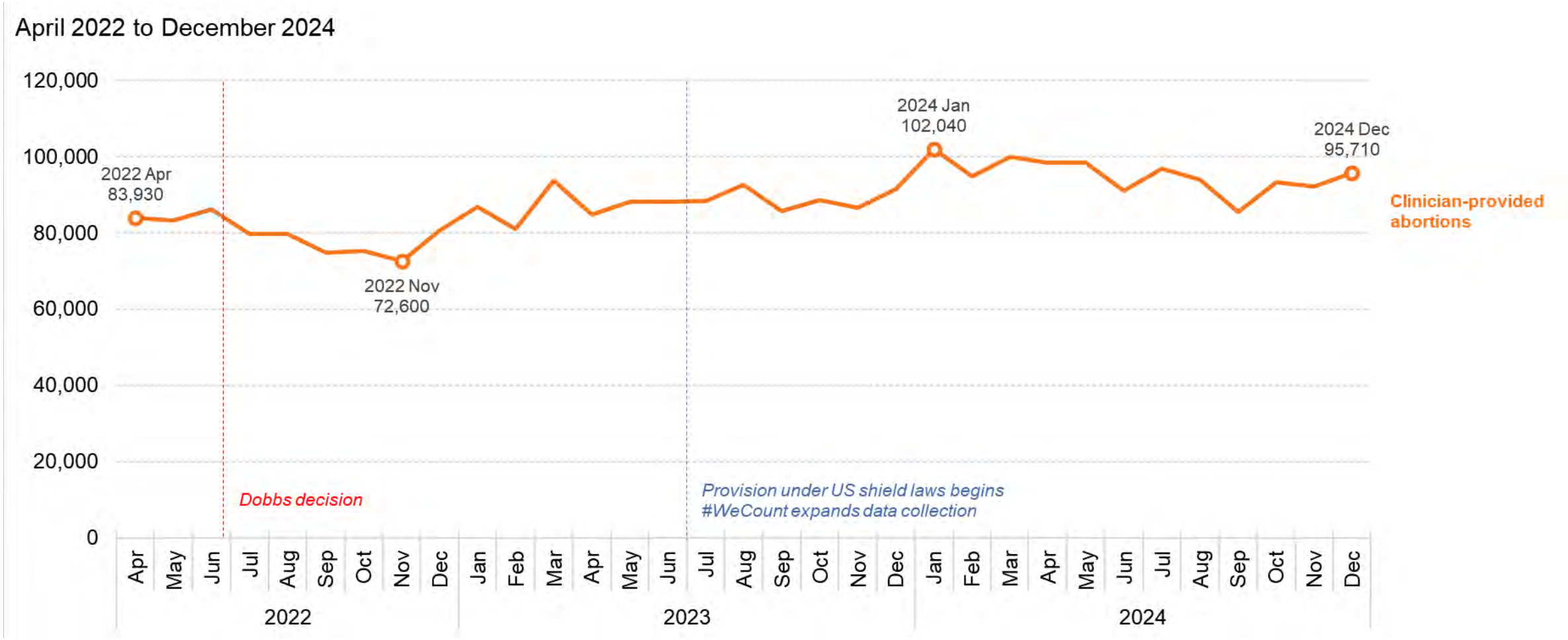
  No brick-and-mortar facilities providing
- States with total bans as of December 2024:

  Alabama, Arkansas, Idaho, Indiana, Kentucky, Louisiana, Mississippi, Missouri, Oklahoma, South Dakota, Tennessee, Texas, West Virginia
- States with 6-week bans as of December 2024:

  Florida, Georgia, Iowa, South Carolina

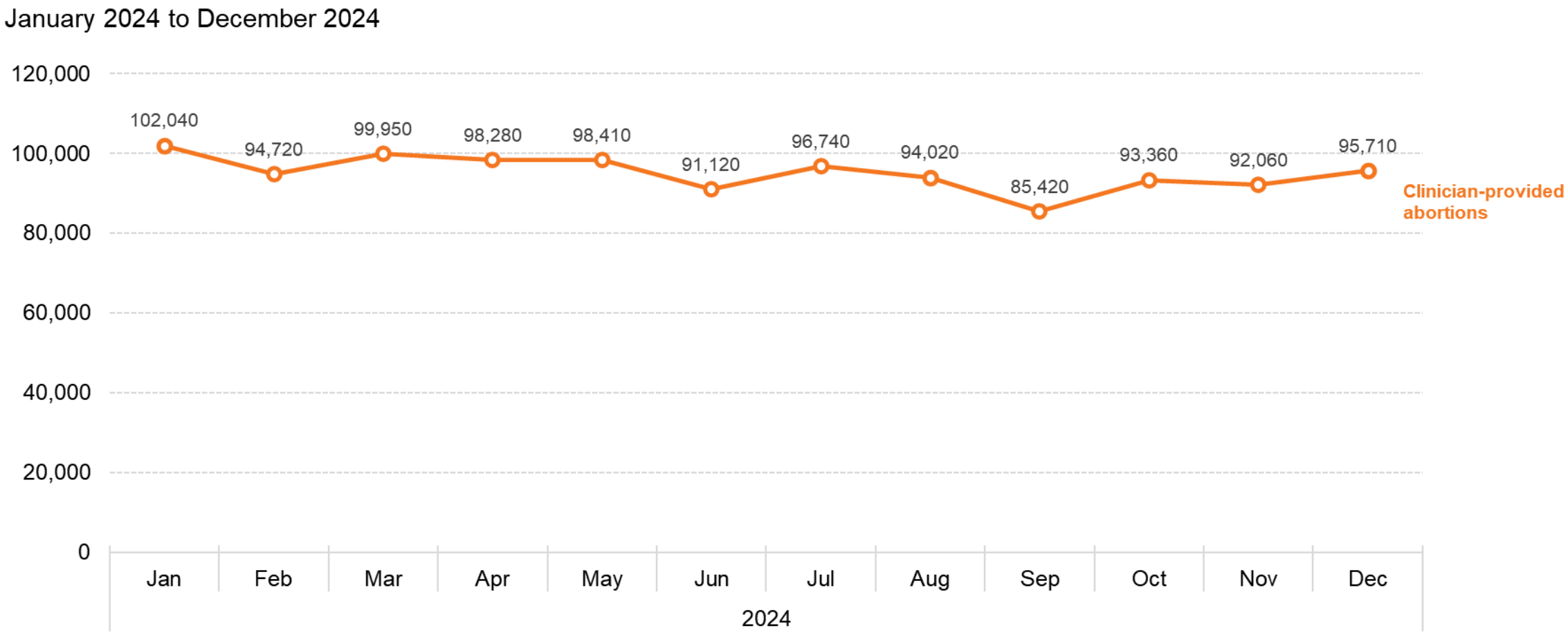


Total abortions in the US have increased since *Dobbs*



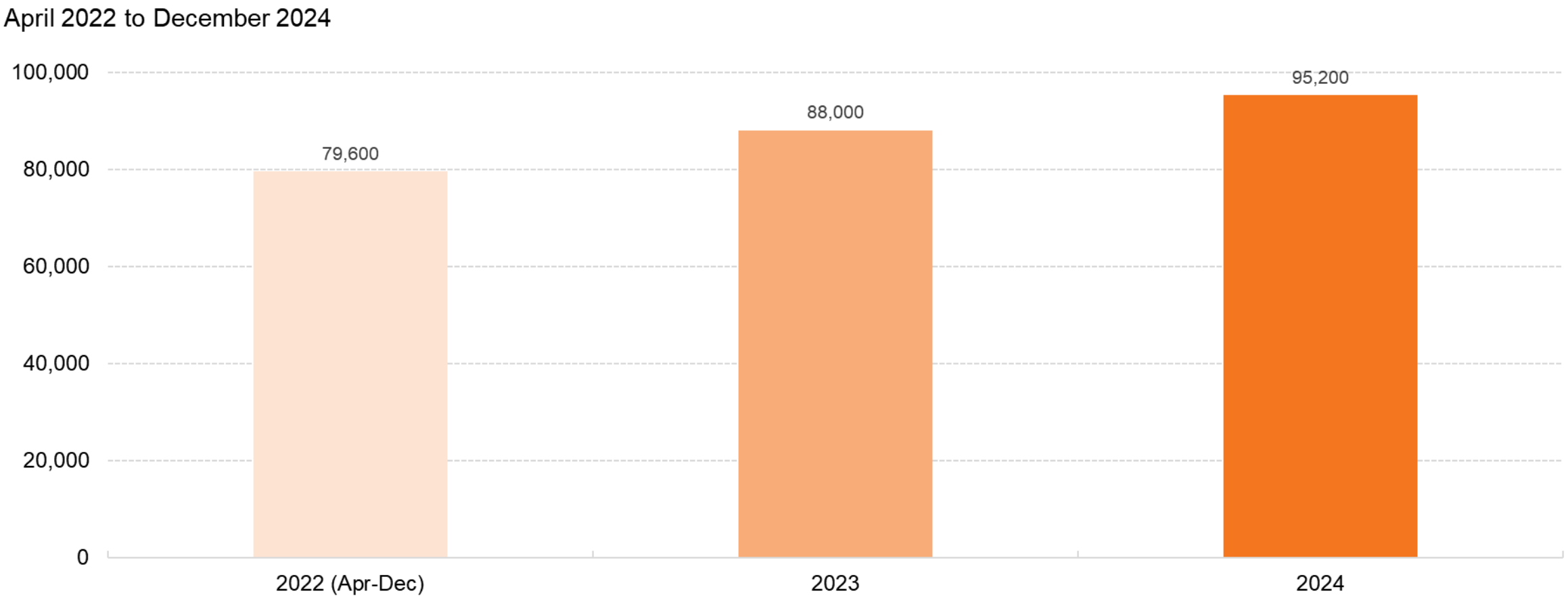
Source: Society of Family Planning, June 2025

US abortions totaled 1.14 million in 2024



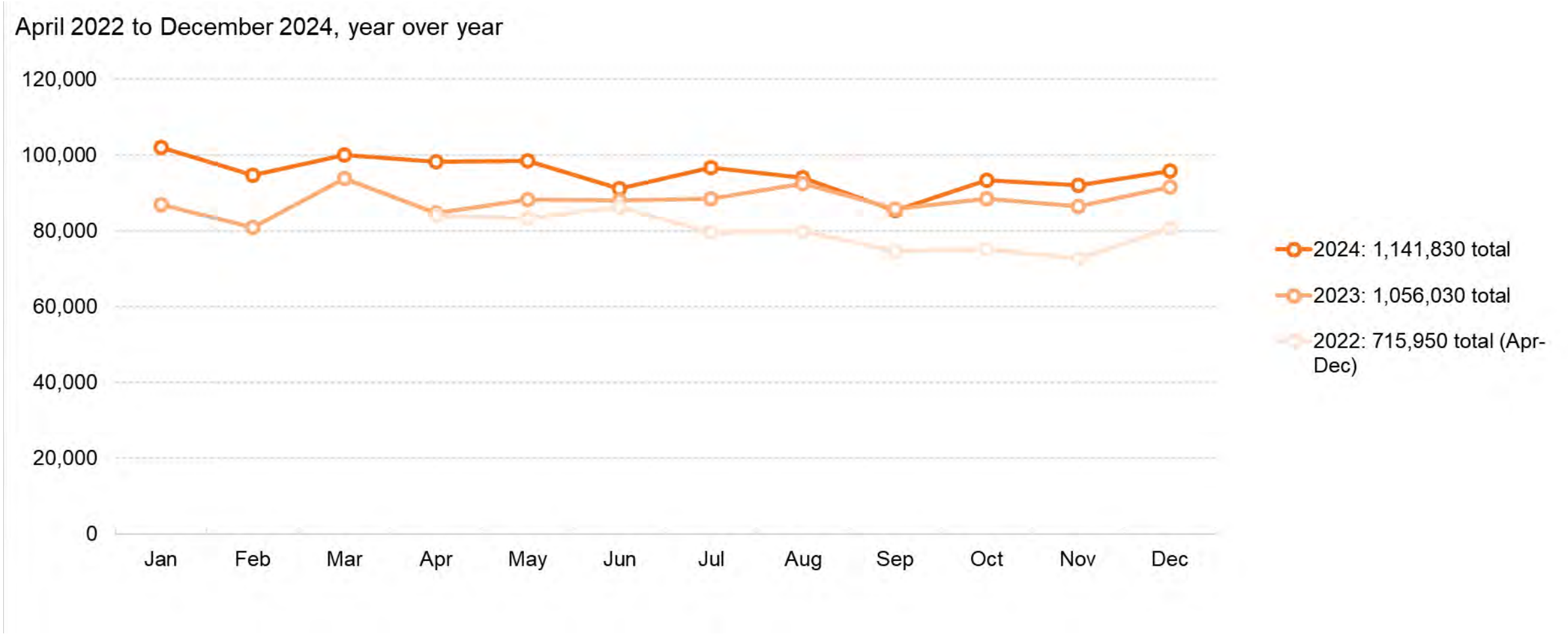
Source: Society of Family Planning, June 2025

Monthly average number of abortions increased each year



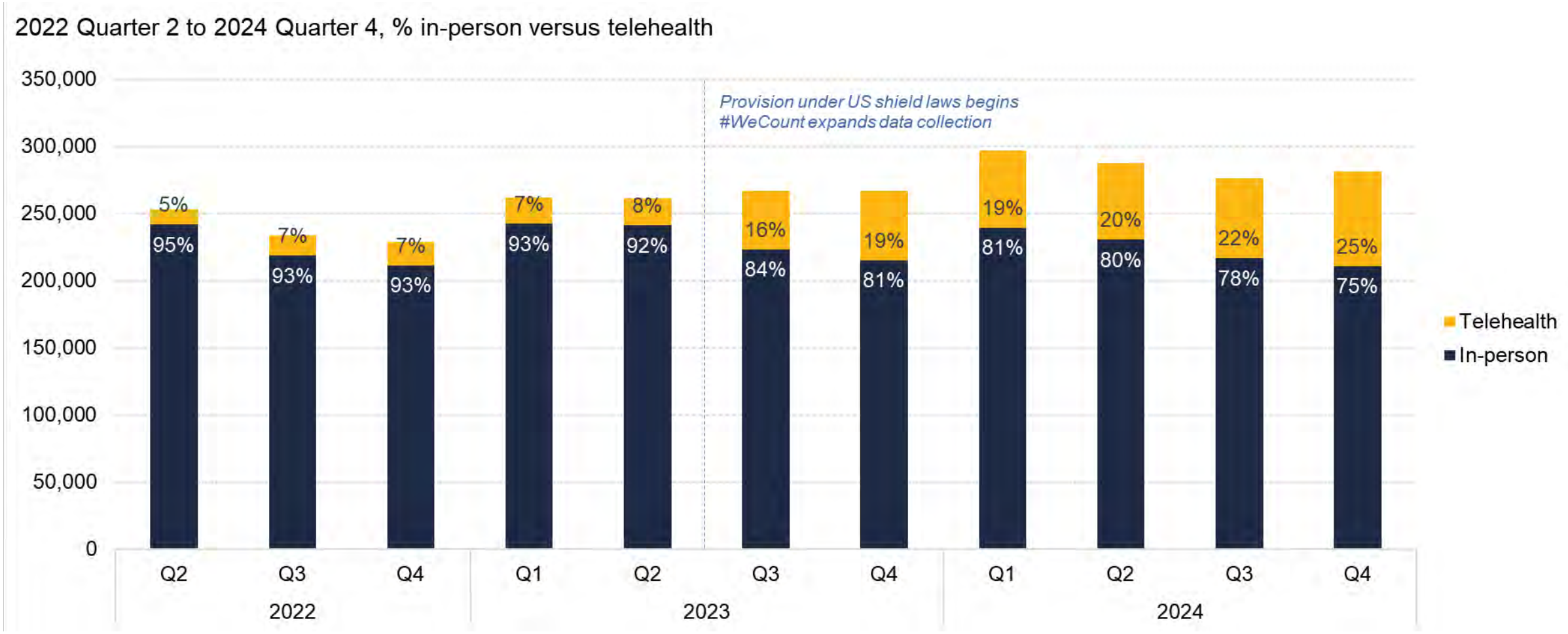
Source: Society of Family Planning, June 2025

The monthly number of abortions increased each year



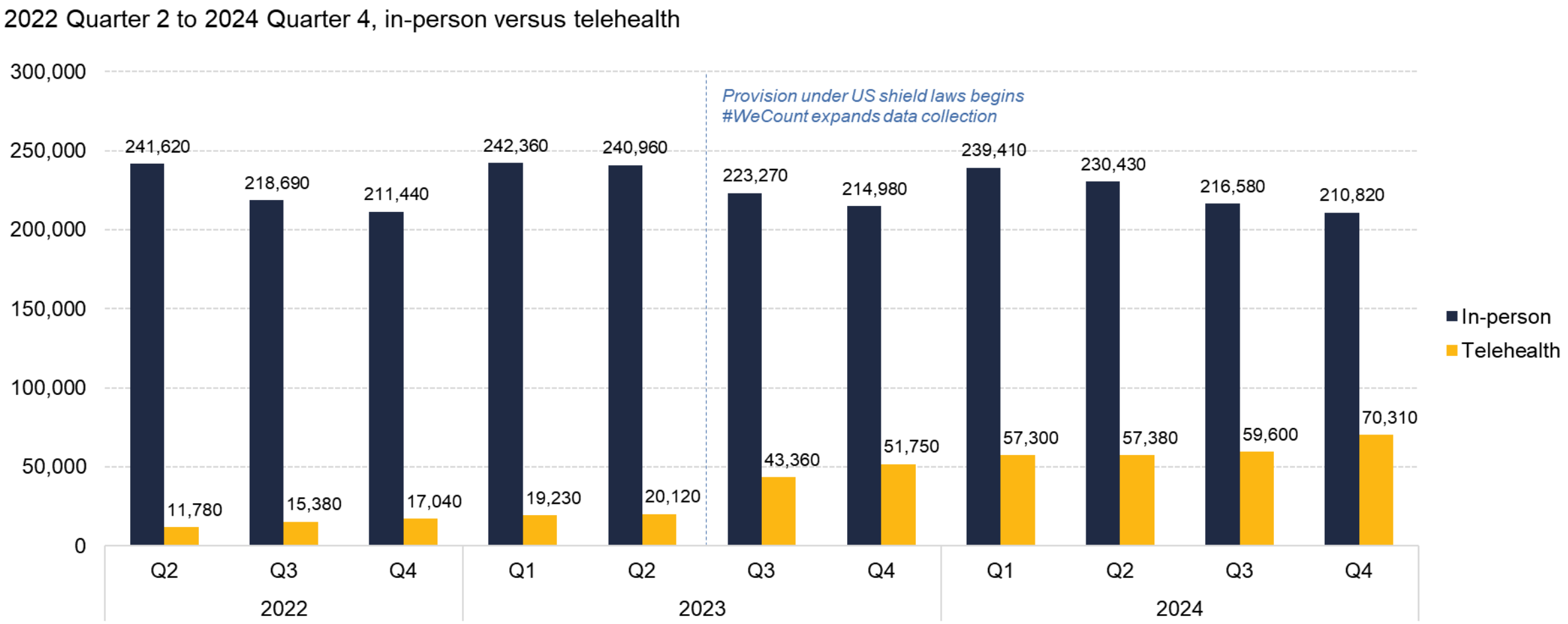
Source: Society of Family Planning, June 2025

By Q4 of 2024, 1 in 4 abortions were provided via telehealth



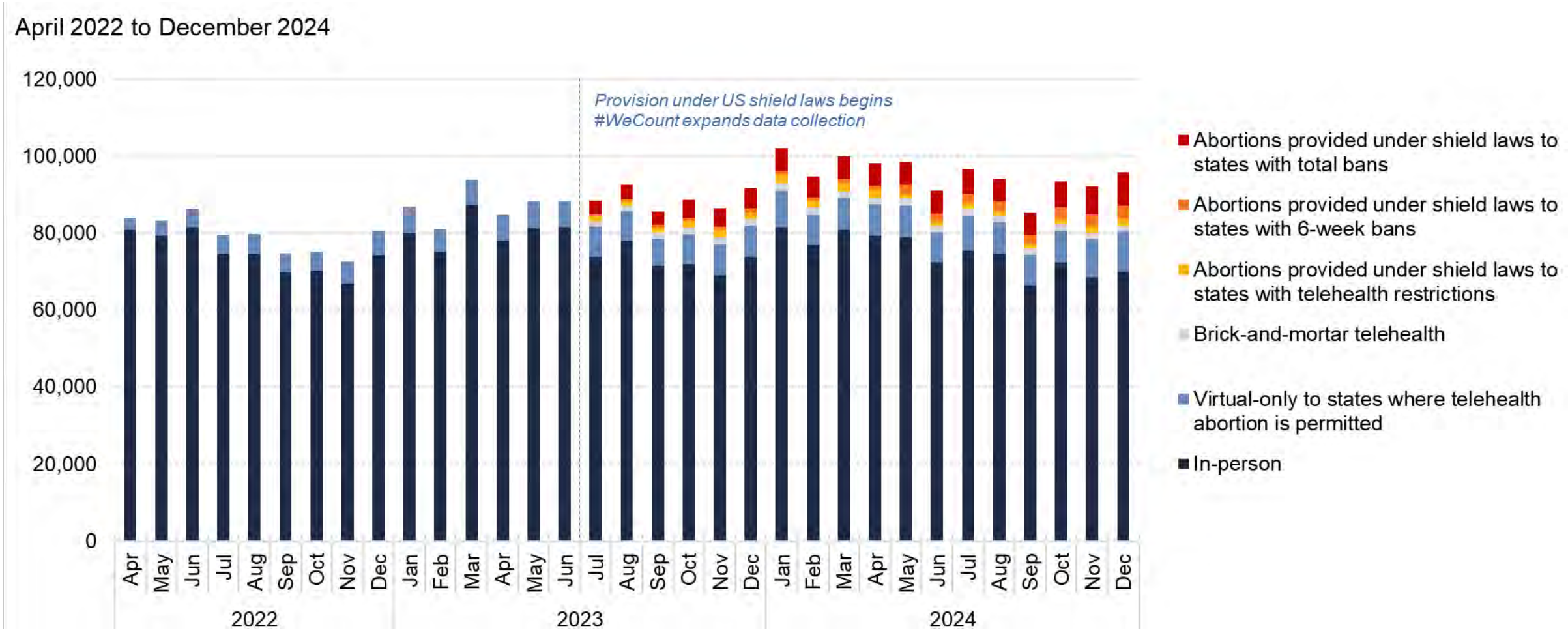
Source: Society of Family Planning, June 2025

In-person abortion care declined slightly, while telehealth grew



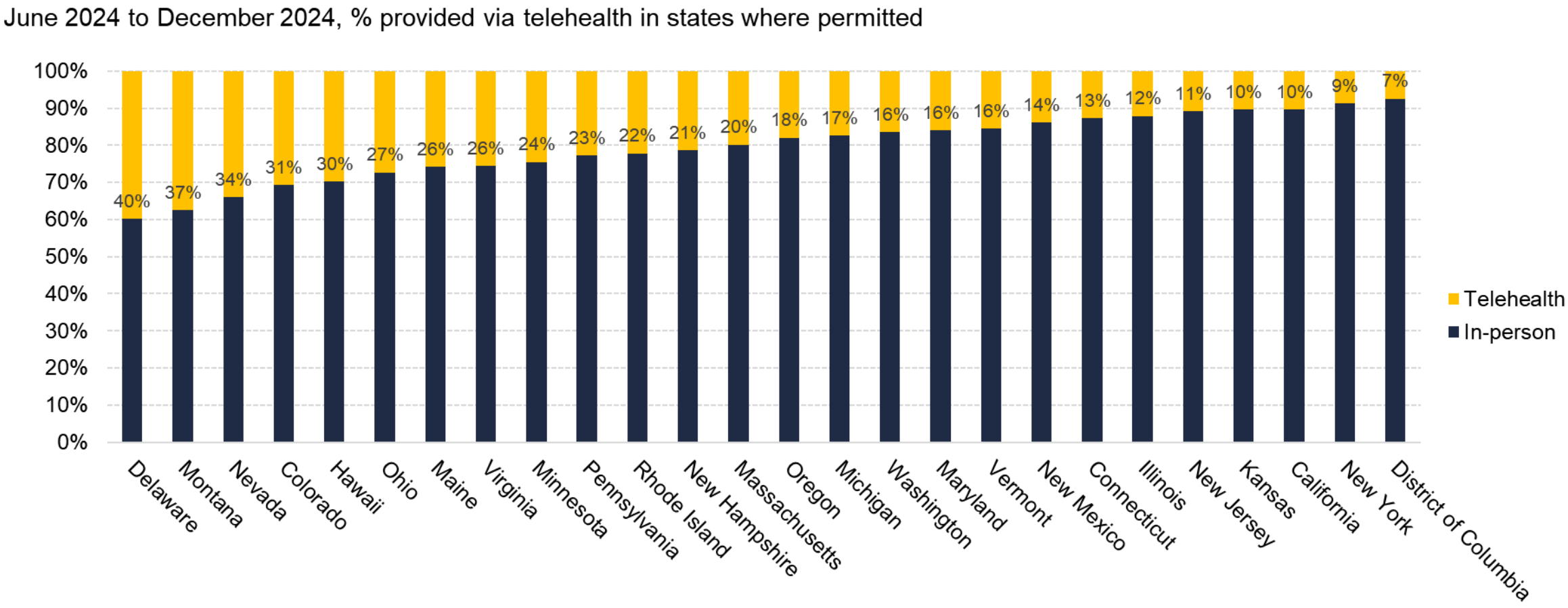
Source: Society of Family Planning, June 2025

The majority of abortions still take place in-person



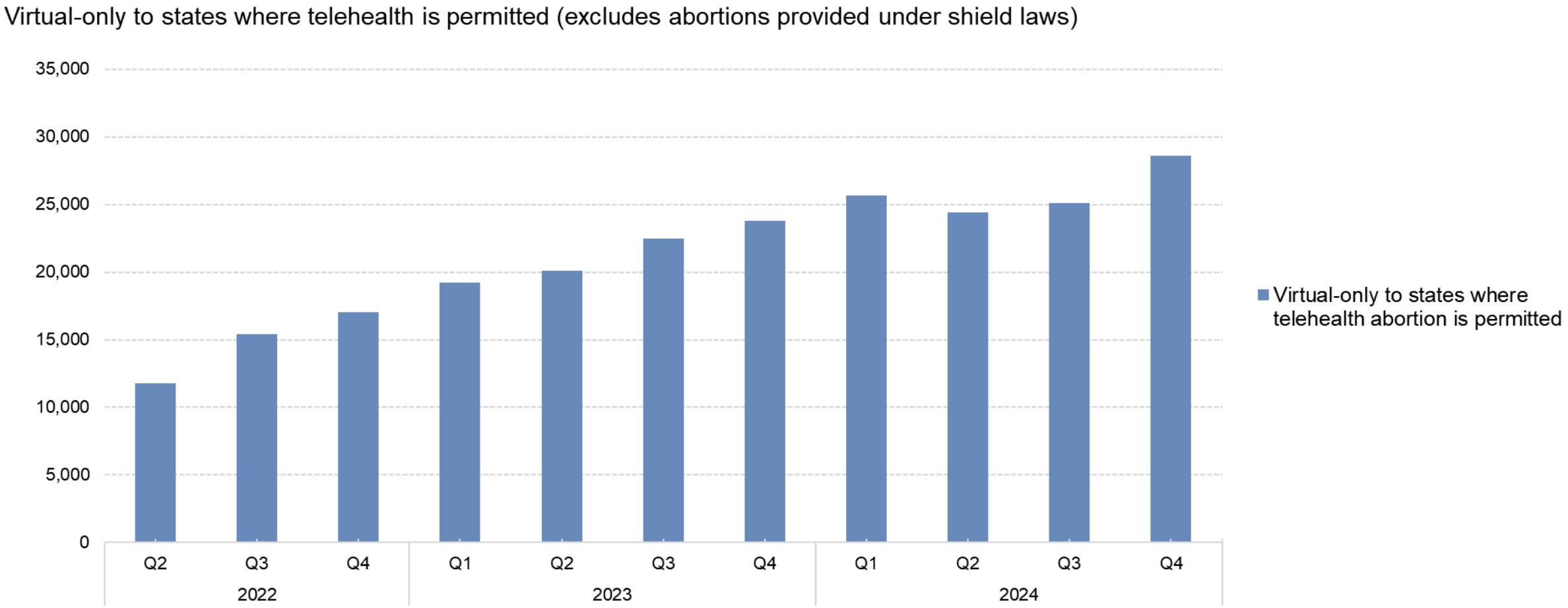
Source: Society of Family Planning, June 2025

The proportion of abortions provided via telehealth varied by state, 2024



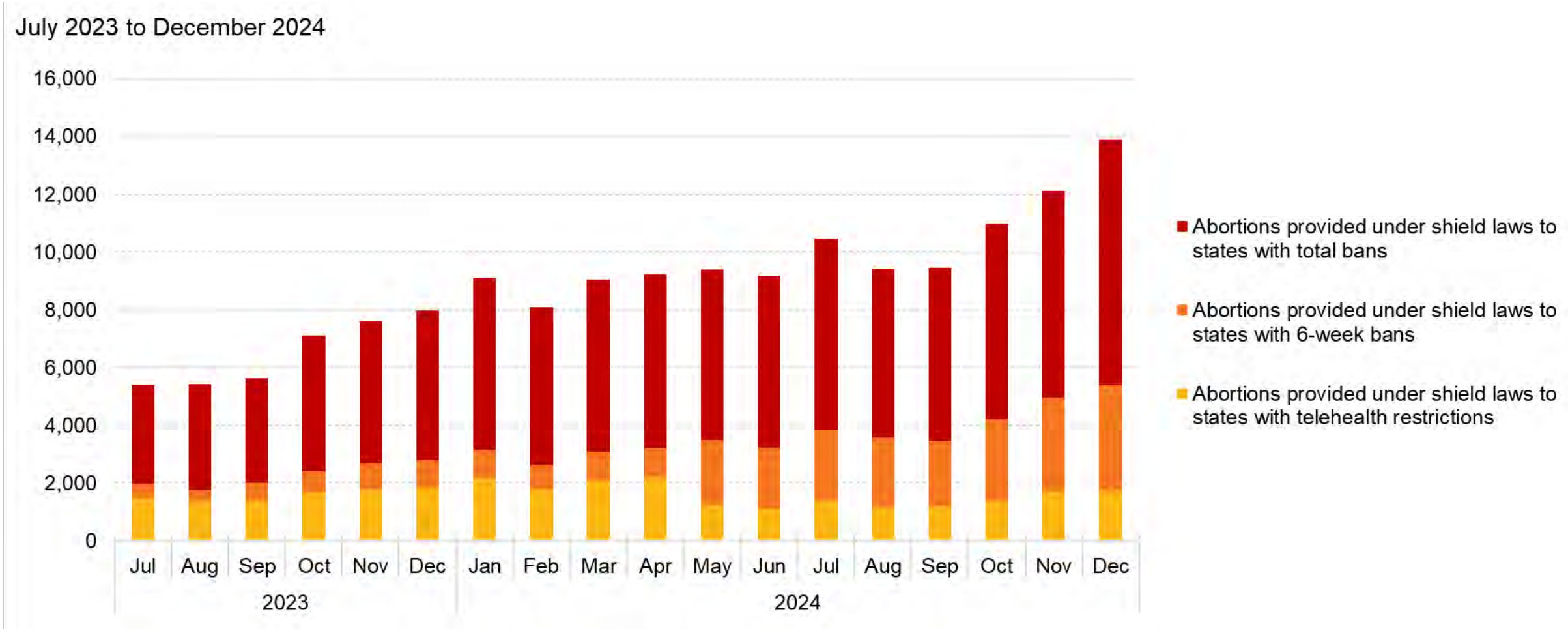
Source: Society of Family Planning, June 2025

Abortions provided by virtual-only clinics have increased since *Dobbs*



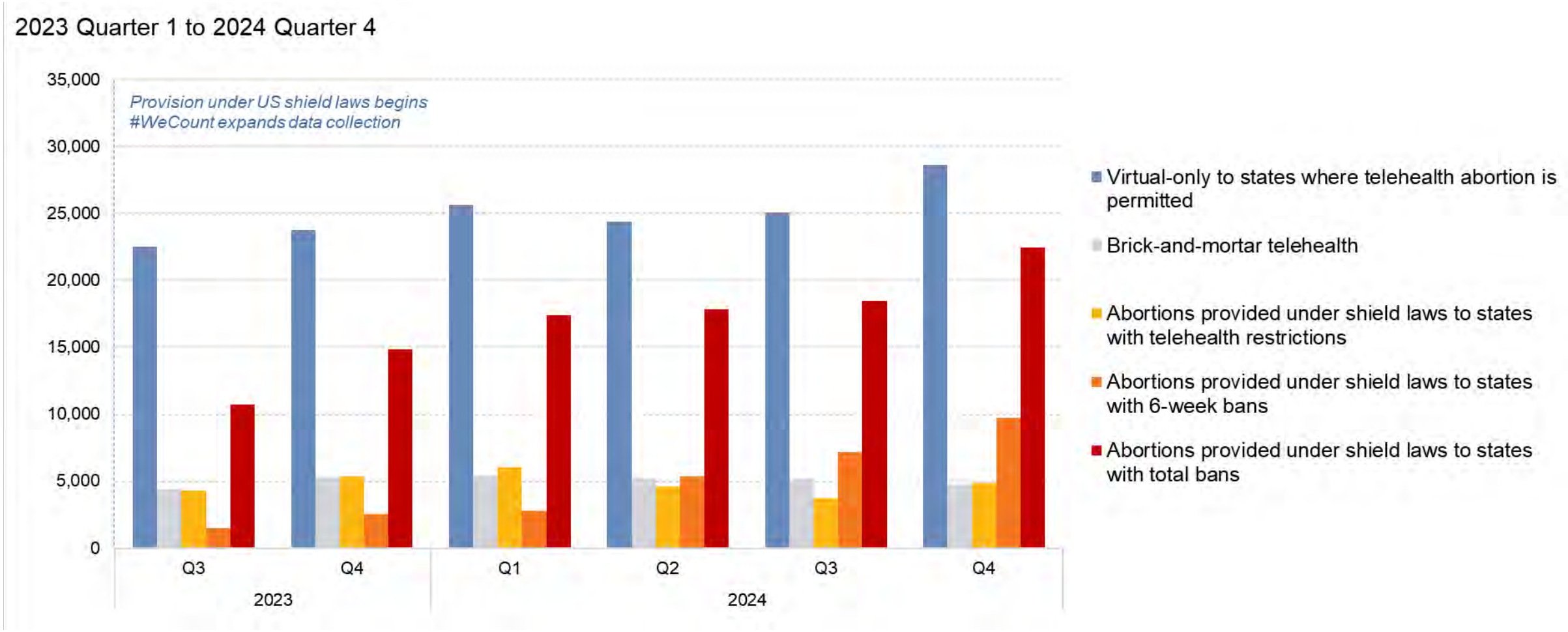
Source: Society of Family Planning, June 2025

Abortions provided under shield laws have increased since this route to care became available



Source: Society of Family Planning, June 2025

Legal climates appear to play an important role in telehealth use



Source: Society of Family Planning, June 2025

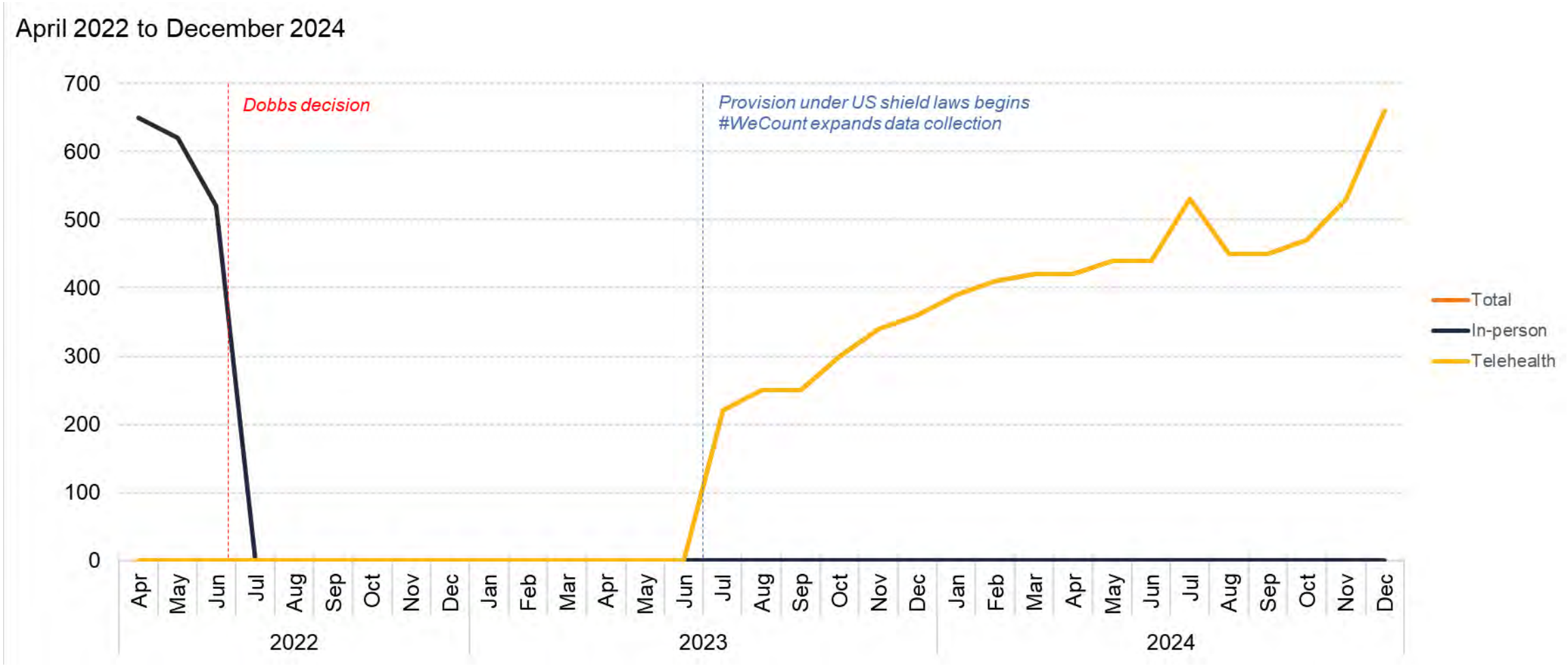
Half of abortions provided via telehealth in 2024 were facilitated by shield laws

2024 monthly average number of abortions		
	In-person	Telehealth
Abortion and telehealth permitted	60,780	10,360
Abortion permitted, telehealth restricted	8,610	1,610
6-week abortion ban, telehealth restricted	5,350	2,080
Abortion is totally banned	30	6,350

Source: Society of Family Planning, June 2025

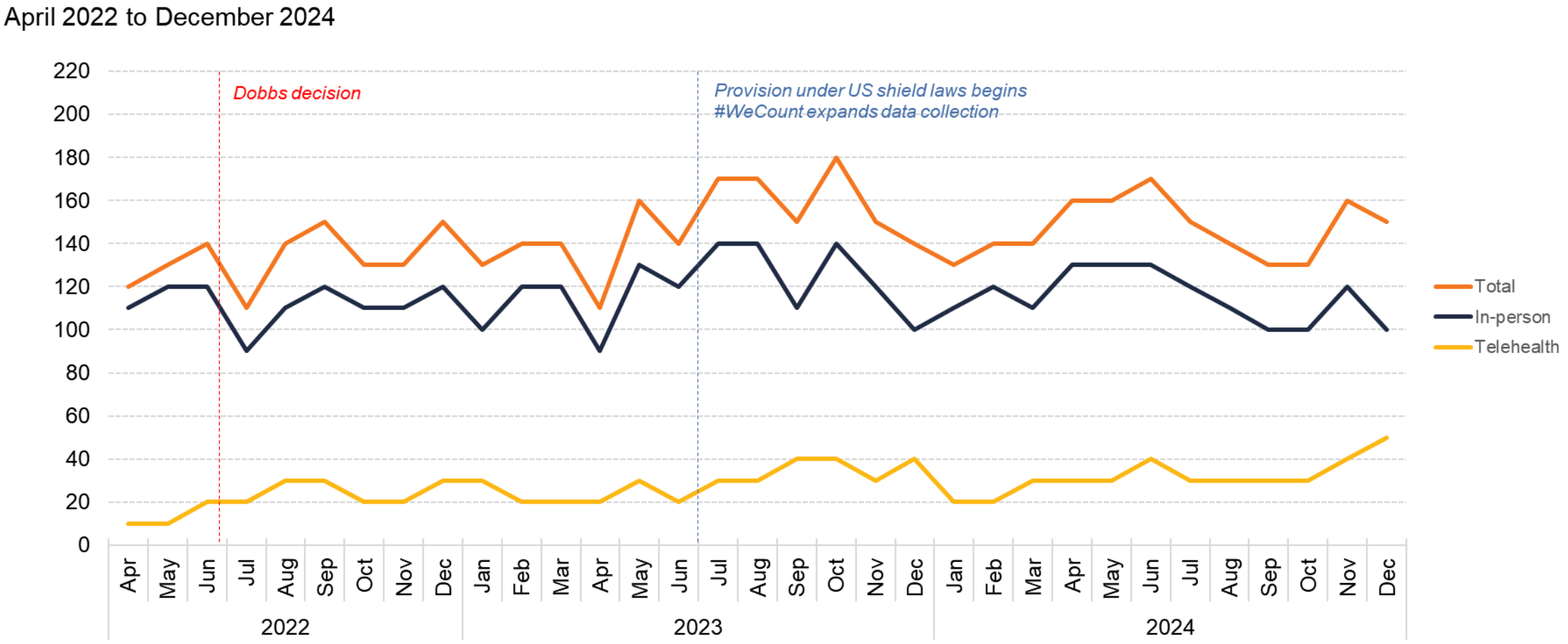
State-level findings

Alabama



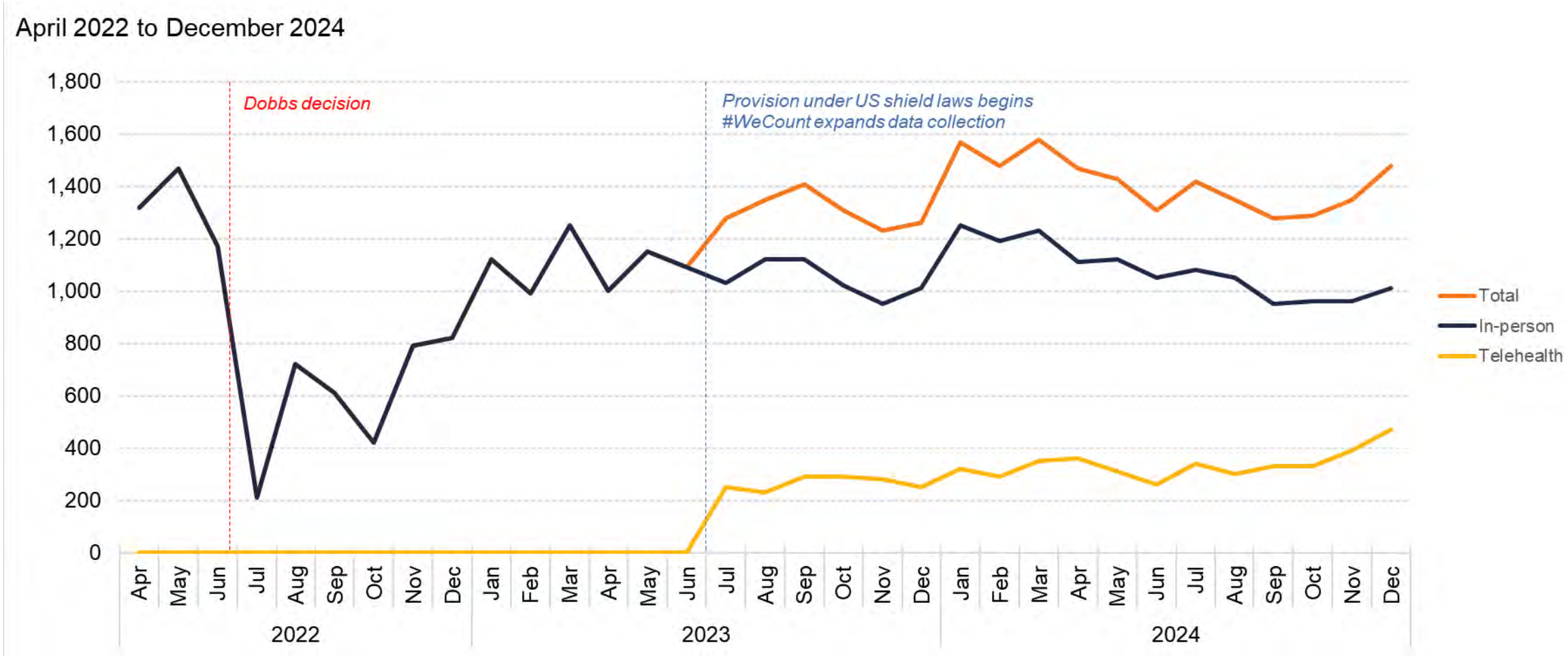
Source: Society of Family Planning, June 2025

Alaska



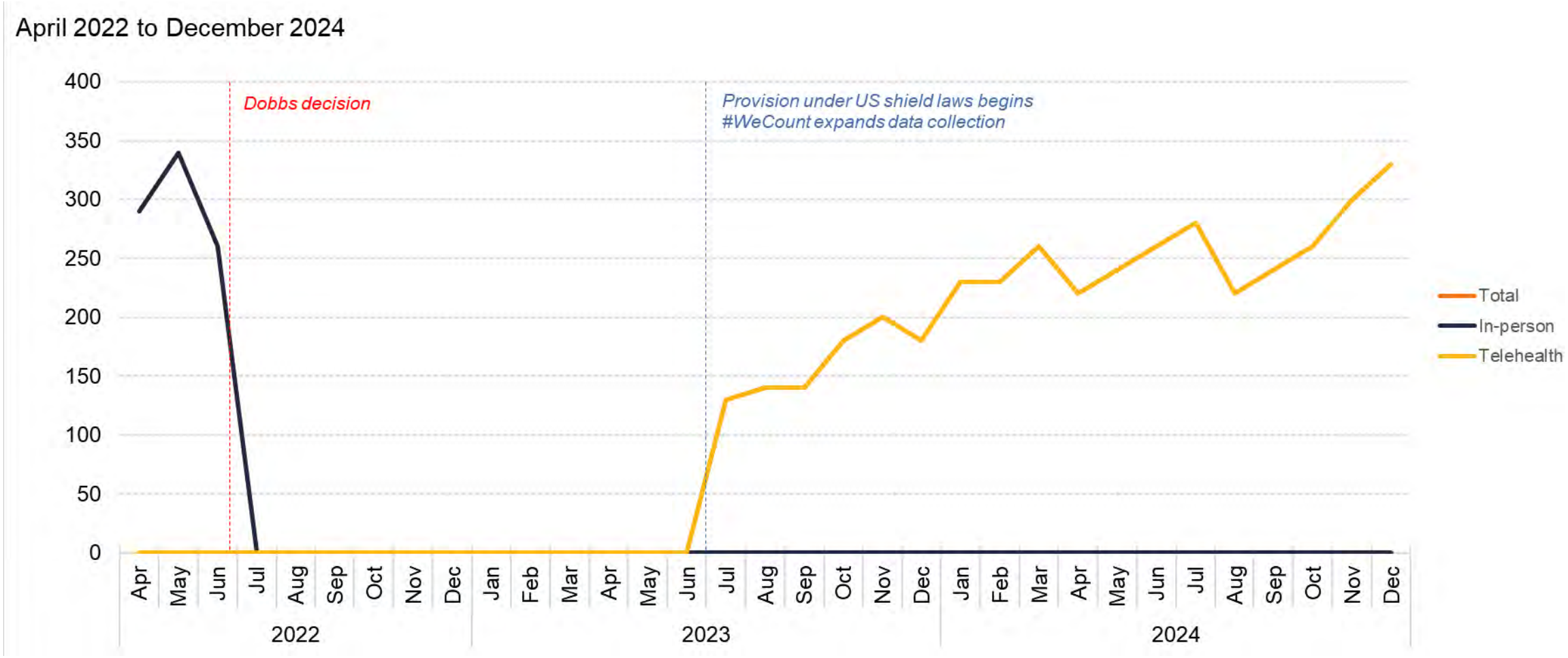
Source: Society of Family Planning, June 2025

Arizona



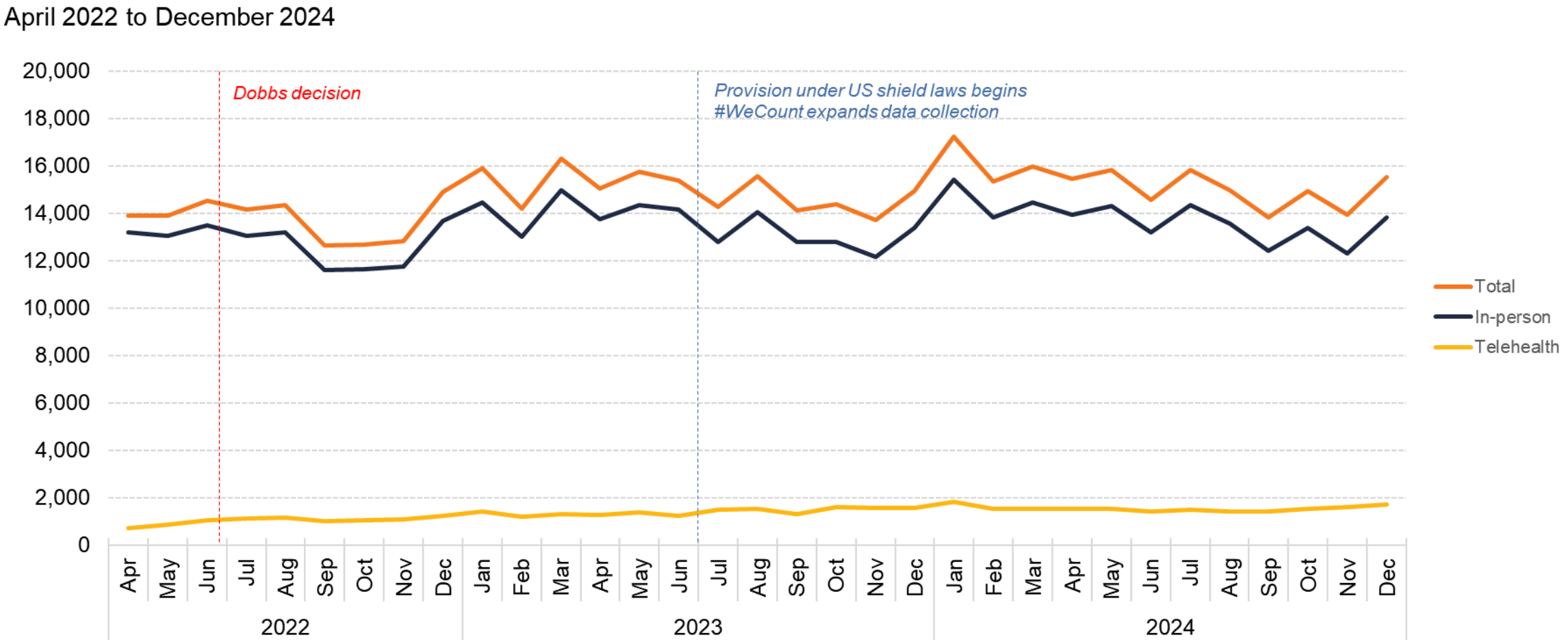
Source: Society of Family Planning, June 2025

Arkansas



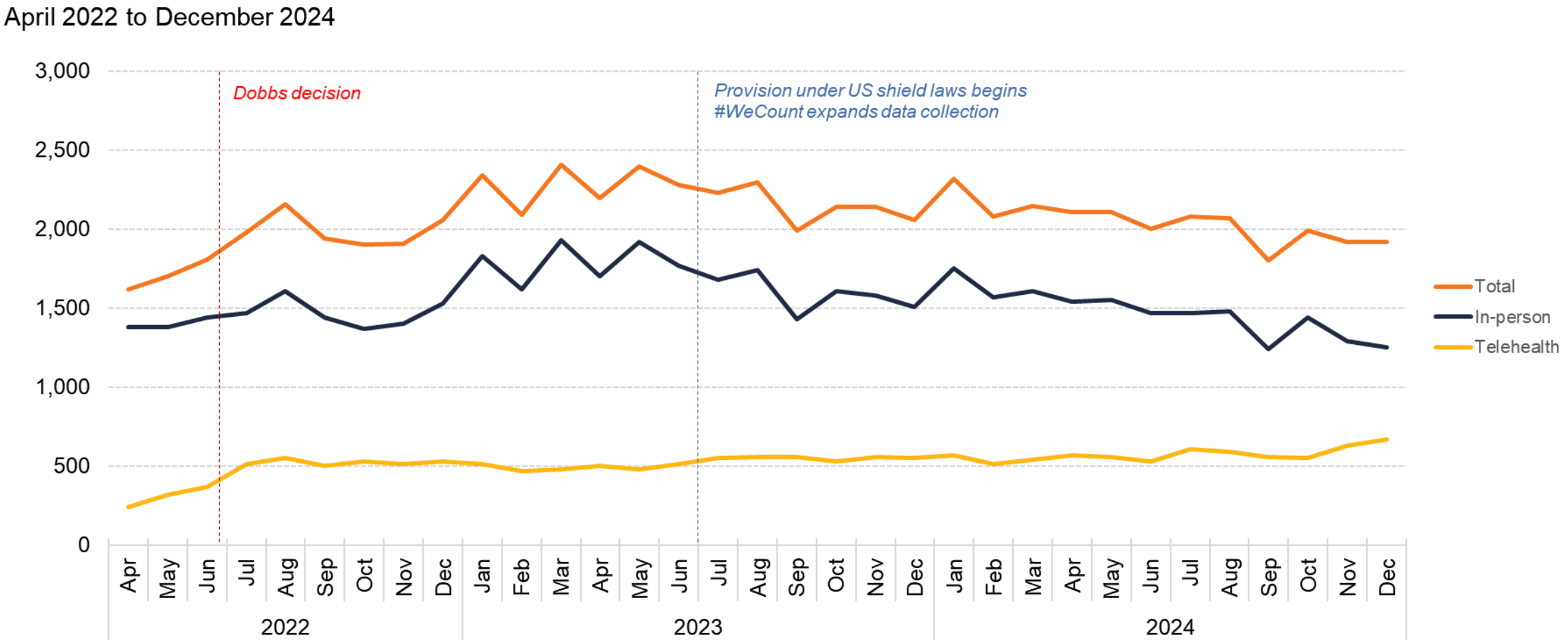
Source: Society of Family Planning, June 2025

California



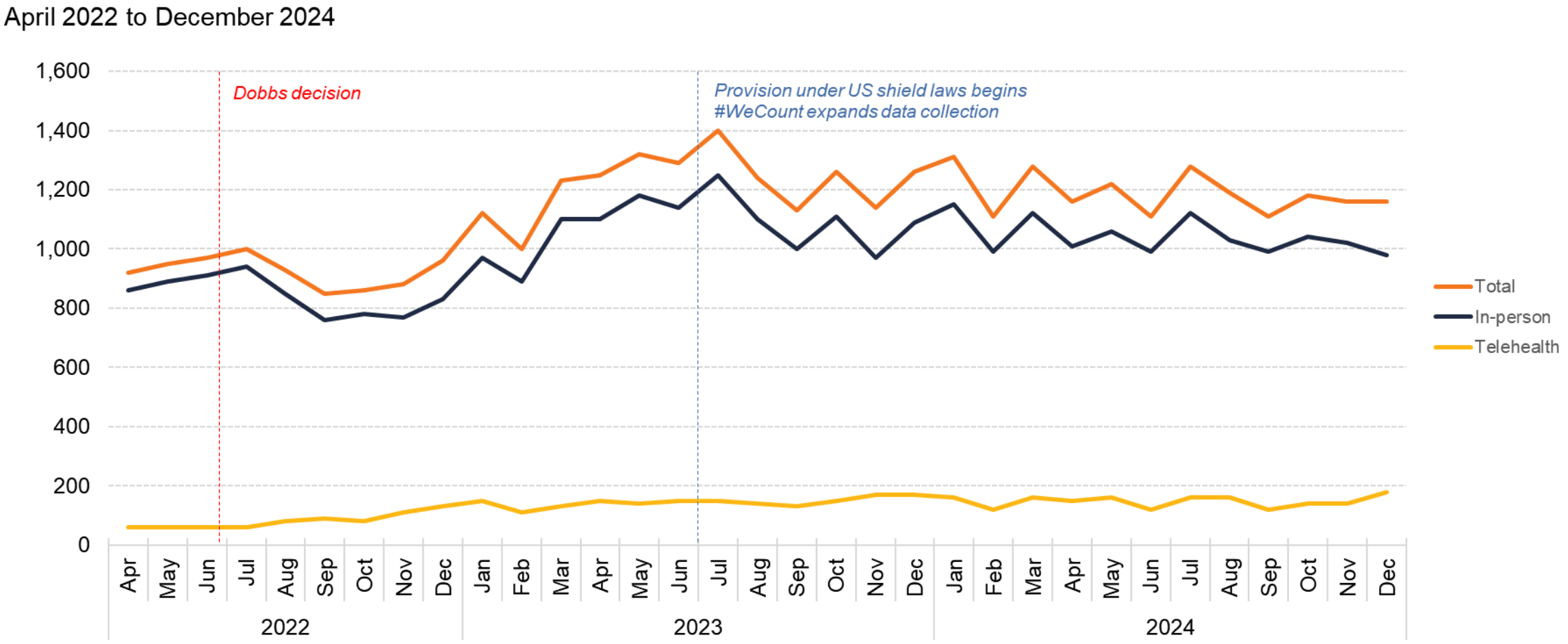
Source: Society of Family Planning, June 2025

Colorado



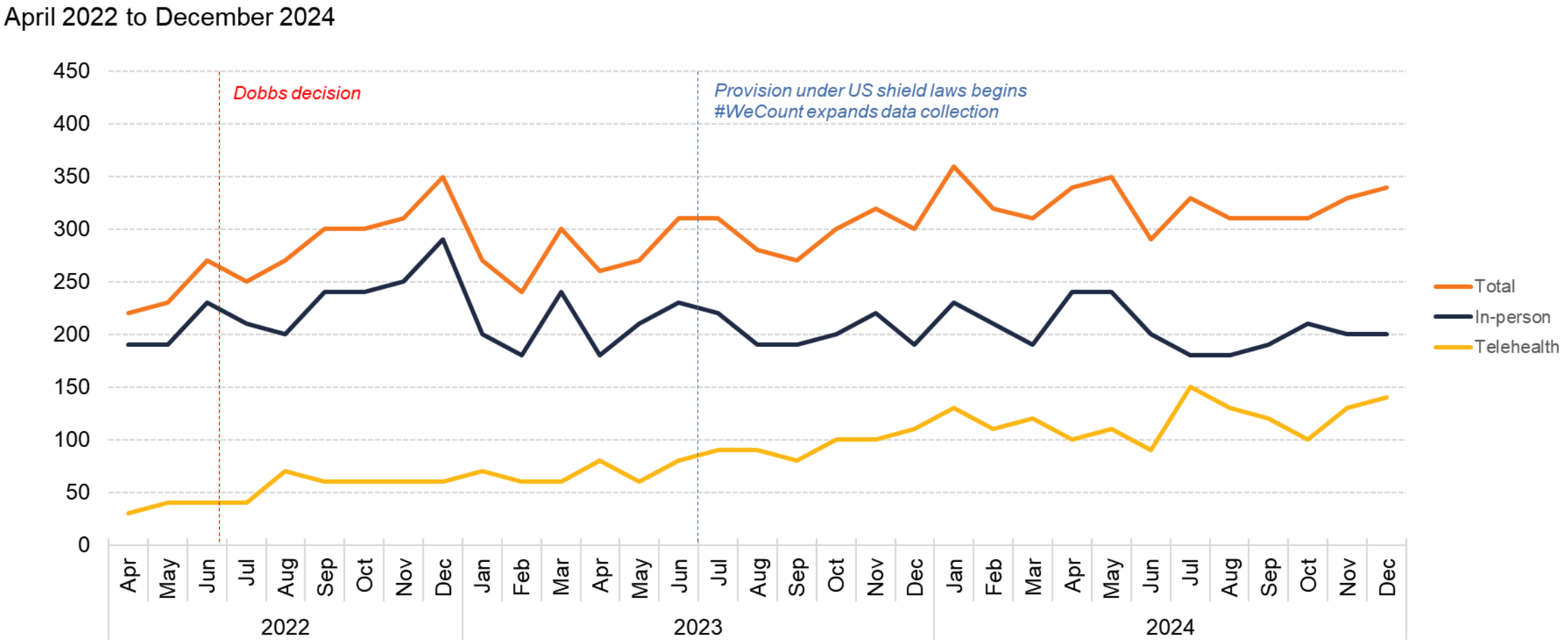
Source: Society of Family Planning, June 2025

Connecticut



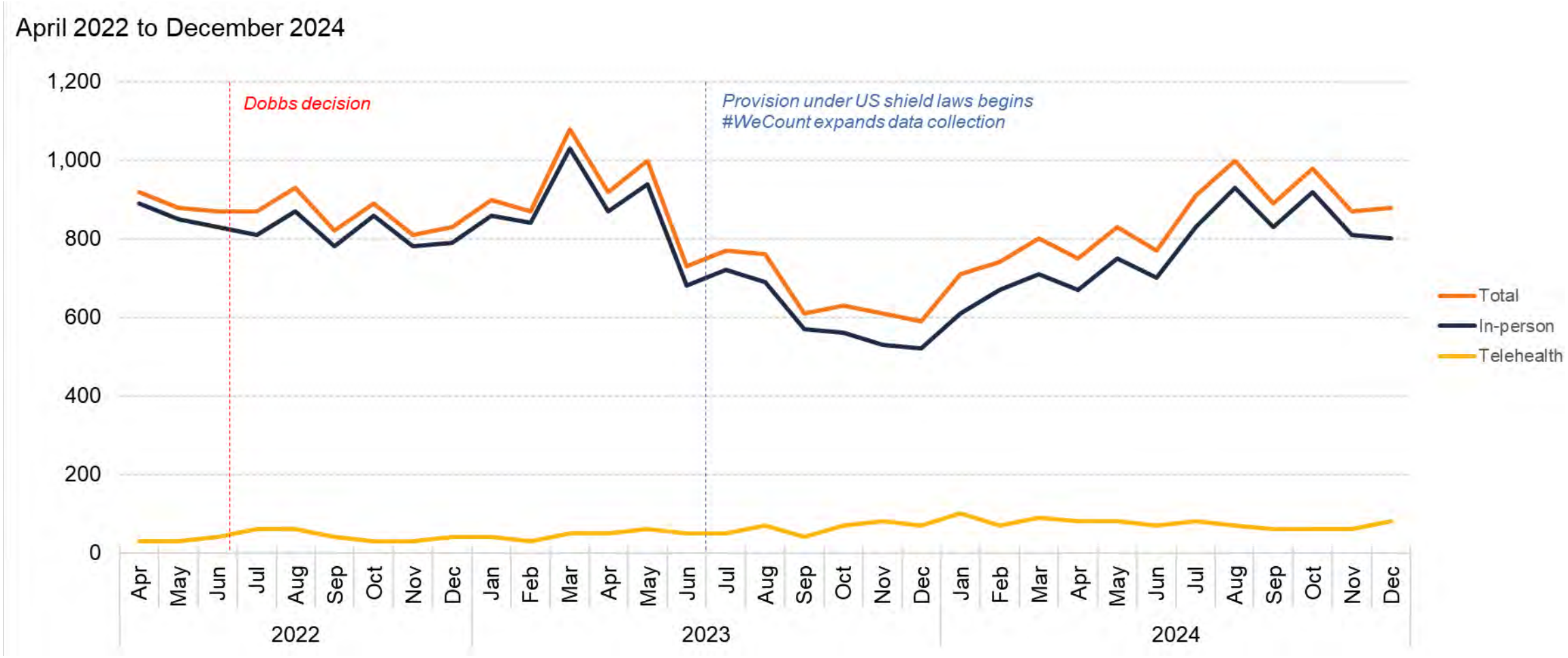
Source: Society of Family Planning, June 2025

Delaware



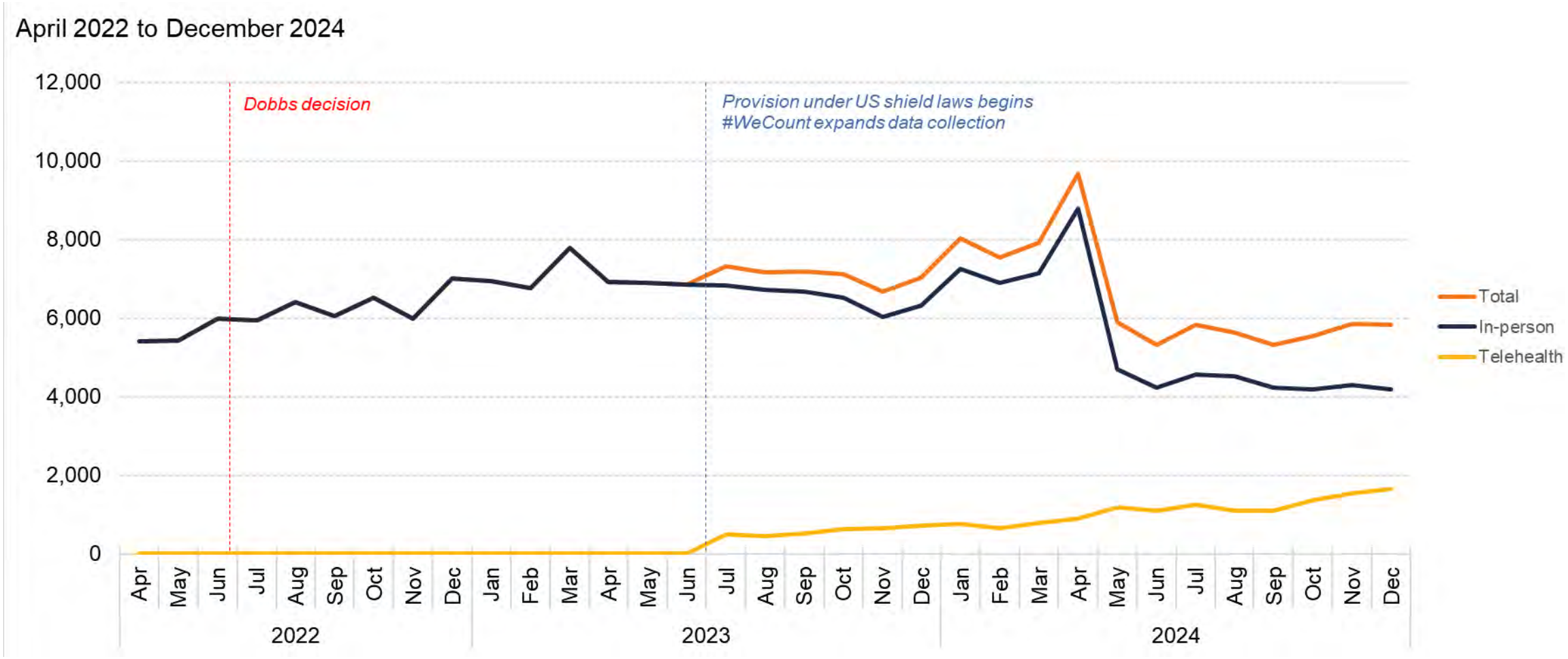
Source: Society of Family Planning, June 2025

District of Columbia



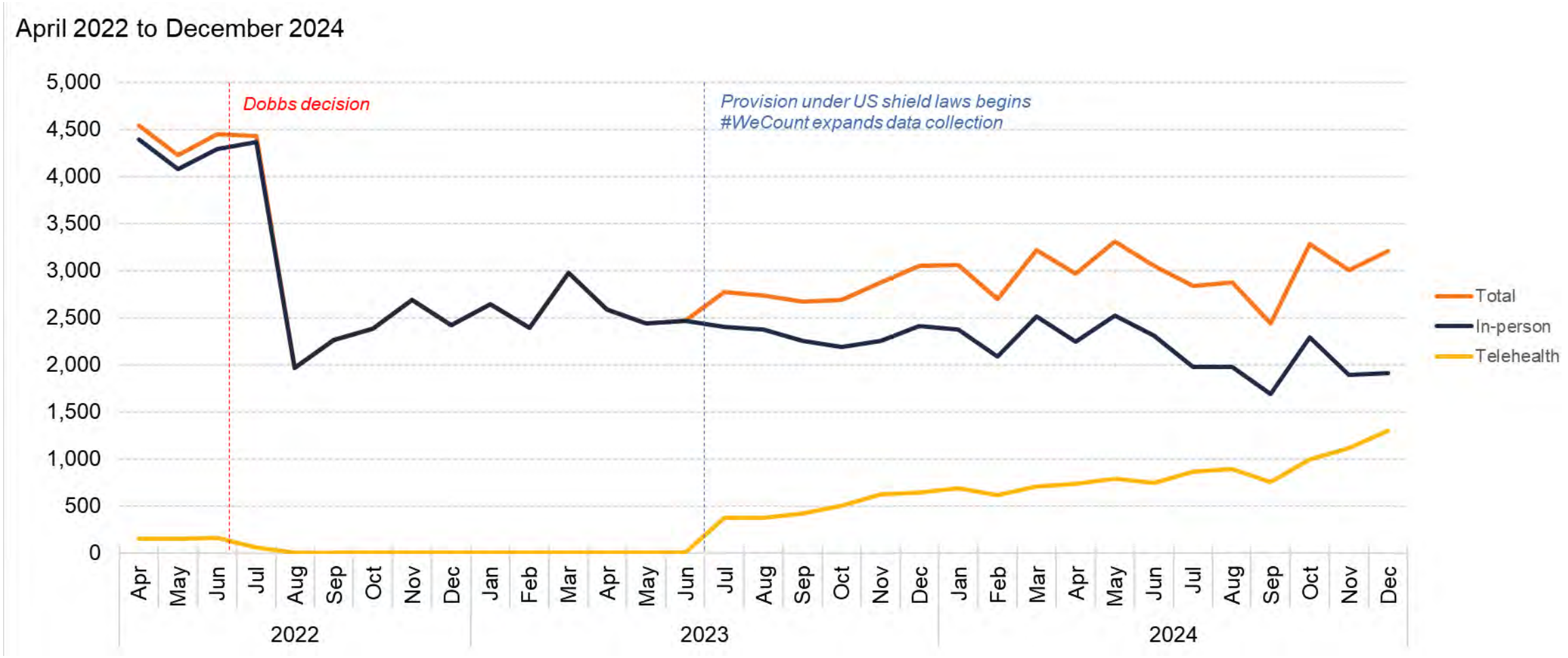
Source: Society of Family Planning, June 2025

Florida



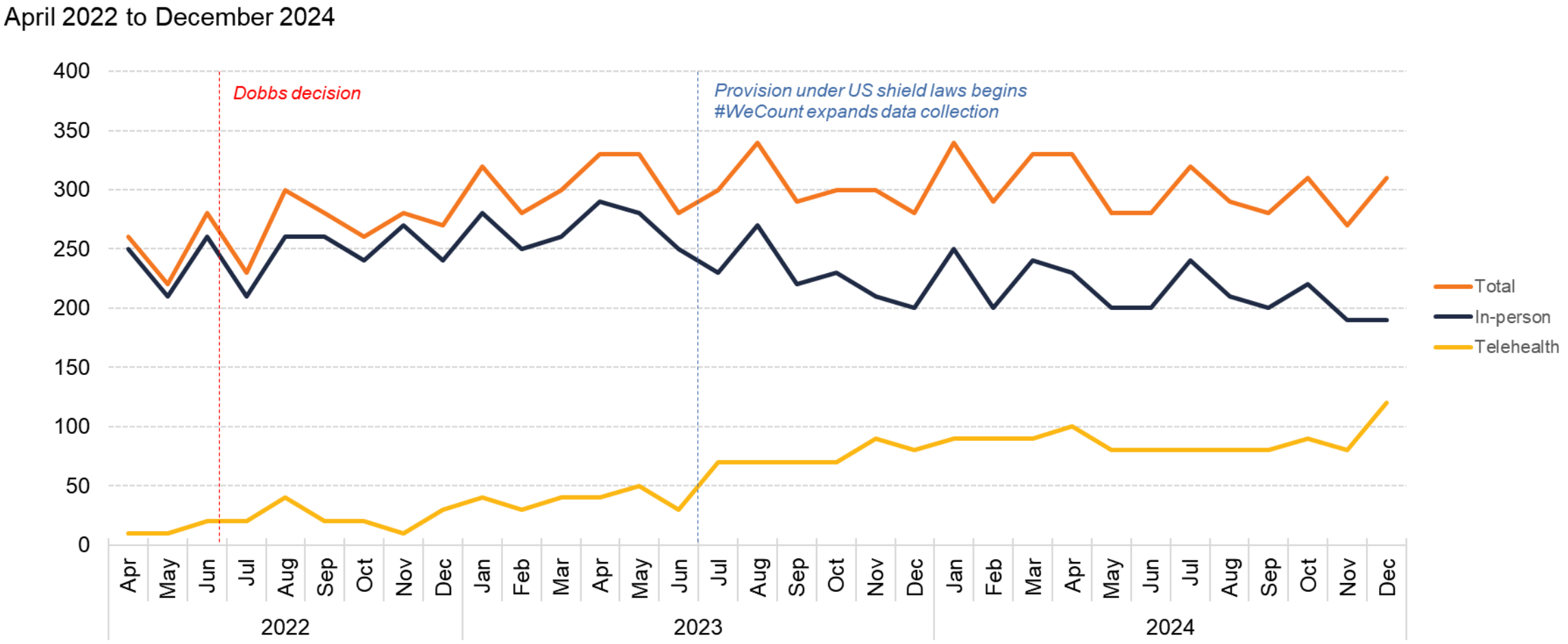
Source: Society of Family Planning, June 2025

Georgia



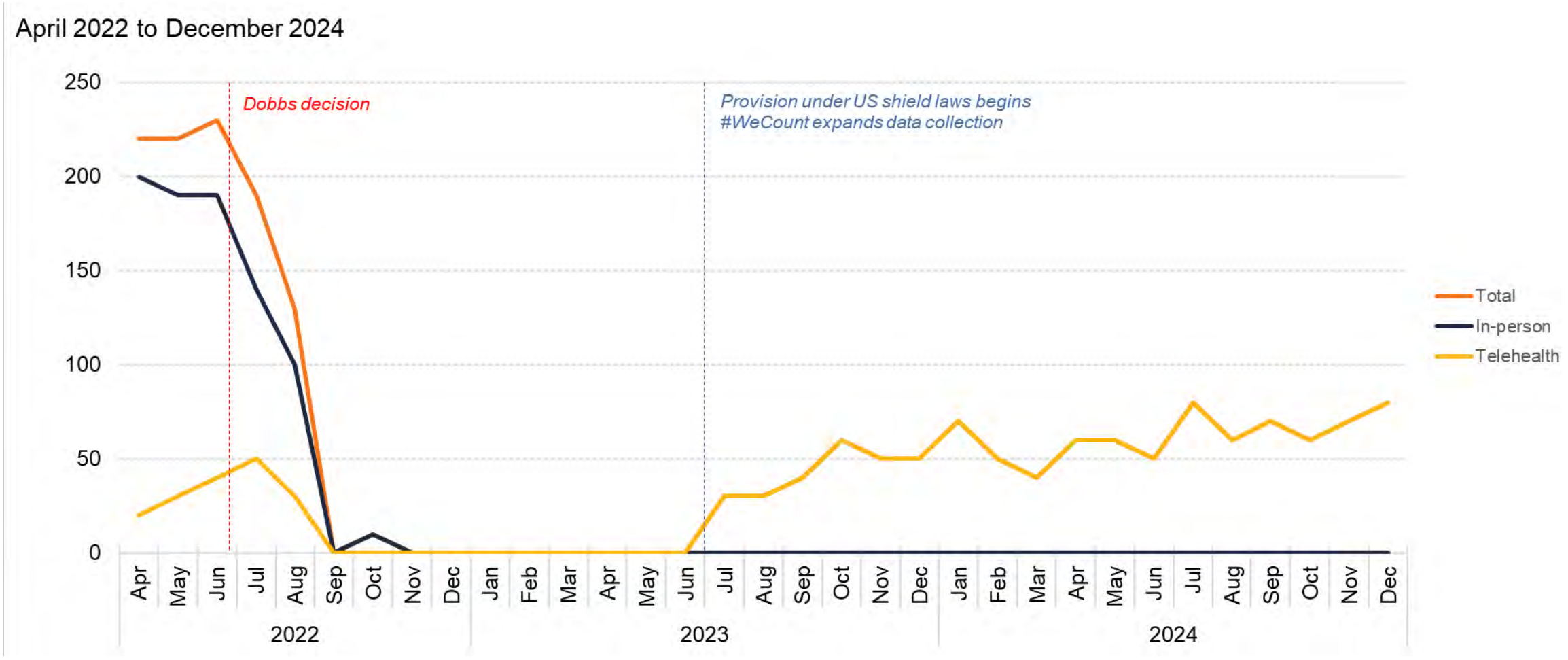
Source: Society of Family Planning, June 2025

Hawaii



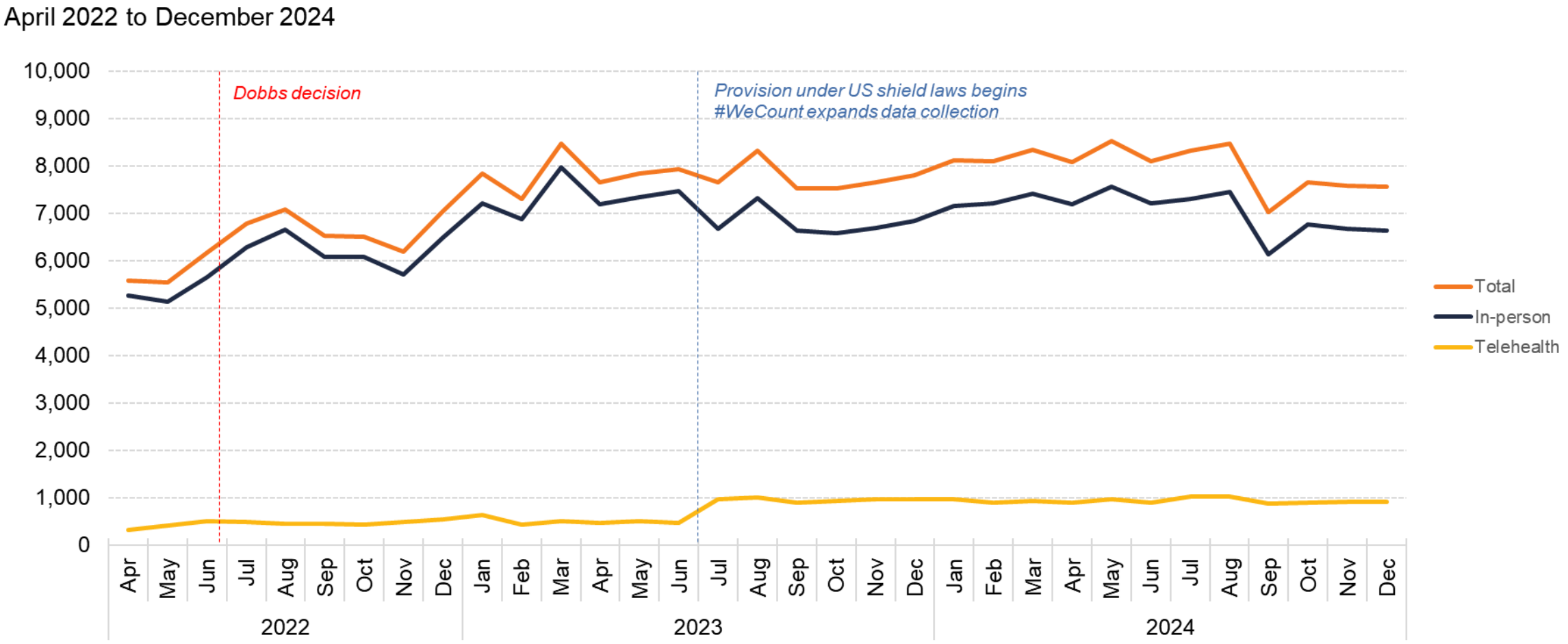
Source: Society of Family Planning, June 2025

Idaho



Source: Society of Family Planning, June 2025

Illinois



Source: Society of Family Planning, June 2025

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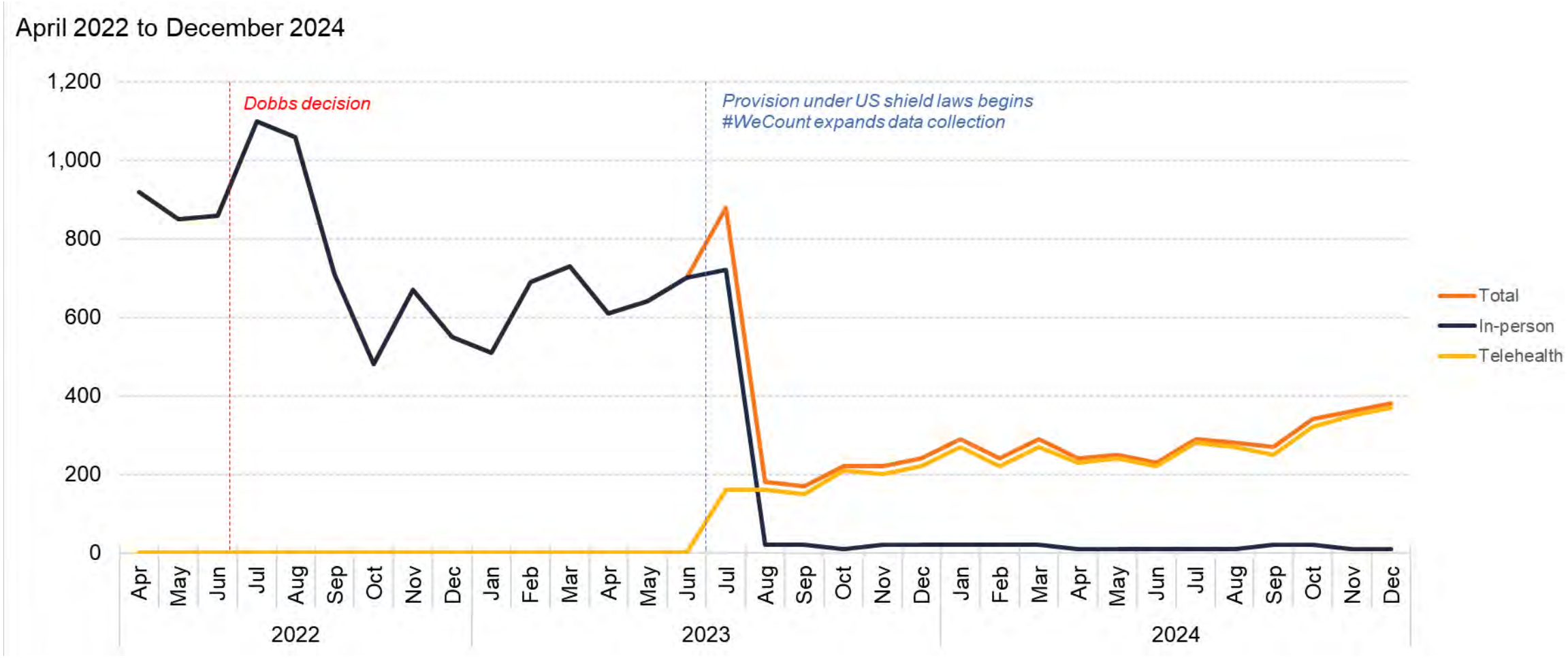

Source: Society of Family Planning, June 2025

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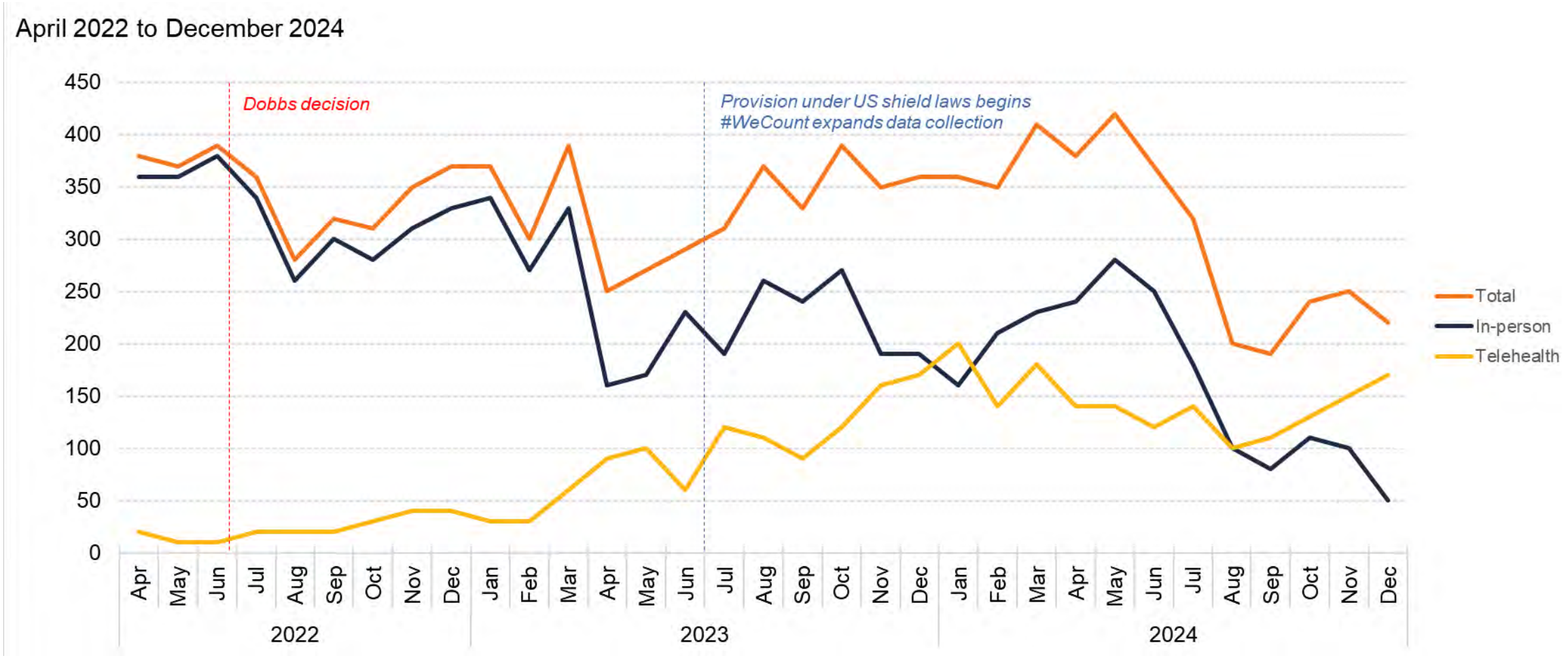
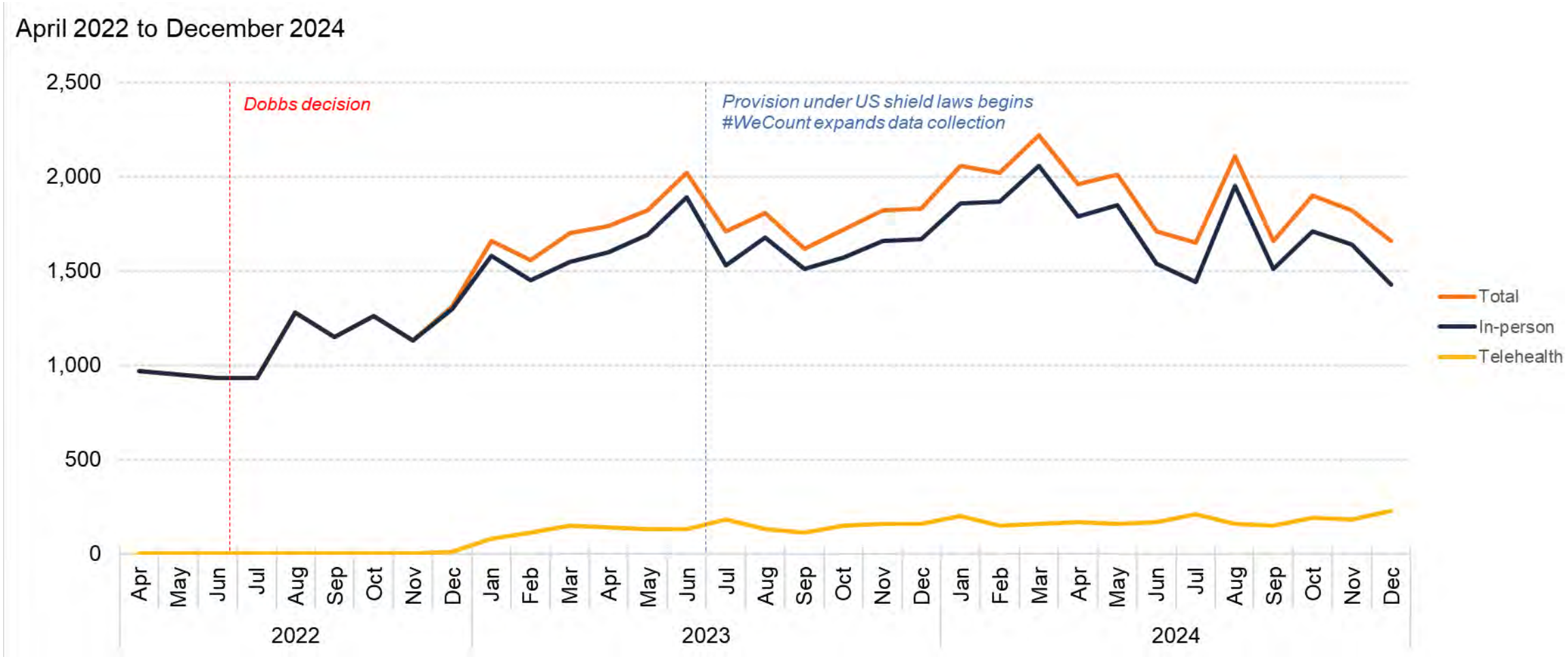


Source: Society of Family Planning, June 2025

Kansas



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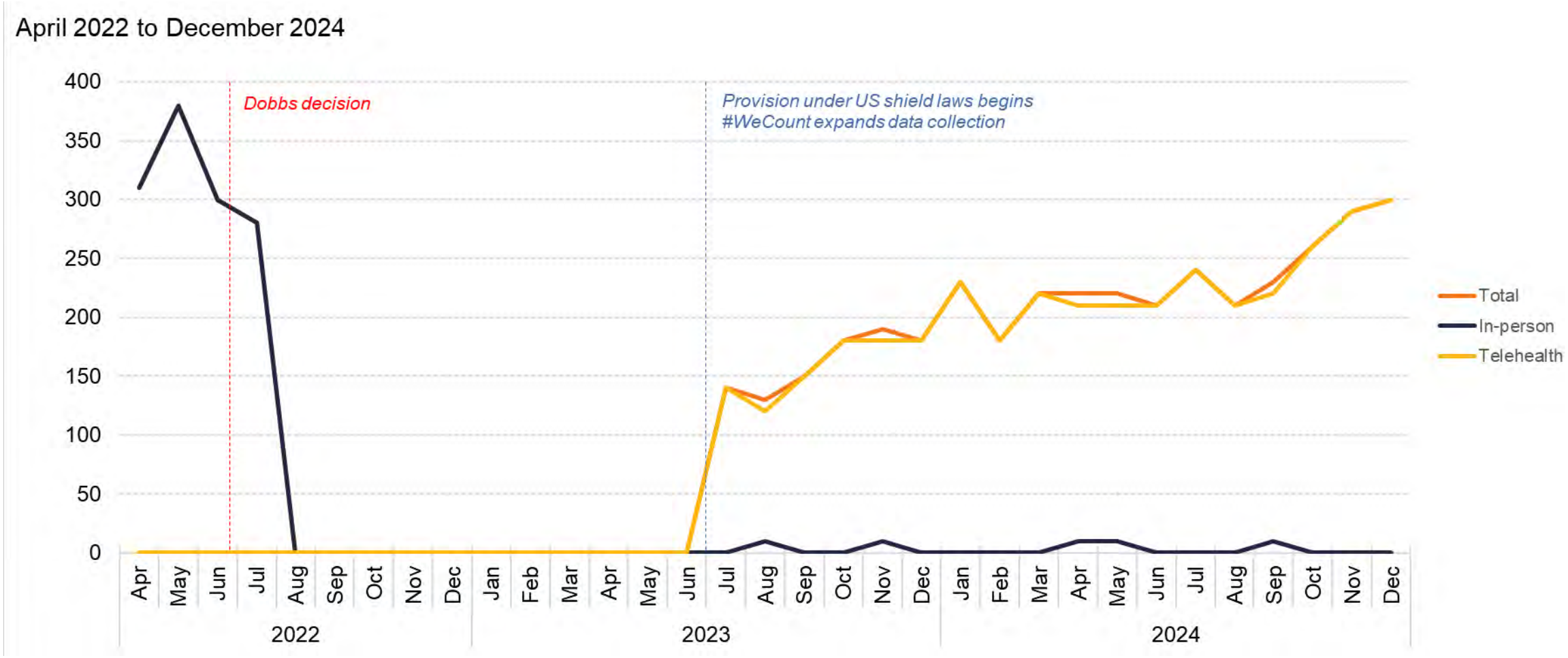

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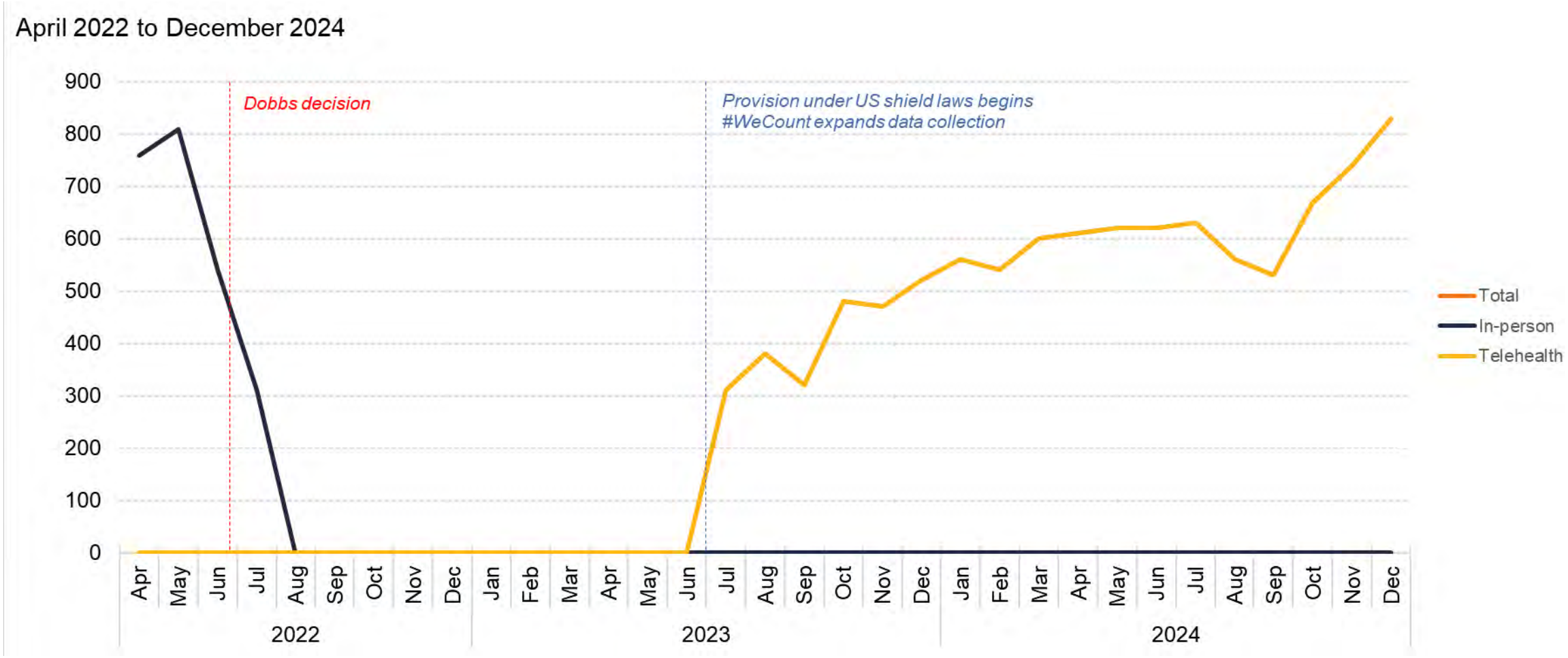

Source: Society of Family Planning, June 2025

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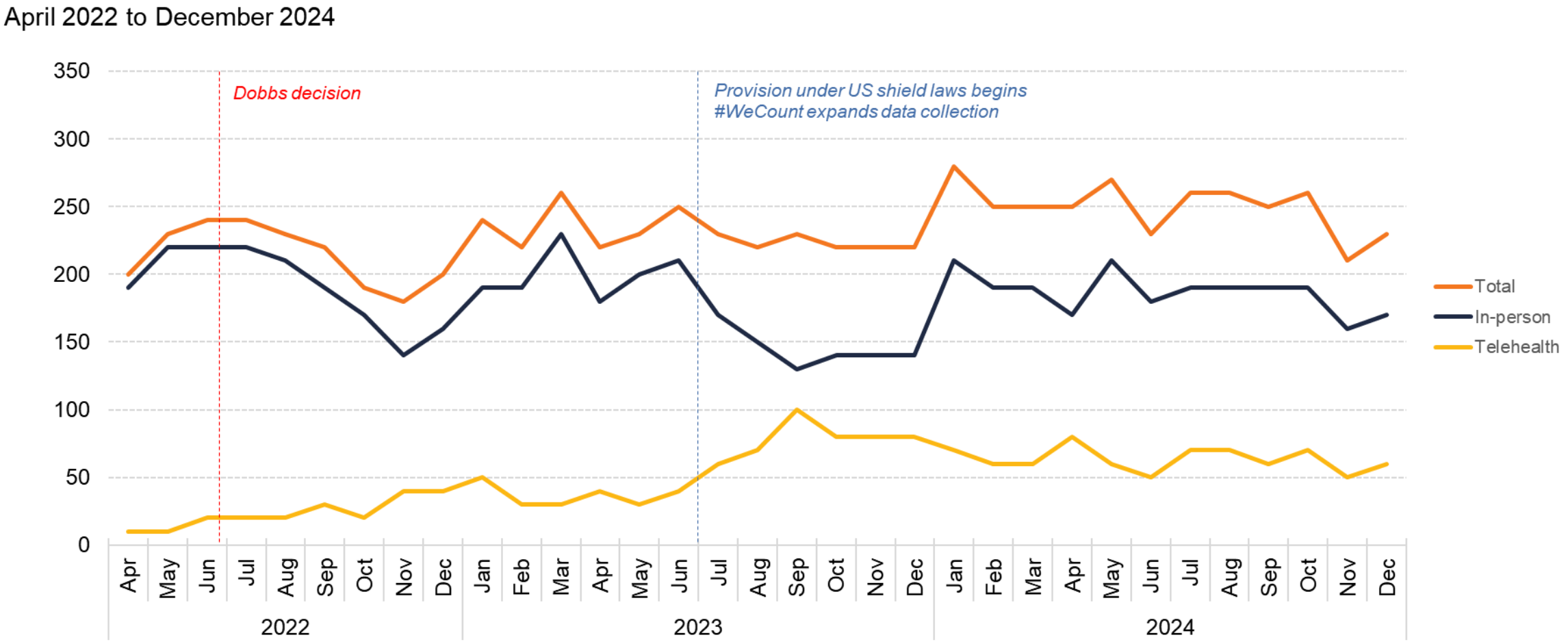
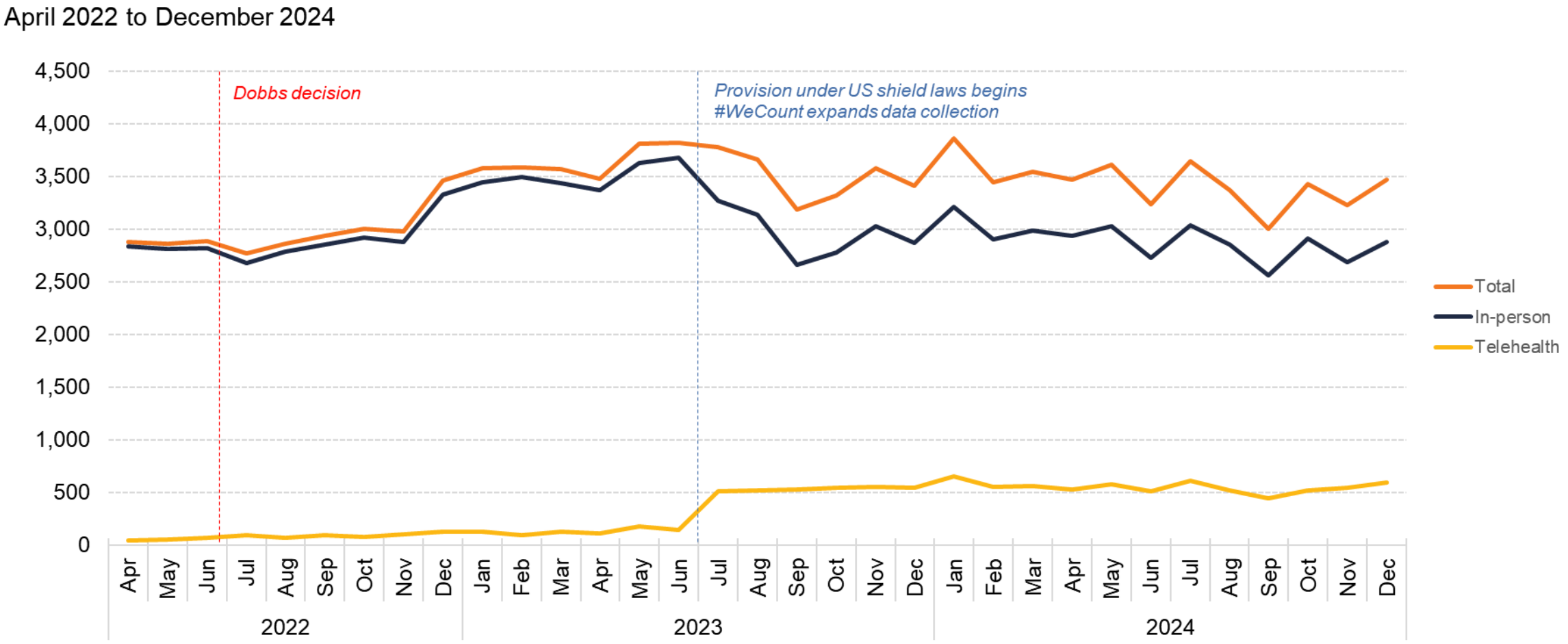


Source: Society of Family Planning, June 2025

Maryland



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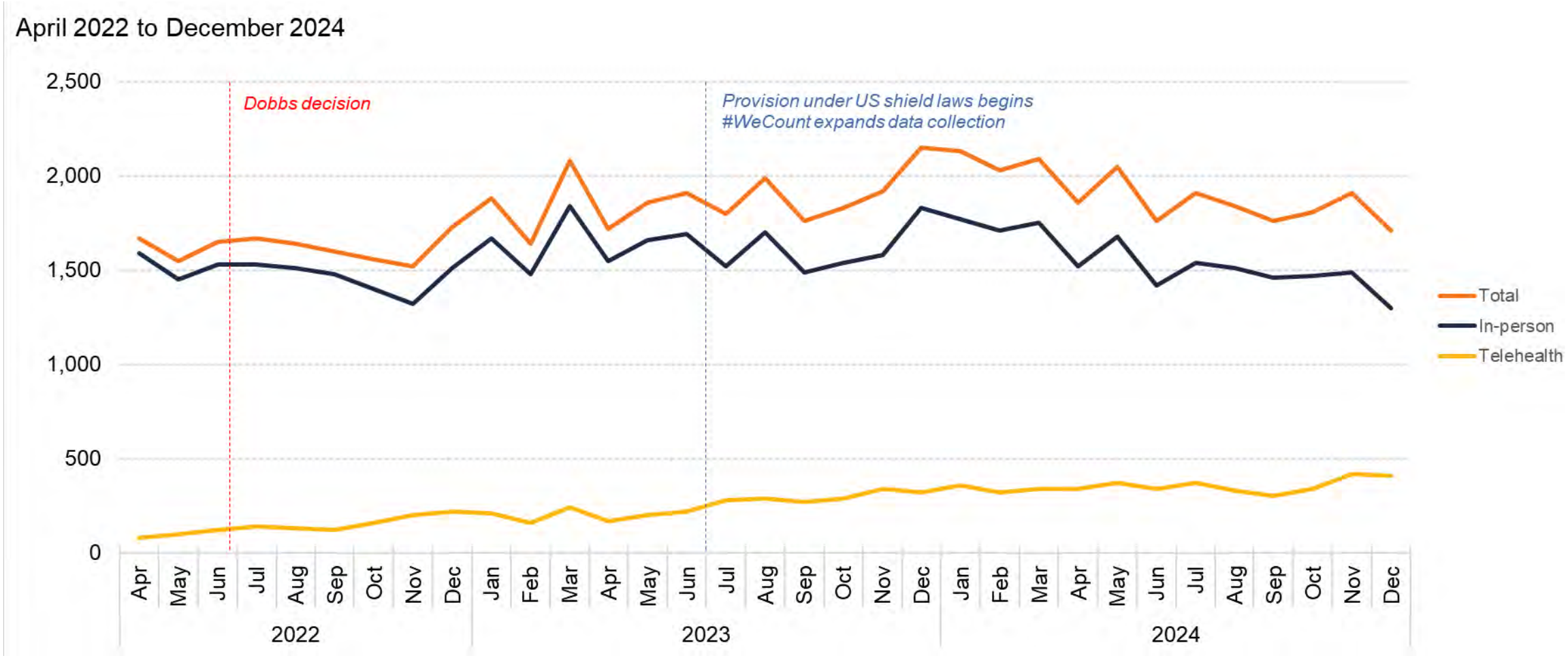
Massachusetts



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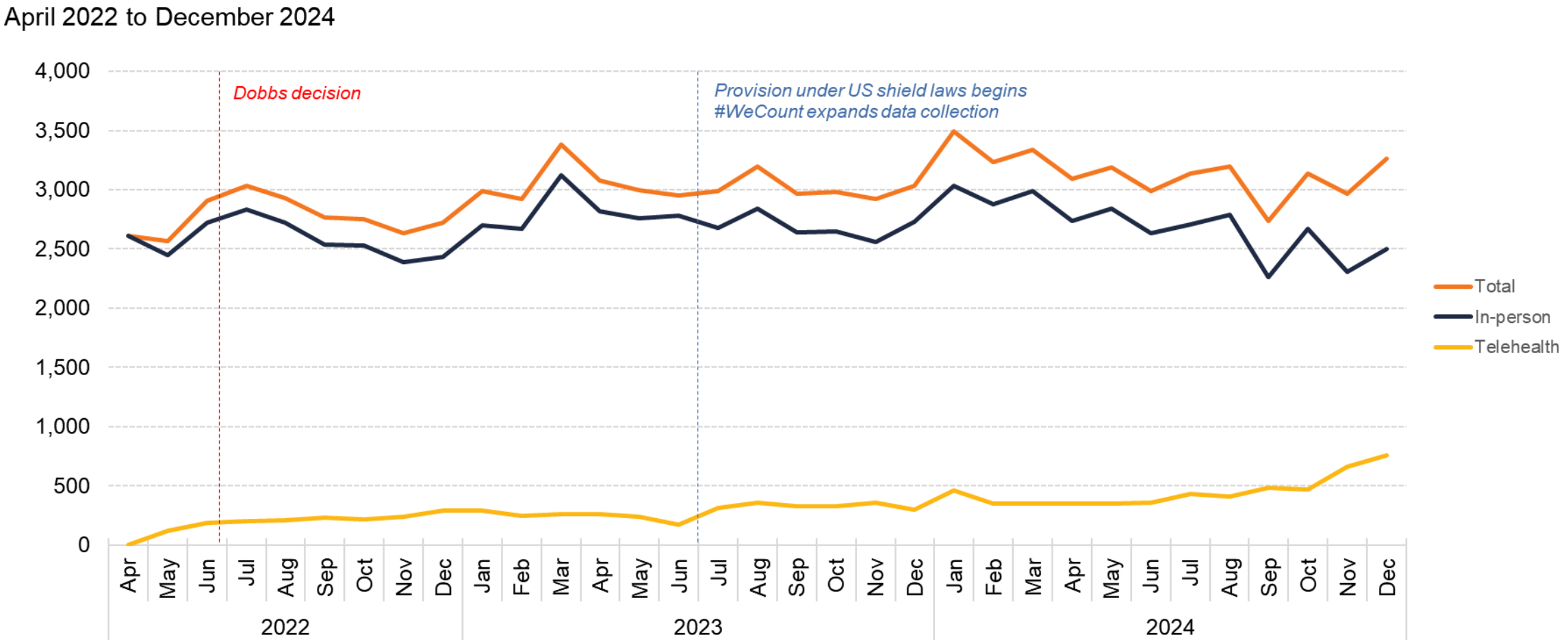

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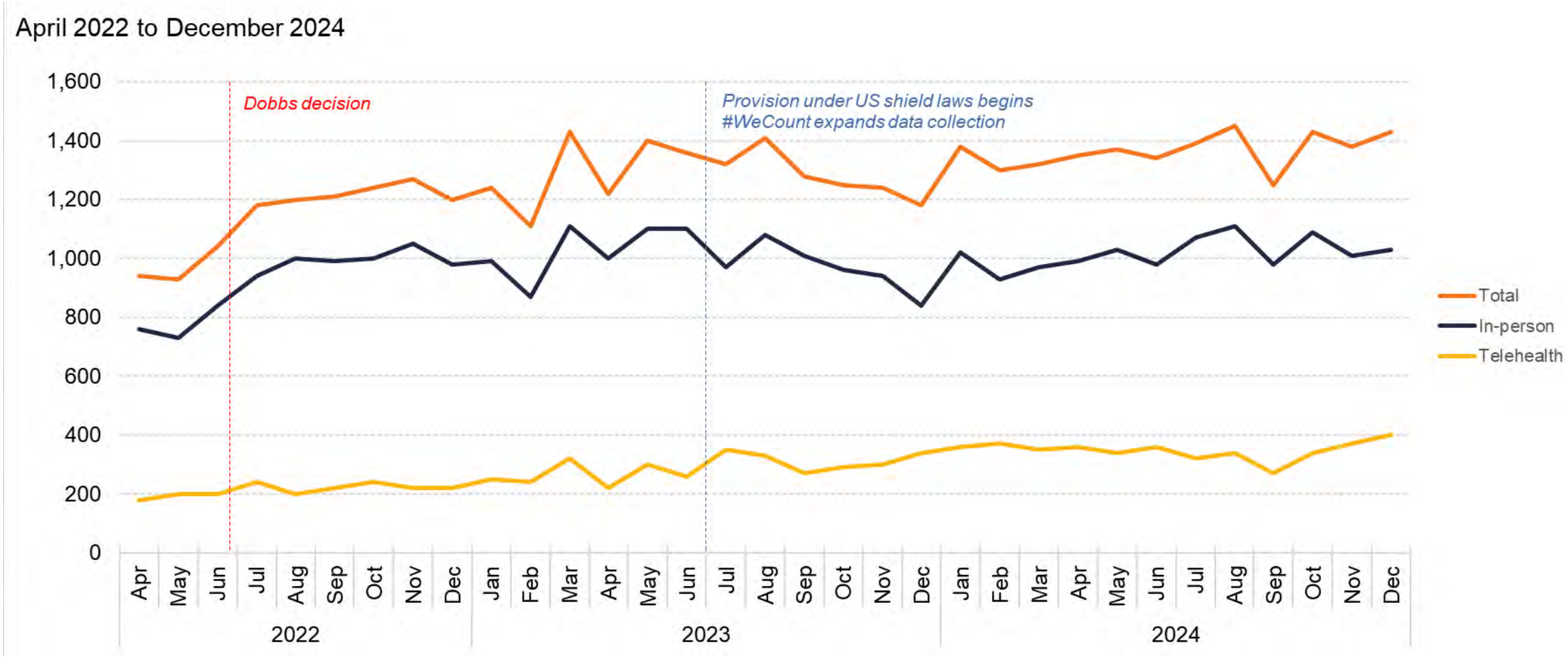

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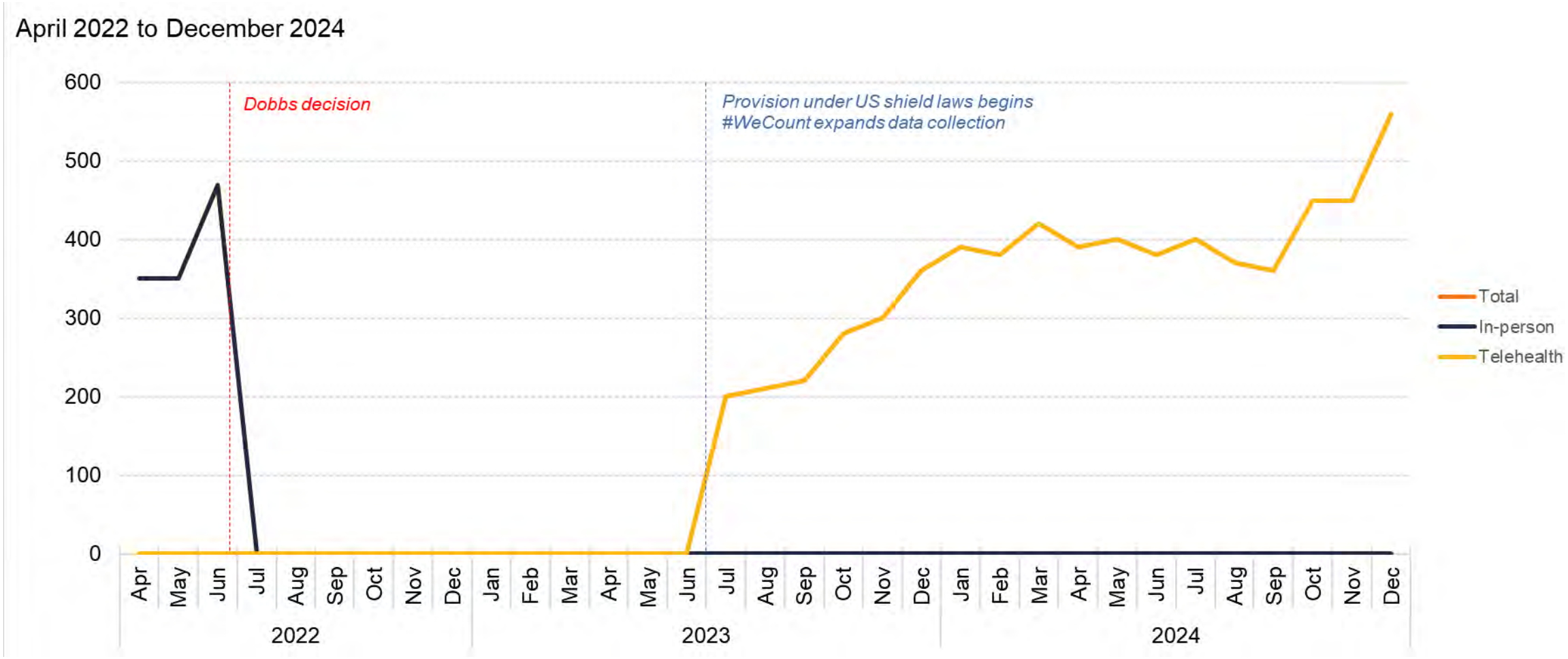

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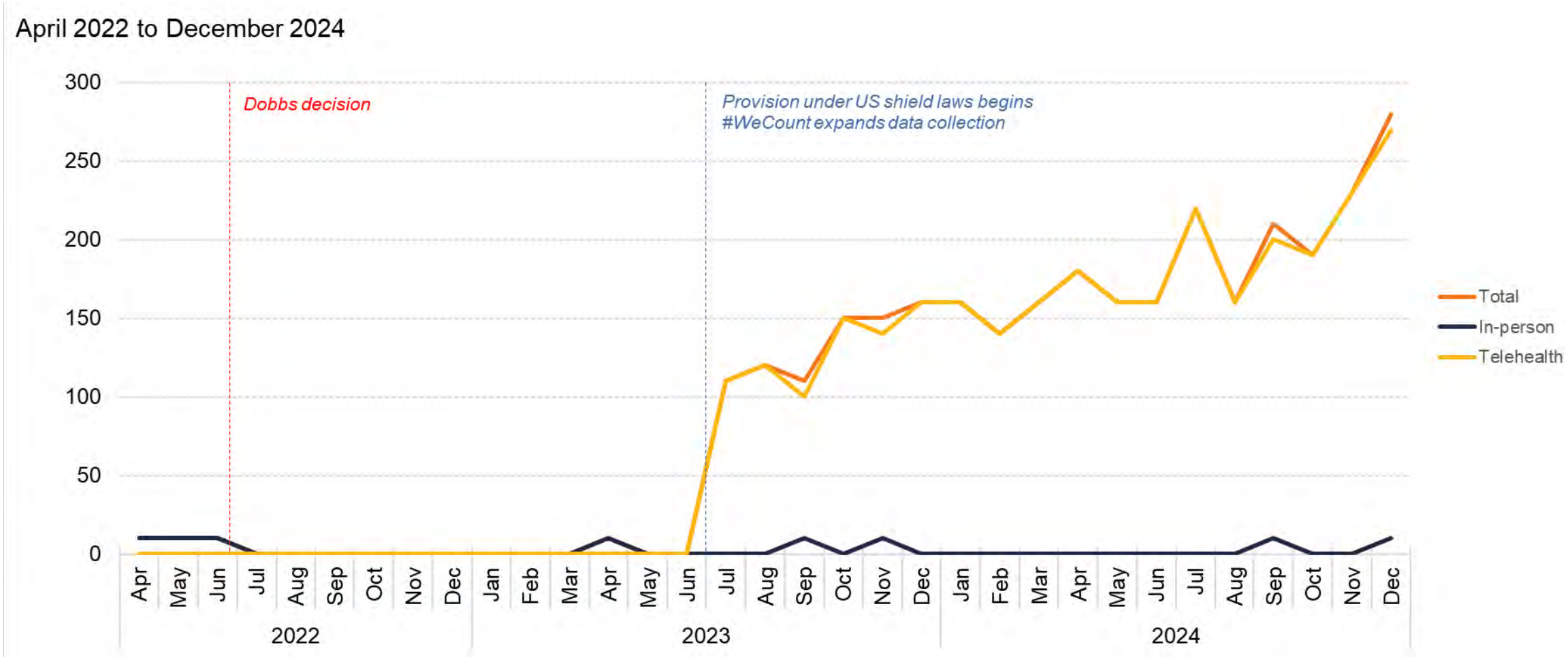

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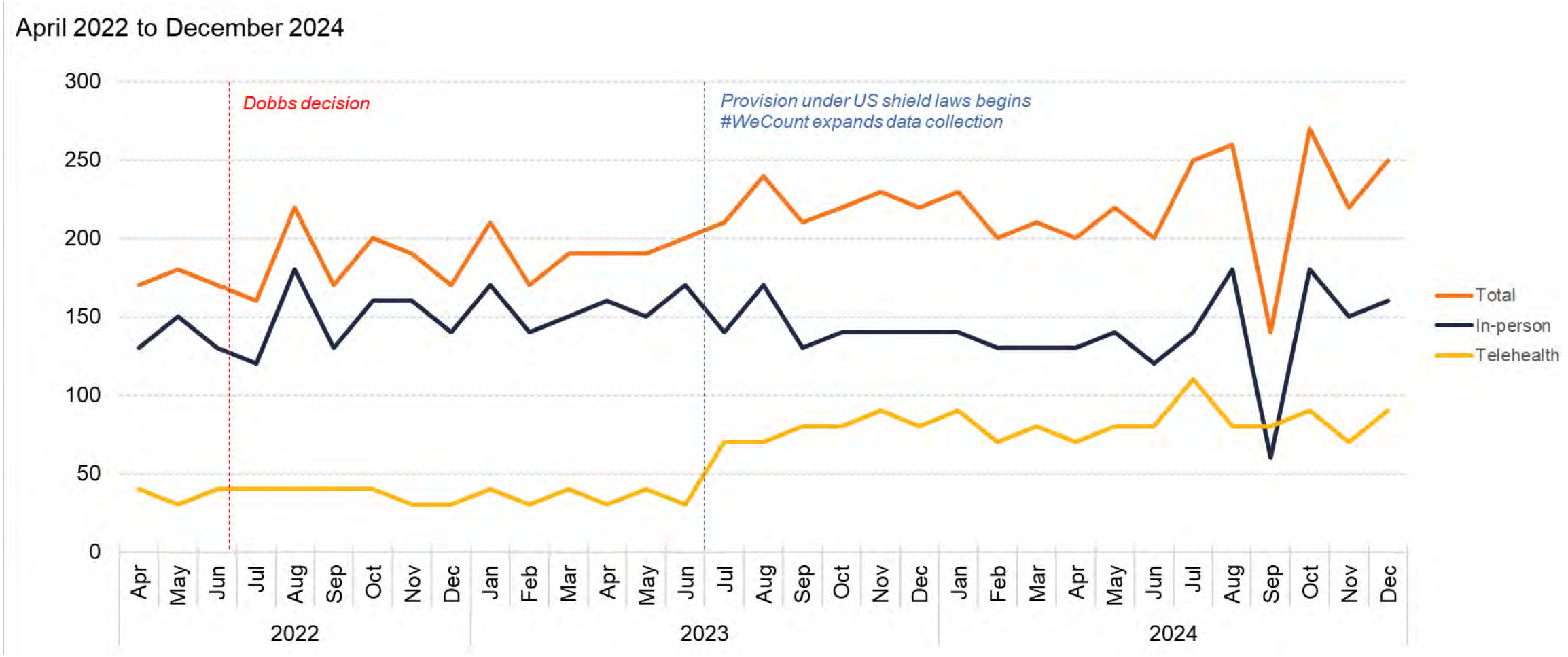
Montana



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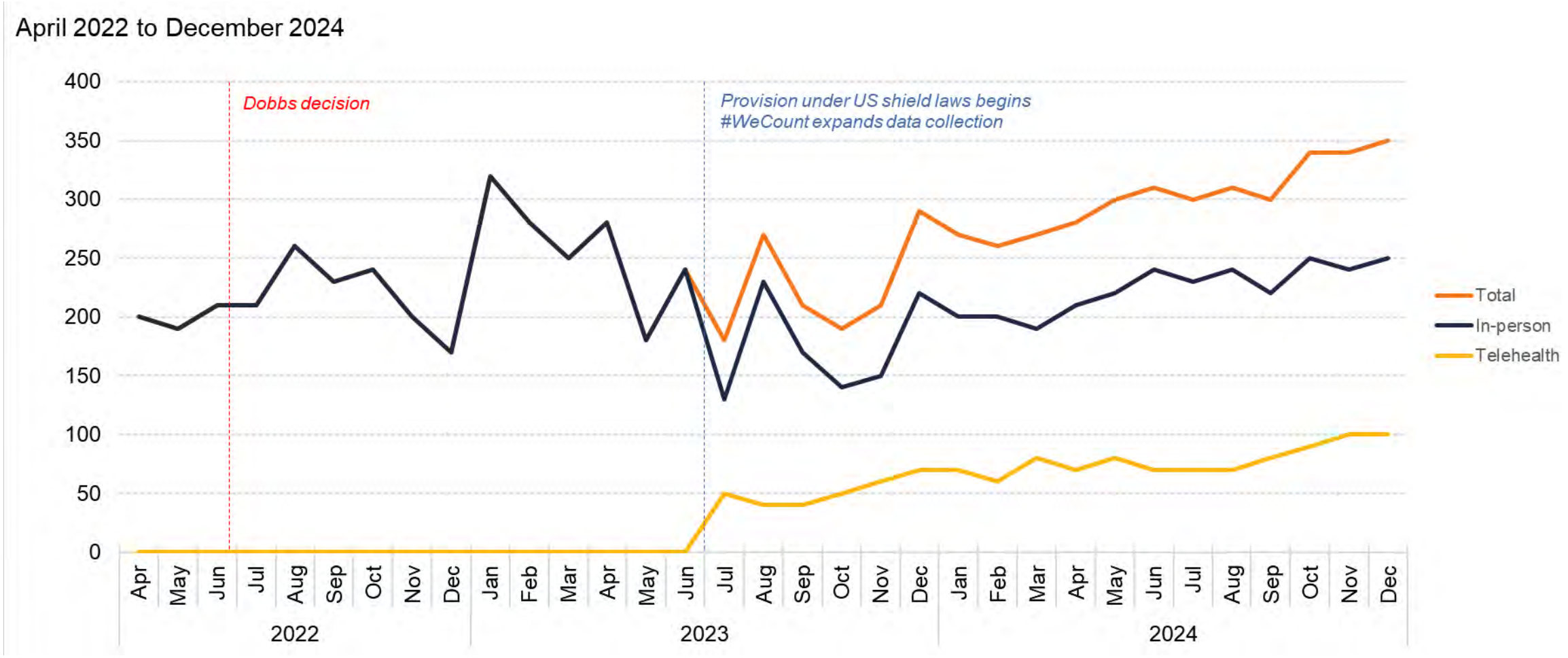

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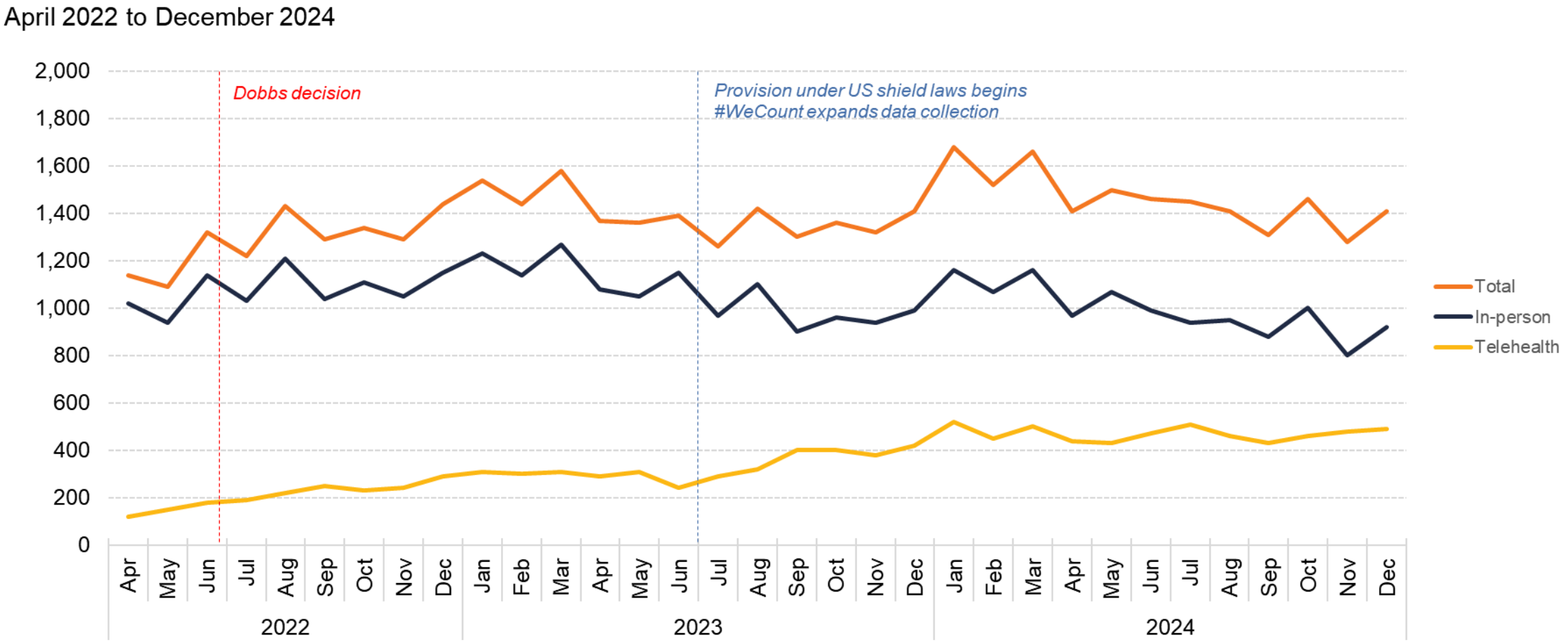

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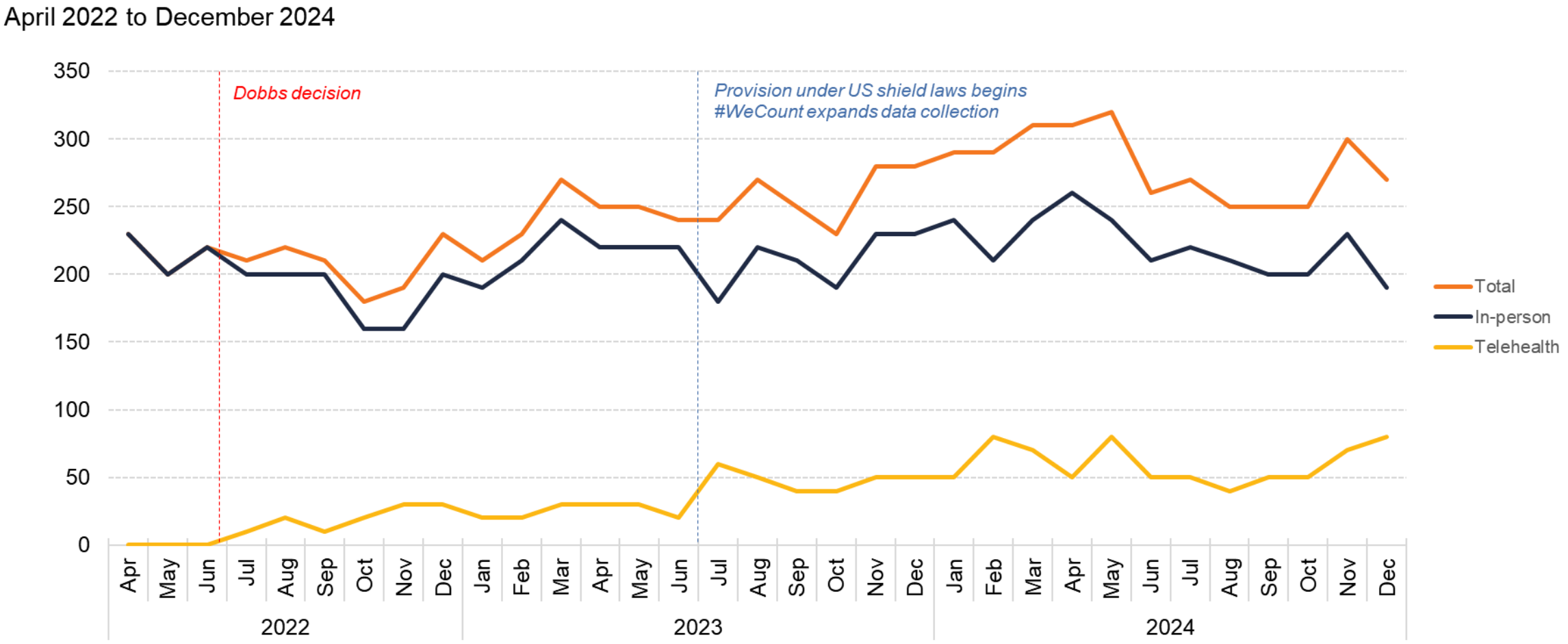
New Hampshire



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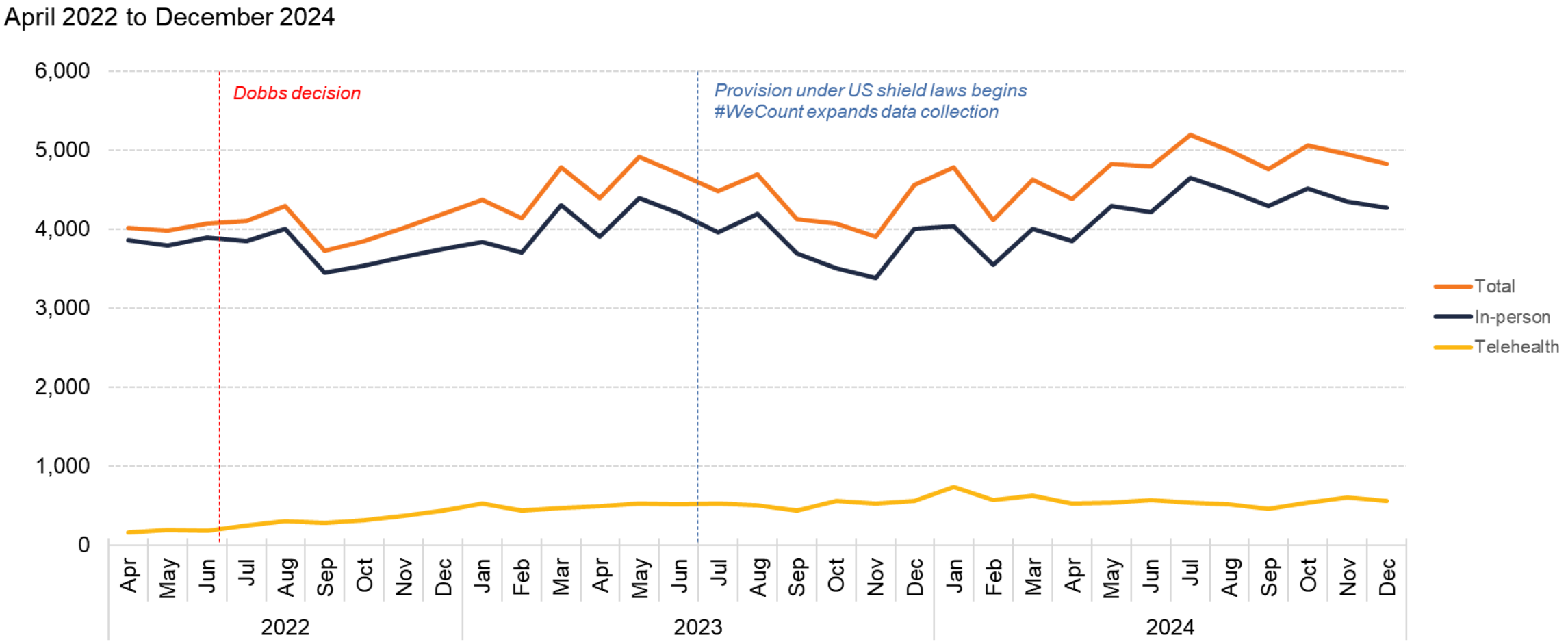

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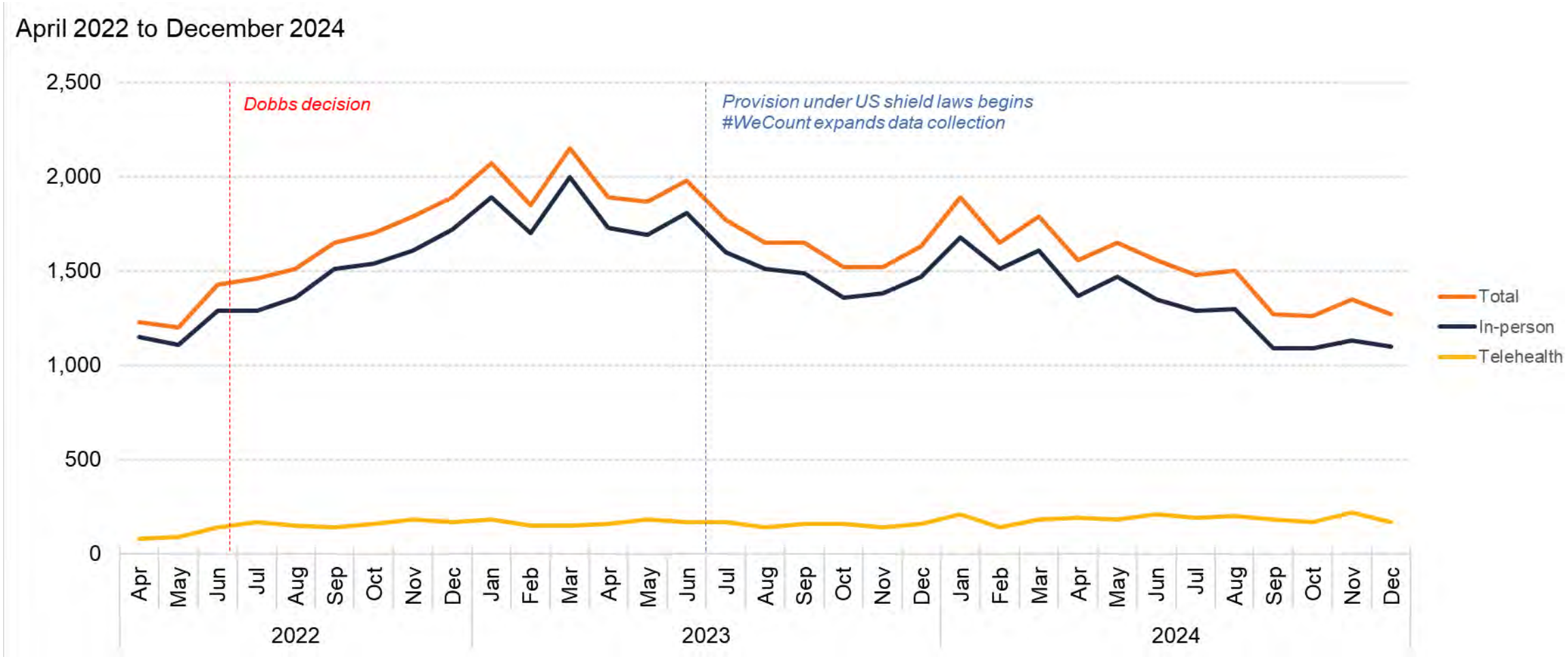

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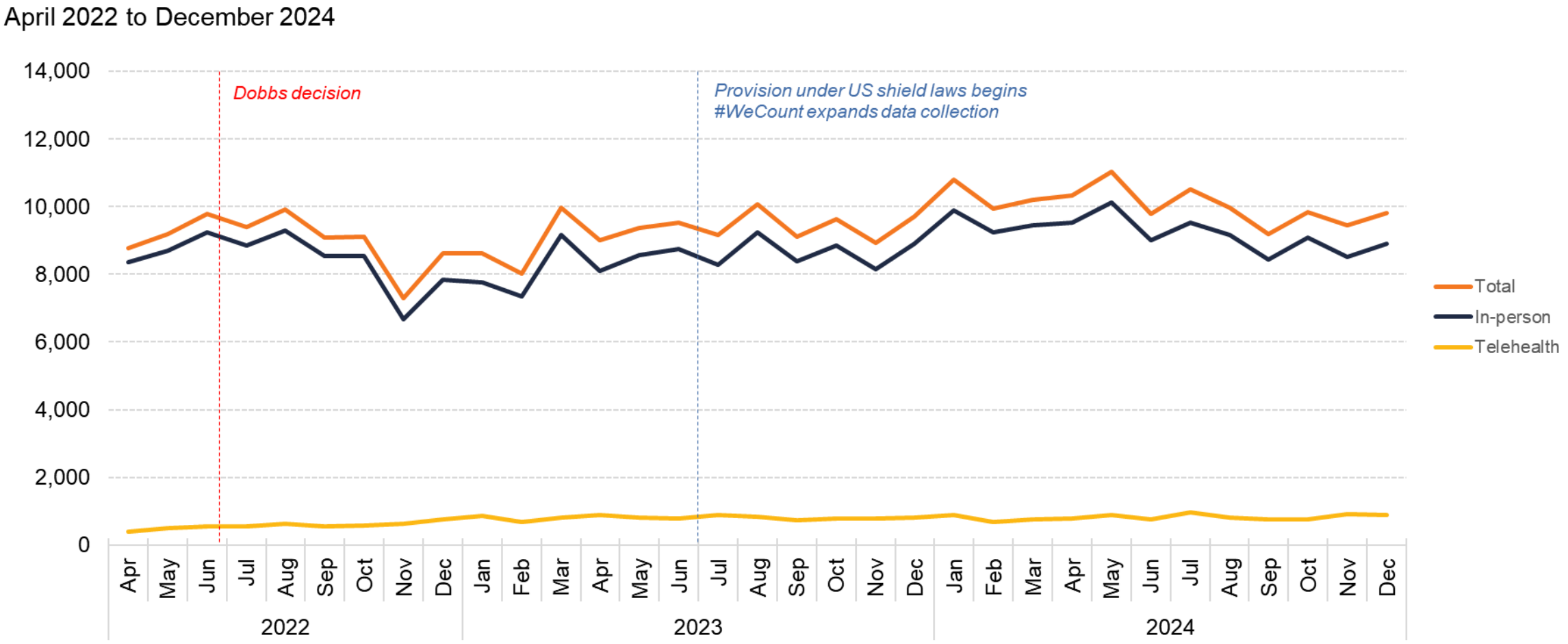
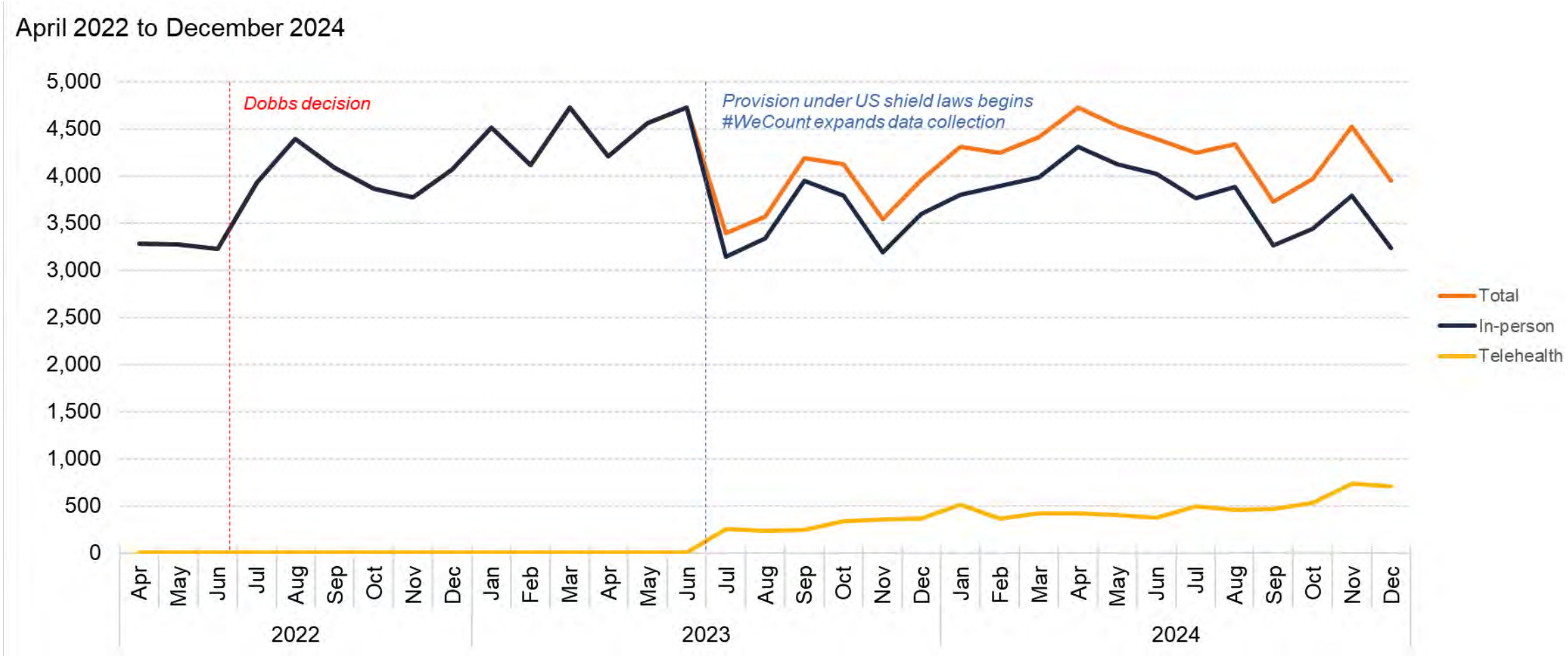


Source: Society of Family Planning, June 2025

North Carolina



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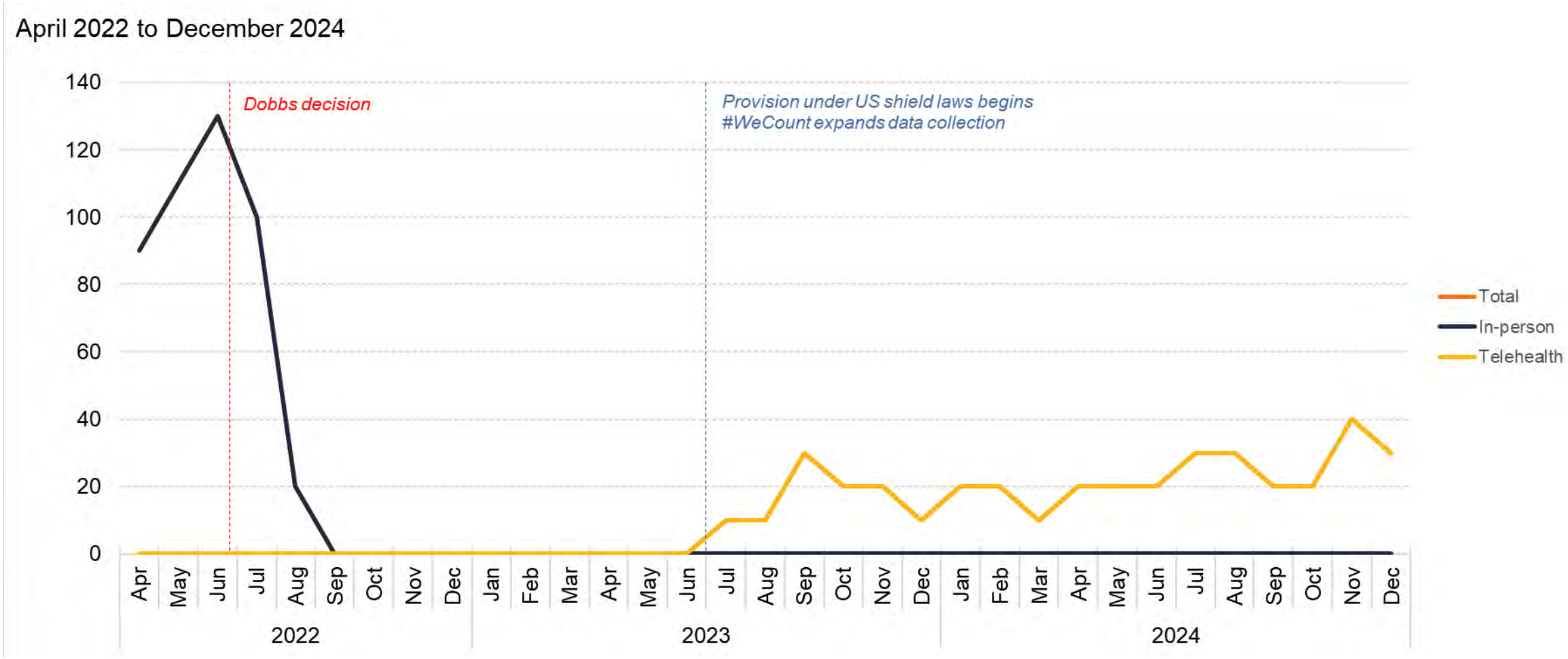

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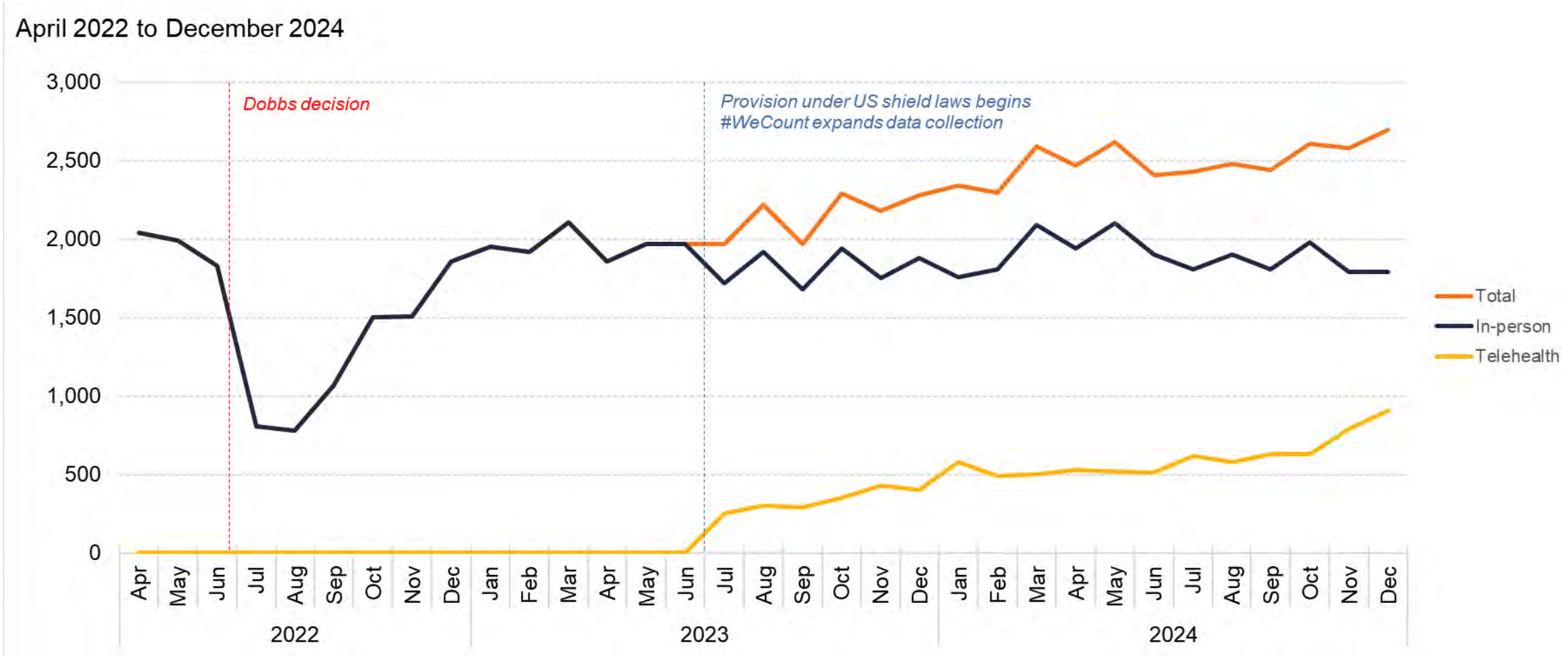
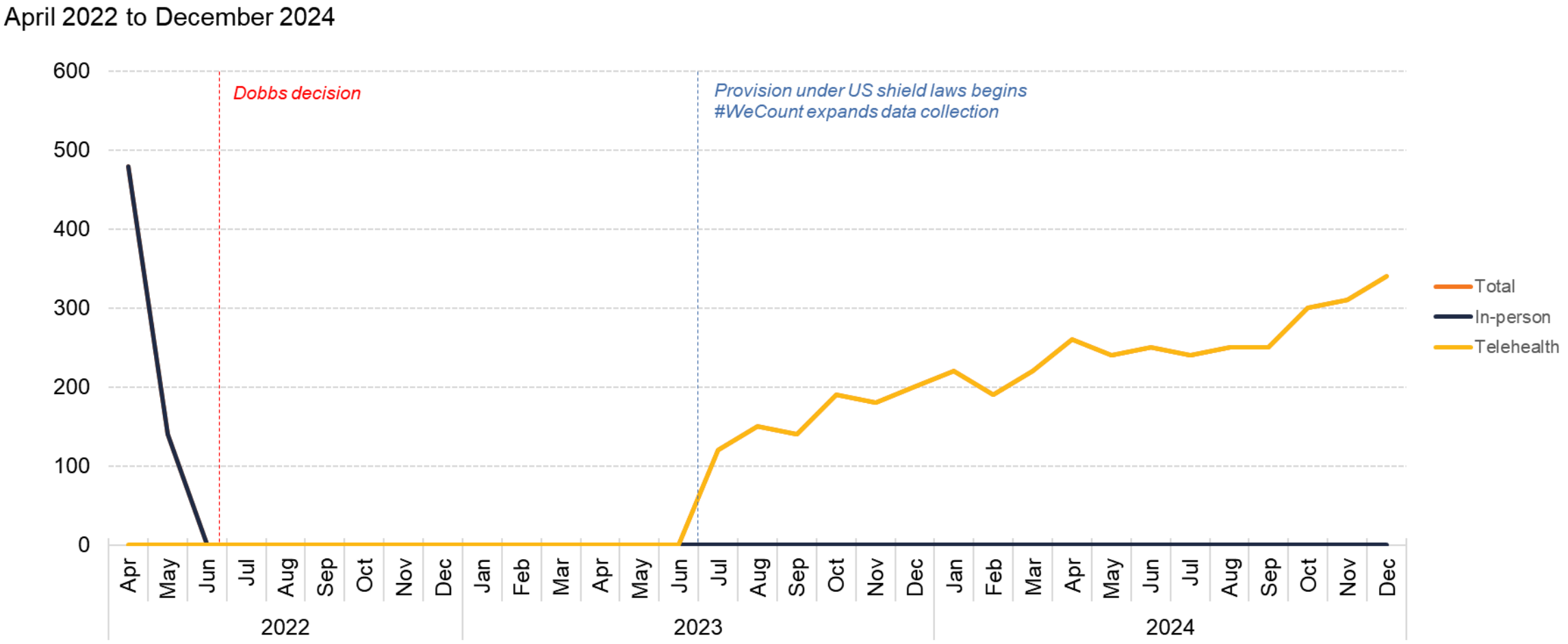
Ohio



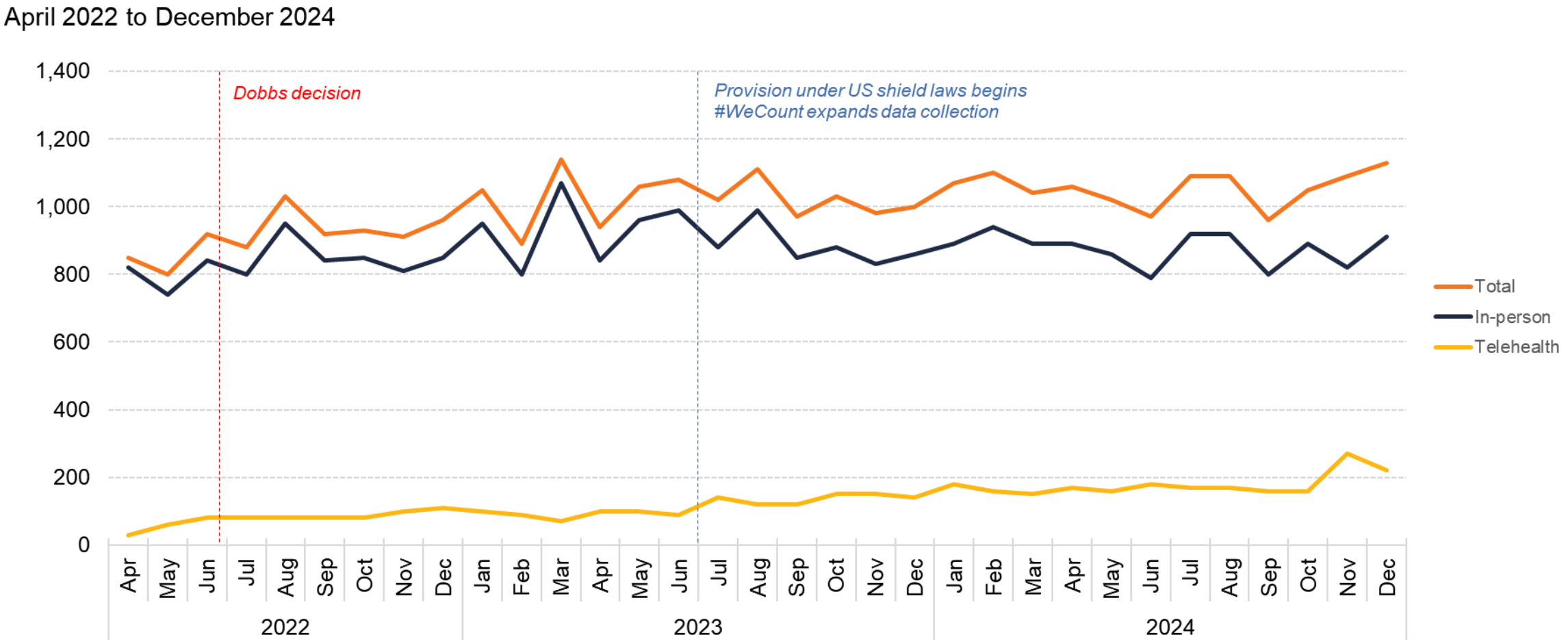
Source: Society of Family Planning, June 2025

Oklahoma



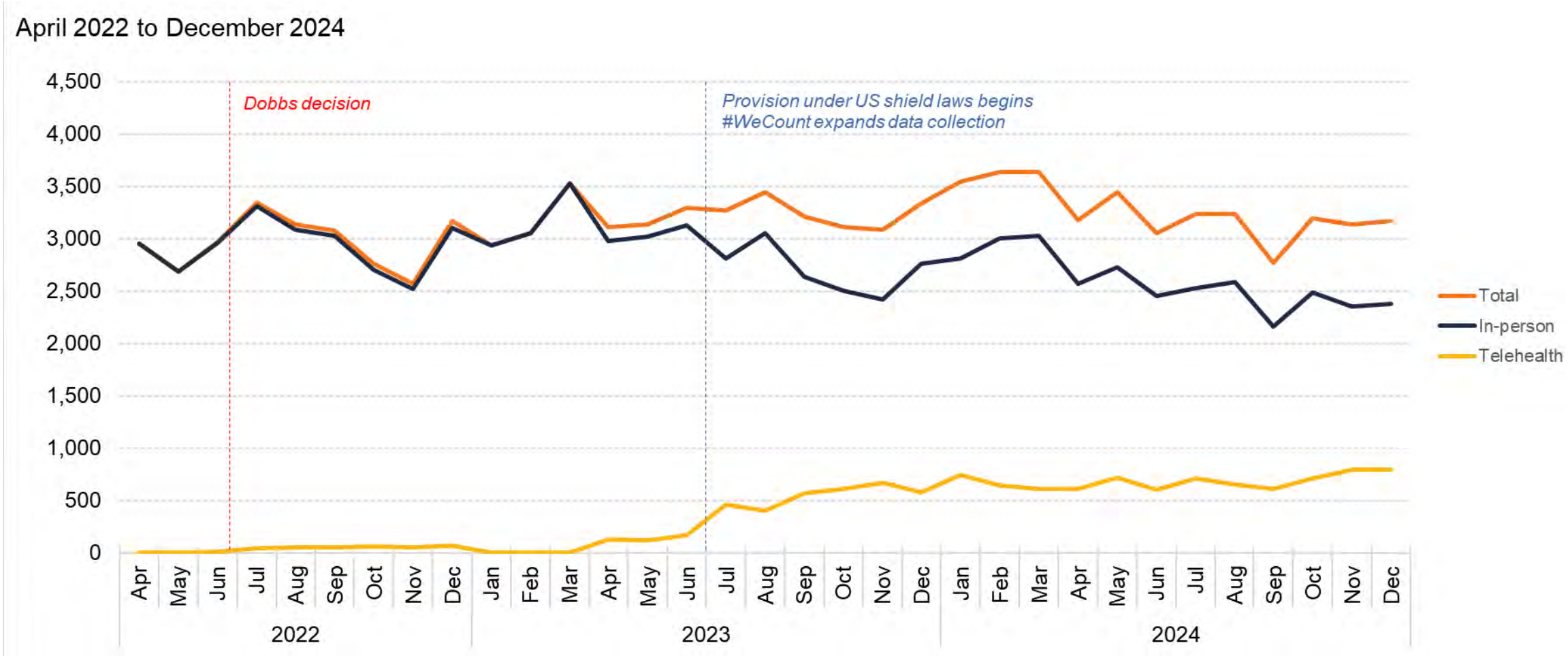
Source: Society of Family Planning, June 2025

Oregon



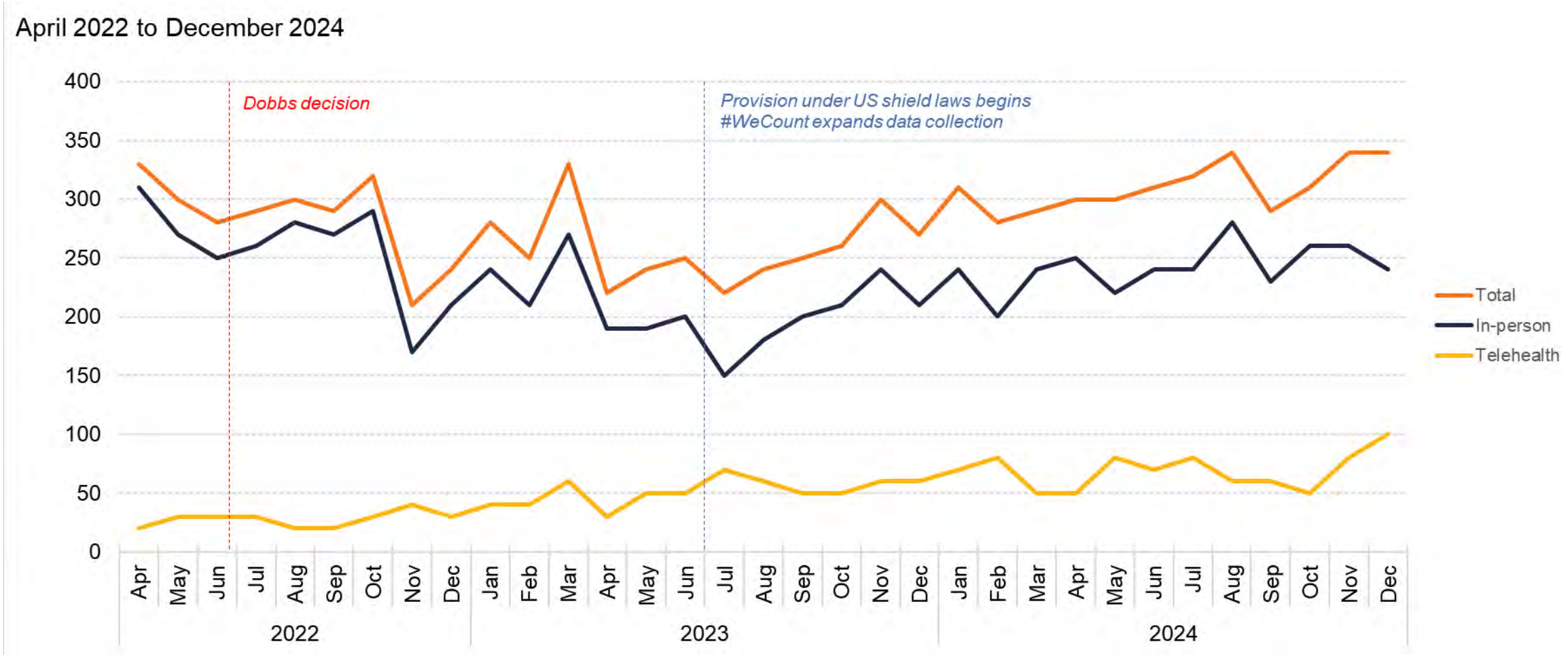
Source: Society of Family Planning, June 2025

Pennsylvania



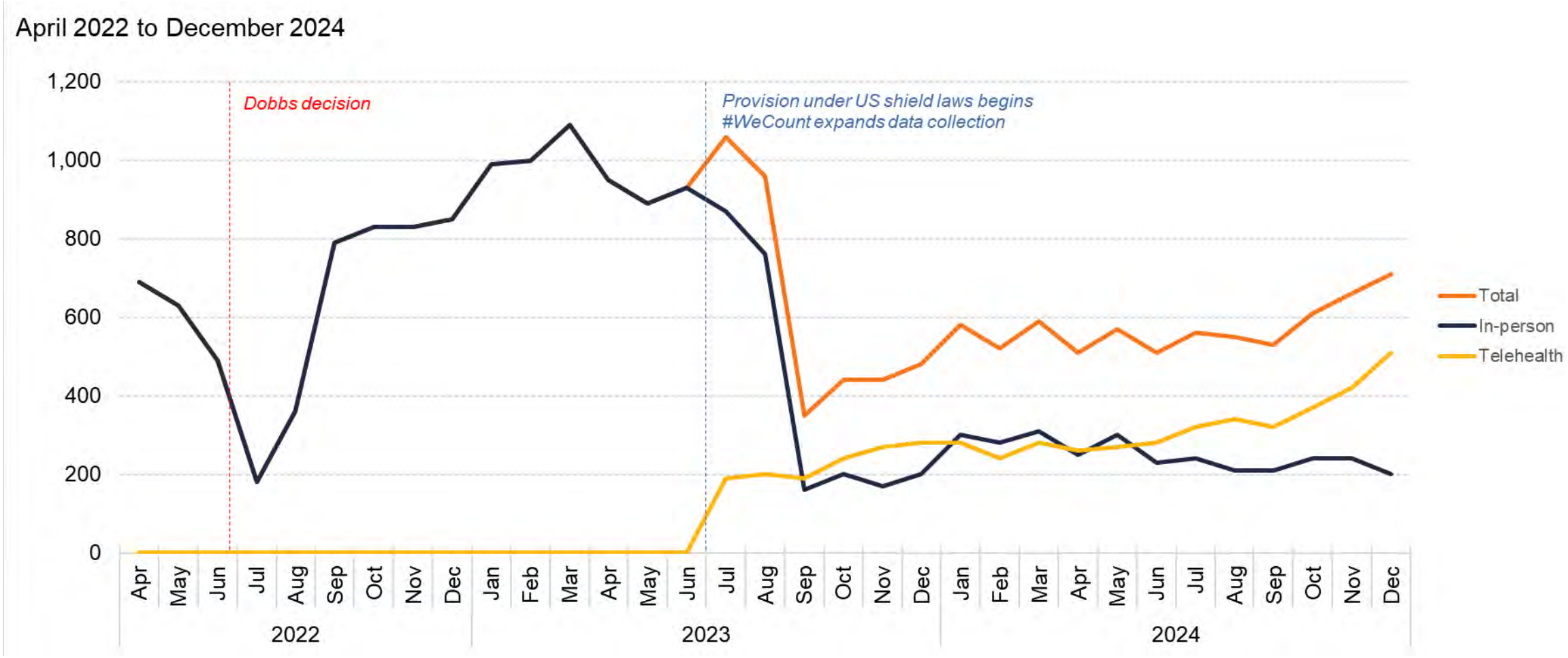
Source: Society of Family Planning, June 2025

Rhode Island



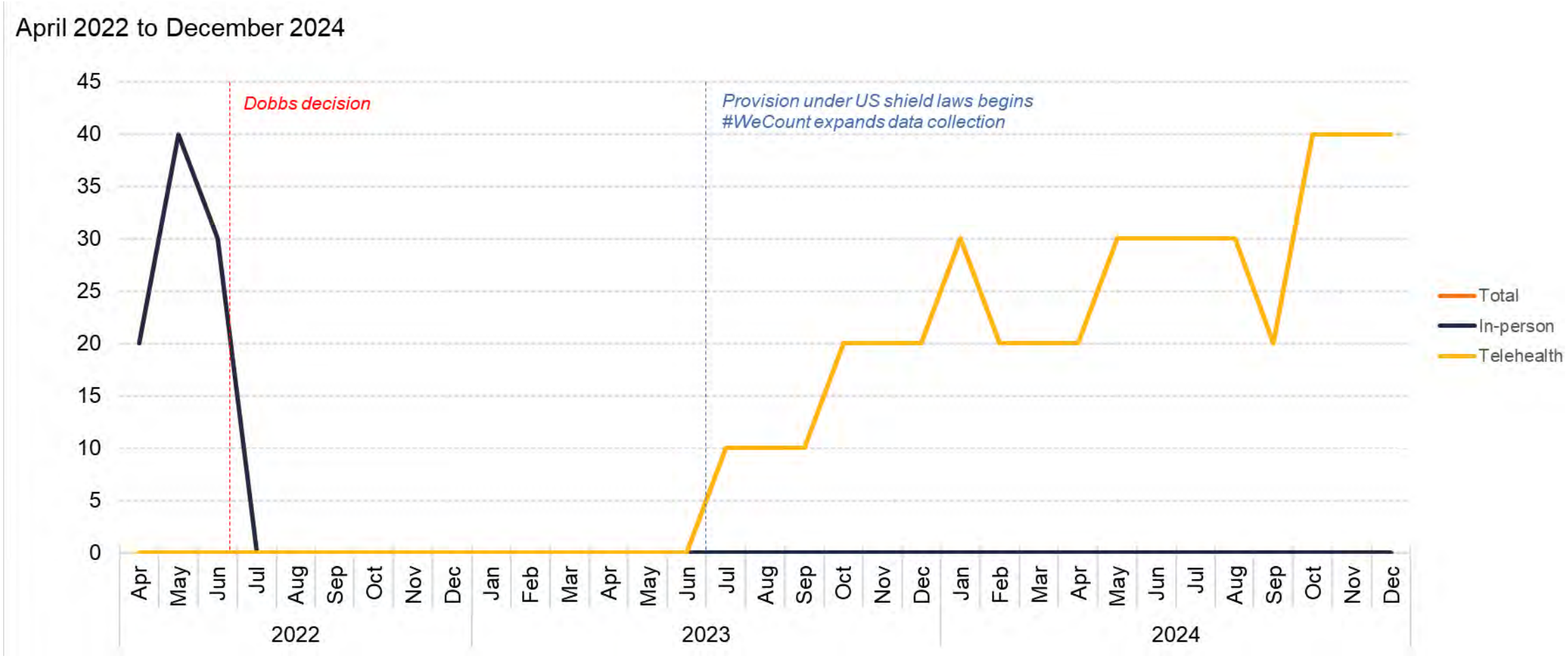
Source: Society of Family Planning, June 2025

South Carolina



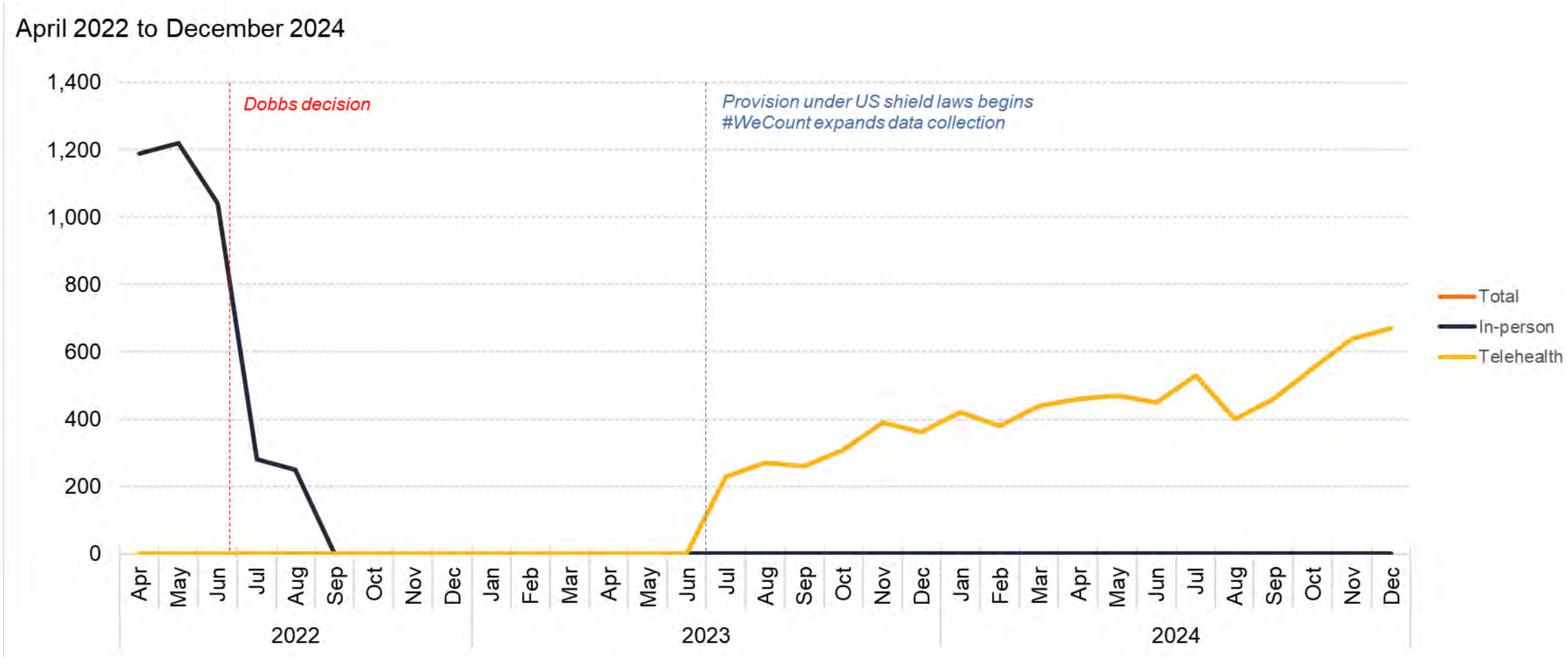
Source: Society of Family Planning, June 2025

South Dakota



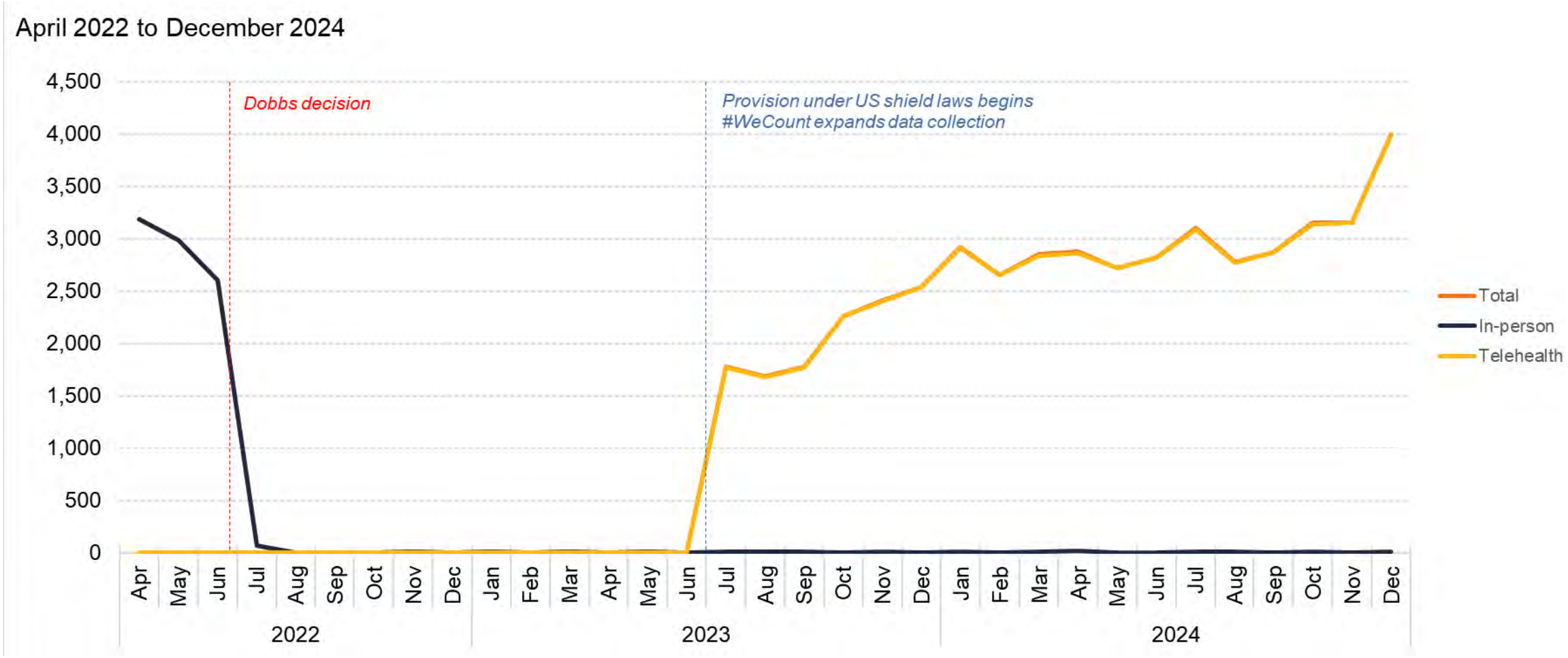
Source: Society of Family Planning, June 2025

Tennessee



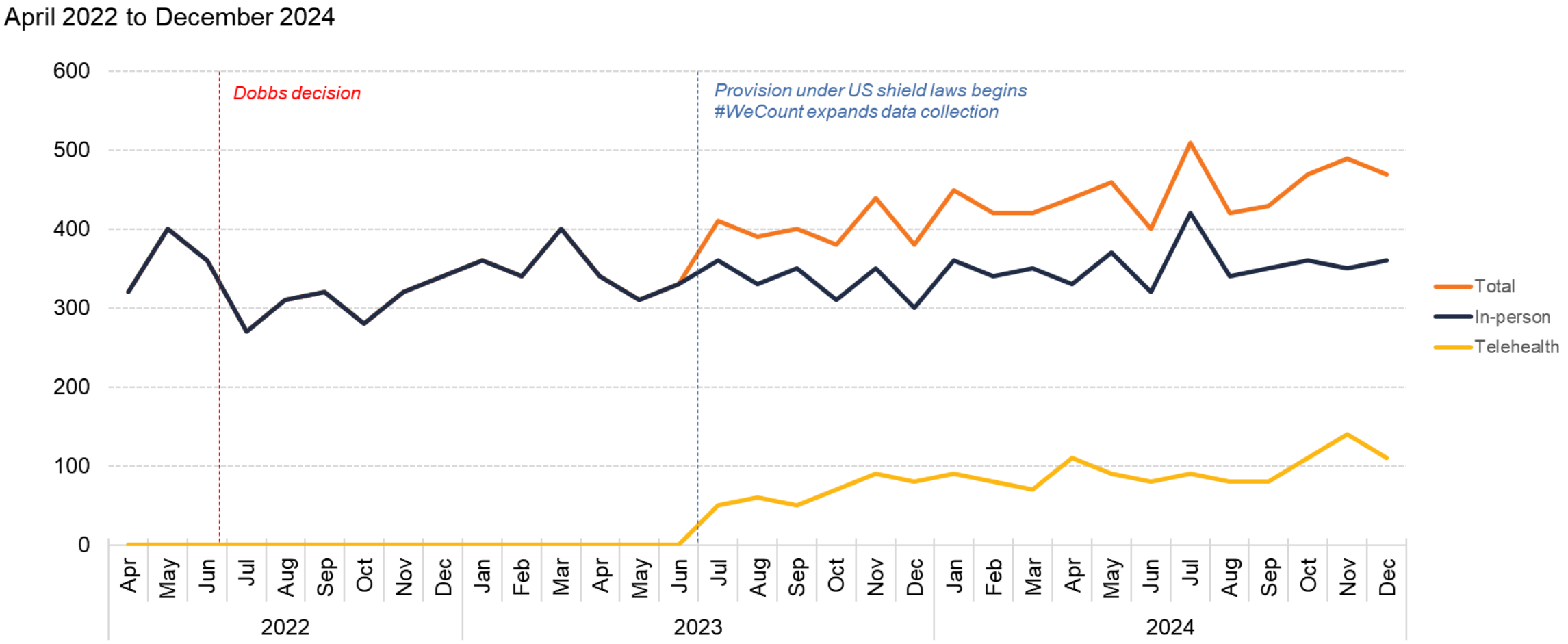
Source: Society of Family Planning, June 2025

Texas



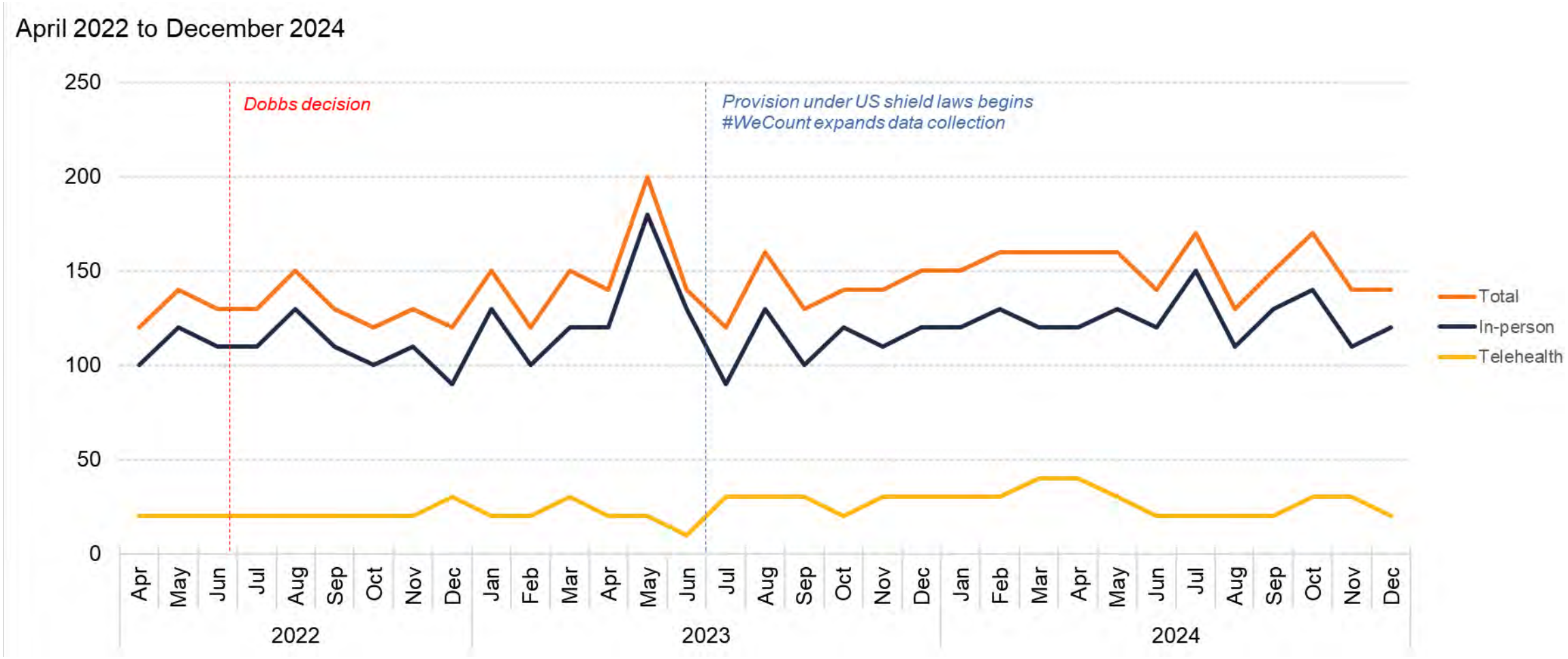
Source: Society of Family Planning, June 2025

Utah



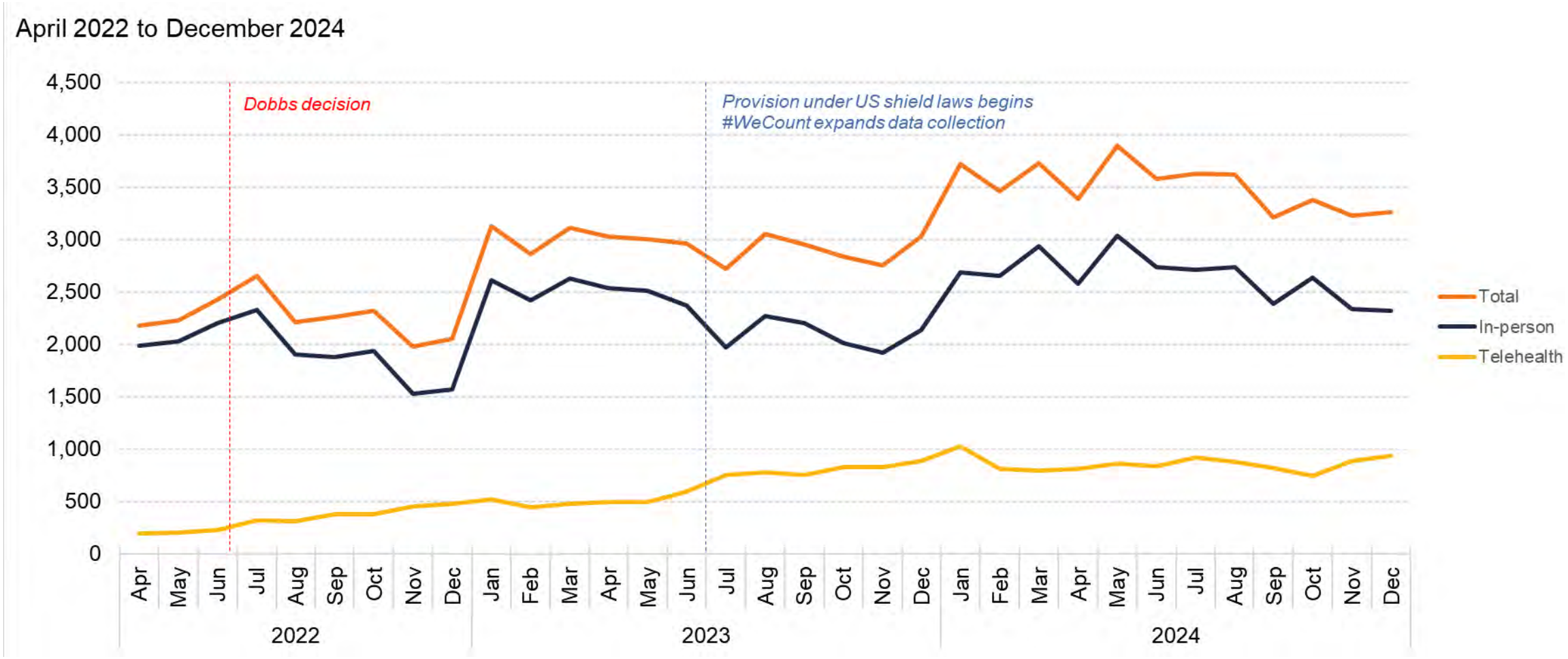
Source: Society of Family Planning, June 2025

Vermont



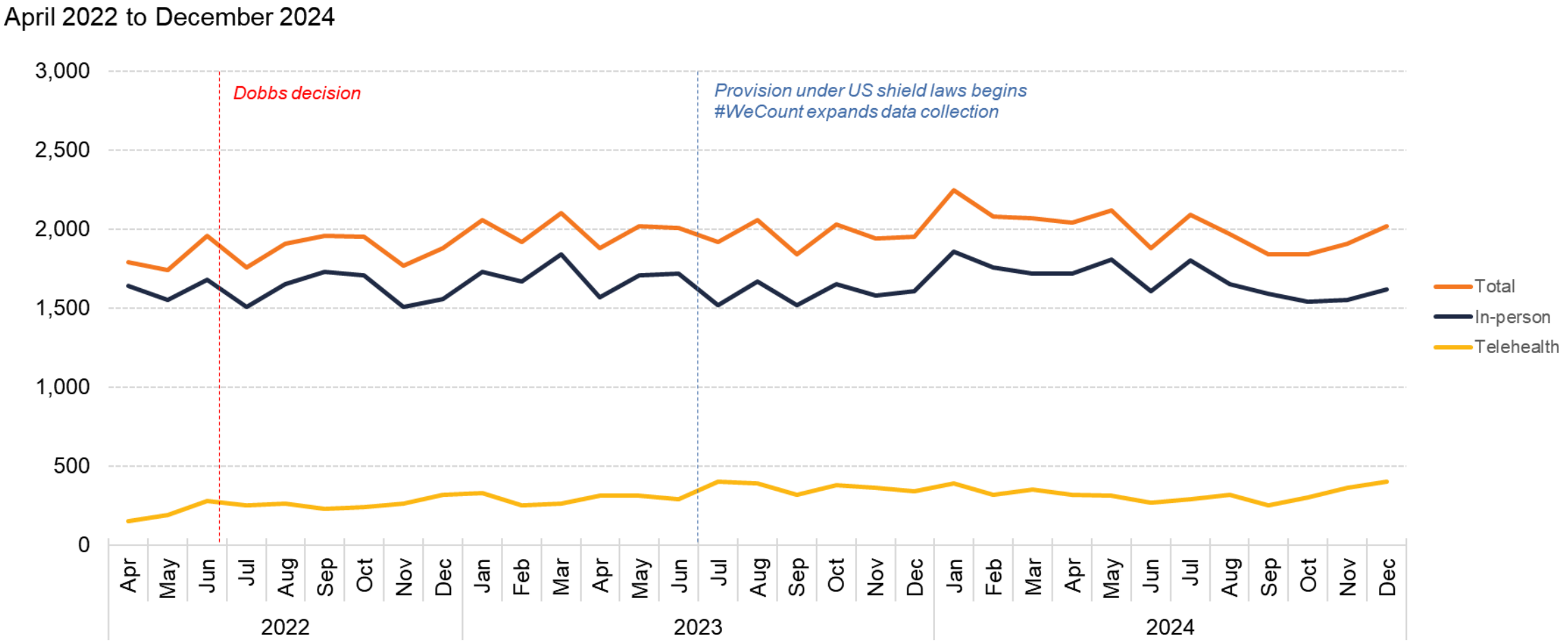
Source: Society of Family Planning, June 2025

Virginia



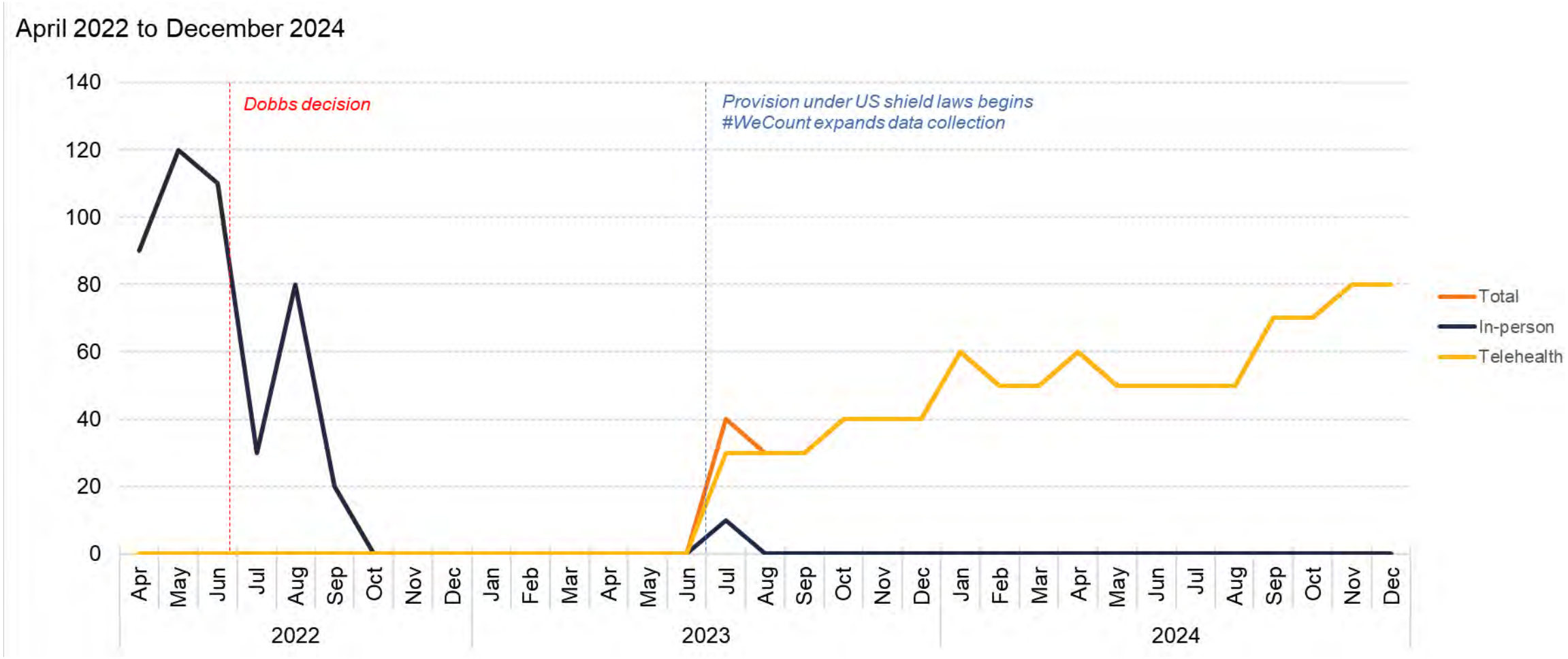
Source: Society of Family Planning, June 2025

Washington



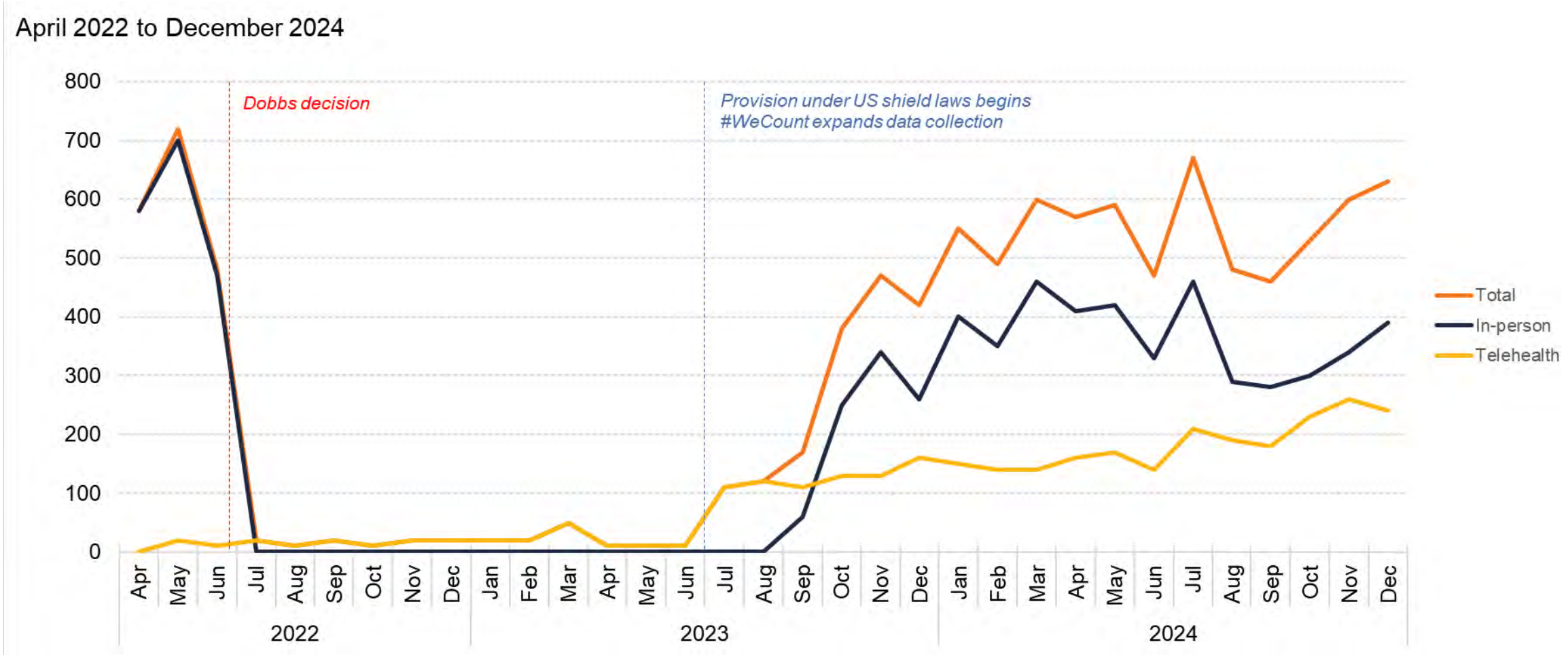
Source: Society of Family Planning, June 2025

West Virginia



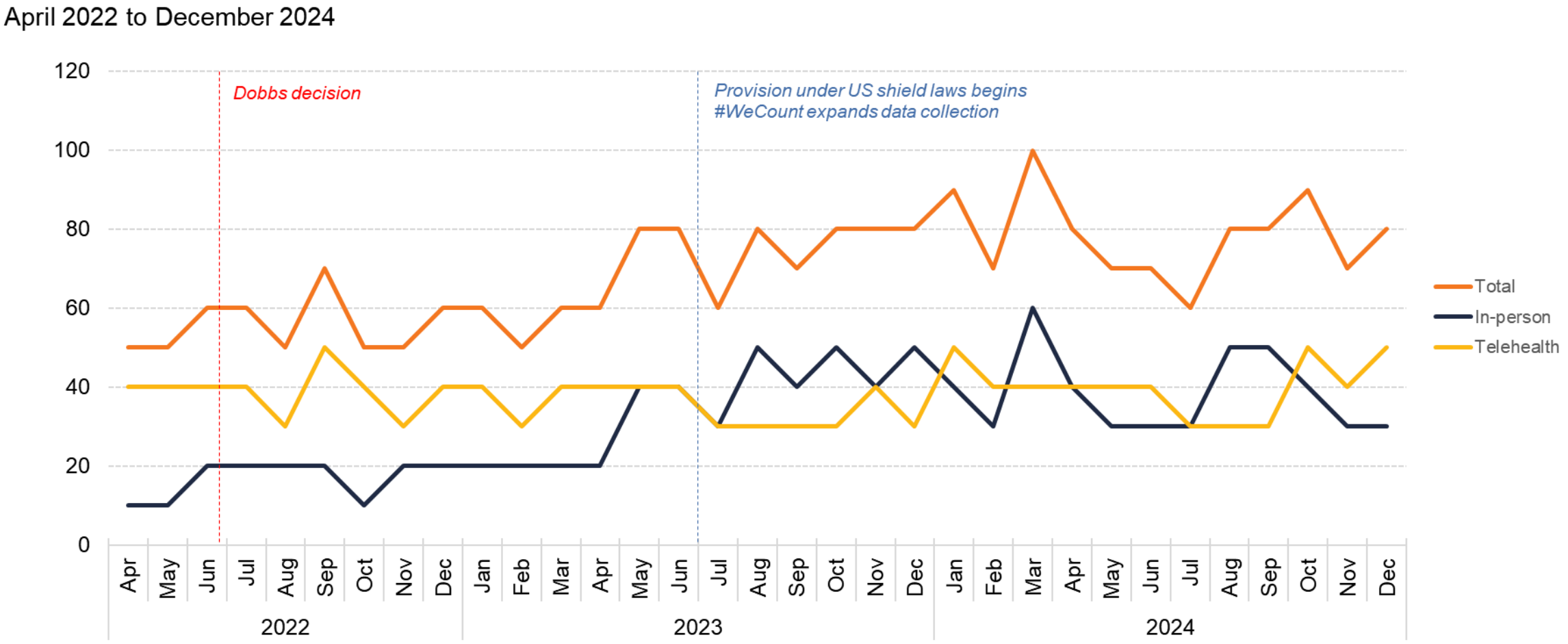
Source: Society of Family Planning, June 2025

Wisconsin



Source: Society of Family Planning, June 2025

Wyoming



Source: Society of Family Planning, June 2025

EXHIBIT

202 FDA etter to AC and SMFM
About Mifepri tone R MS
(Apr. 2, 202)

U.S. FOOD & DRUG ADMINISTRATION

April 12, 2021

Maureen G. Phipps, MD, MPH, FACOG
Chief Executive Officer
American College of Obstetricians and Gynecologists
c/o Rachel Tetlow, Federal Affairs Director
rtetlow@acog.org

Skye Perryman, General Counsel
sperryman@acog.org

William Grobman, MD, MBA
President
Society for Maternal-Fetal Medicine
w-grobman@northwestern.edu

Dear Drs. Phipps and Grobman,

In your letter of April 20, 2020, to former Commissioner Stephen Hahn, you expressed concerns about the in-person dispensing requirements for certain prescription drugs during the current public health emergency. In my letter to you of March 19, 2021, I indicated that staff in the Food and Drug Administration's (FDA) Center for Drug Evaluation and Research (CDER) were evaluating the issues you raised.

Following up on my March 19, 2021, letter I am writing to report the results of CDER's review and analysis.

CDER conducted a literature search for studies pertinent to the in-person dispensing requirement in the Mifepristone REMS Program during the COVID-19 pandemic. Based on this literature search, CDER identified four publications that included relevant clinical outcome data.[1] CDER

[1] Chong E, et al. Expansion of a Direct-to-Patient Telemedicine Abortion Service in the United States and Experience during the COVID-19 Pandemic. Contraception 2021 (accepted manuscript). https://www.sciencedirect.com/science/article/pii/S0010782421000913; Kerestes C, et al. Provision of medication abortion in Hawai'i during COVID-19: Practical experience with multiple care delivery models. Contraception 2021 (accepted manuscript). https://doi.org/10.1016/j.contraception.2021.03.025; Aiken A et al. Effectiveness, Safety and Acceptability of No-test Medical Abortion Provided Via Telemedicine: a National Cohort Study. British J Obstet Gynecol 2021. https://obgyn.onlinelibrary.wiley.com/doi/10.1111/1471-0528.16668; Reynolds-Wright JJ et al. Telemedicine medical abortion at home under 12 weeks' gestation: a prospective observational cohort study during the COVID-19 pandemic. BMJ Sex Reprod Health 2021. https://srh.bmj.com/content/early/2021/02/04/bmjsrh-2020-200976

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

found that although there are limitations to the study designs, the overall findings from these studies do not appear to show increases in serious safety concerns (such as hemorrhage, ectopic pregnancy, or surgical interventions) occurring with medical abortion as a result of modifying the in-person dispensing requirement during the COVID-19 pandemic.

CDER also reviewed postmarketing adverse events that reportedly occurred from January 27, 2020 - January 12, 2021, with mifepristone use for medical termination of early pregnancy, along with available information about deviations or noncompliance events associated with the Mifepristone REMS Program.[2] CDER found that the small number of adverse events reported to FDA during the COVID-19 public health emergency (PHE) provide no indication that any program deviation or noncompliance with the Mifepristone REMS Program contributed to the reported adverse events.

In summary, provided the other requirements of the Mifepristone REMS Program are met, and given that the in-person dispensing of mifepristone for medical termination of early pregnancy may present additional COVID-related risks to patients and healthcare personnel because it may involve a clinic visit solely for this purpose, CDER intends to exercise enforcement discretion during the COVID-19 PHE with respect to the in-person dispensing requirement of the Mifepristone REMS Program, including any in-person requirements that may be related to the Patient Agreement Form. Further, to the extent all of the other requirements of the Mifepristone REMS Program are met, CDER intends to exercise enforcement discretion during the COVID-19 PHE with respect to the dispensing of mifepristone through the mail either by or under the supervision of a certified prescriber, or through a mail-order pharmacy when such dispensing is done under the supervision of a certified prescriber.

CDER is communicating this decision to the approved application holders subject to the Mifepristone REMS Program.

Sincerely yours,

Janet Woodcock, M.D.
Acting Commissioner of Food and Drugs

[2] See Mifepristone REMS Program at https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=RemsDetails.page&REMS=390. CDER's analysis covers both products that are subject to the Mifepristone REMS Program (Mifeprex and the approved generic, Mifepristone Tablets, 200 mg).

EXHIBIT

Dr. Margaret Carpenter indictment

Clerk of Court Demographic Information Report for

Judicial District:	18th
DA Name:	Tony Clayton
Judge:	
Parish:	West Baton Rouge
Defendant Name:	Dr. Margaret D Carpenter, and Nightingale Medical, PC
DOB:	12/17/1969
Race:	
Sex:	
Date of Arrest:	
Arr. Agency:	Attorney Generals Office
SID:	
US Citizen:	
Drivers License #:	
Drivers License State:	
City:	New Paltz
State:	NY
Deputy Clerk:	Sharon Saul
Minute Clerk:	Kelli Arnold
Charge:	14:87.9.B(1)
Plea:	
Date Filed:	JAN 31 2025
Date Arraigned:	

THE EIGHTEENTH JUDICIAL DISTRICT COURT
FOR THE PARISH OF WEST BATON ROUGE

STATE OF LOUISIANA

STATE OF LOUISIANA

FILED: January 31, 2025
Sharon Paul
Deputy Clerk of Court

VERSUS

DR. MARGARET D. CARPENTER AND NIGHTINGALE MEDICAL, PC
[redacted]

NO. 250187

A TRUE BILL
Foreman
Date: 1-31-2025

BILL OF INDICTMENT

The GRAND JURY OF THE STATE OF LOUISIANA, *duly impaneled sworn and charge in and for the body of the Parish of West Baton Rouge, in the name and by authority of said State, upon their oath, PRESENT: that one DR. MARGARET D. CARPENTER AND NIGHTINGALE MEDICAL, PC, late of the State of New York, County of Ulster, with force and arms, in the Parish of West Baton Rouge, State of Louisiana, aforesaid, and within the jurisdiction of the Eighteenth Judicial District Court in and for the Parish of West Baton Rouge charges that* :

LA R.S. 14:87.9 (A) AND (B)(1) CRIMINAL ABORTION BY MEANS OF ABORTION-INDUCING DRUGS, Dr. Margaret D Carpenter, and Nightingale Medical, PC, on or about April 5, 2024, did knowingly cause an abortion to occur by means of delivering, dispensing, distributing, or providing a pregnant women with an abortion-inducing drug.

Contrary to the law of the State of Louisiana and against the peace and dignity of the same.

TONY CLAYTON
DISTRICT ATTORNEY

BY: Tony Clayton #21191
Assistant District Attorney
Eighteenth Judicial District
State of Louisiana

EXHIBIT

FDA Appro ed abel for Mifepri tone
(Mifepre) (Jan. 2023)
(Mifepre 2023 abel)

This label may not be the latest approved by EDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use MIFEPREX safely and effectively. See full prescribing information for MIFEPREX.

MIFEPREX® (mifepristone) tablets, for oral use
Initial U.S. Approval: 2000

WARNING: SERIOUS AND SOMETIMES FATAL INFECTIONS OR BLEEDING

See full prescribing information for complete boxed warning.

Serious and sometimes fatal infections and bleeding occur very rarely following spontaneous, surgical, and medical abortions, including following MIFEPREX use.

- **Atypical Presentation of Infection. Patients with serious bacterial infections and sepsis can present without fever, bacteremia or significant findings on pelvic examination. A high index of suspicion is needed to rule out serious infection and sepsis. (5.1)**
- **Bleeding. Prolonged heavy bleeding may be a sign of incomplete abortion or other complications and prompt medical or surgical intervention may be needed. (5.2)**

MIFEPREX is only available through a restricted program called the mifepristone REMS Program (5.3).
Before prescribing MIFEPREX, inform the patient about these risks. Ensure the patient knows whom to call and what to do if they experience sustained fever, severe abdominal pain, prolonged heavy bleeding, or syncope, or if they experience abdominal pain or discomfort or general malaise for more than 24 hours after taking misoprostol.

----------INDICATIONS AND USAGE----------
MIFEPREX is a progestin antagonist indicated, in a regimen with misoprostol, for the medical termination of intrauterine pregnancy through 70 days gestation. (1)

----------DOSAGE AND ADMINISTRATION----------
- 200 mg MIFEPREX on Day 1, followed 24-48 hours after MIFEPREX dosing by 800 mcg buccal misoprostol. (2.1)
- Instruct the patient what to do if significant adverse reactions occur. (2.2)
- Follow-up is needed to confirm complete termination of pregnancy. (2.3)

----------DOSAGE FORMS AND STRENGTHS----------
Tablets containing 200 mg of mifepristone each, supplied as 1 tablet on one blister card (3)

----------CONTRAINDICATIONS----------
- Confirmed/suspected ectopic pregnancy or undiagnosed adnexal mass (4)
- Chronic adrenal failure (4)
- Concurrent long-term corticosteroid therapy (4)
- History of allergy to mifepristone, misoprostol, or other prostaglandins (4)
- Hemorrhagic disorders or concurrent anticoagulant therapy (4)
- Inherited porphyria (4)
- Intrauterine device (IUD) in place (4)

----------WARNINGS AND PRECAUTIONS----------
- Ectopic pregnancy: Exclude before treatment. (5.4)
- Rhesus immunization: Prevention needed as for surgical abortion. (5.5)

----------ADVERSE REACTIONS----------
Most common adverse reactions (>15%) are nausea, weakness, fever/chills, vomiting, headache, diarrhea, and dizziness. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Danco Laboratories, LLC at 1-877-432-7596 or medicaldirector@earlyoptionpill.com or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

----------DRUG INTERACTIONS----------
- CYP3A4 inducers can lower mifepristone concentrations. (7.1)
- CYP3A4 inhibitors can increase mifepristone concentrations. Use with caution. (7.2)
- CYP3A4 substrate concentrations can be increased. Caution with coadministration of substrates with narrow therapeutic margin. (7.3)

----------USE IN SPECIFIC POPULATIONS----------
- Pregnancy: Risk of fetal malformations in ongoing pregnancy if not terminated is unknown. (8.1)

See 17 for PATIENT COUNSELING INFORMATION, Medication Guide.

Revised: 01/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

WARNING: SERIOUS AND SOMETIMES FATAL INFECTIONS OR BLEEDING
1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
2.1 Dosing Regimen
2.2 Patient Management Following Misoprostol Administration
2.3 Post-treatment Assessment: Day 7 to 14
2.4 Contact for Consultation
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Infections and Sepsis
5.2 Uterine Bleeding
5.3 Mifepristone REMS Program
5.4 Ectopic Pregnancy
5.5 Rhesus Immunization
6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
6.2 Postmarketing Experience
7 DRUG INTERACTIONS
7.1 Drugs that May Reduce MIFEPREX Exposure (Effect of CYP 3A4 Inducers on MIFEPREX)
7.2 Drugs that May Increase Exposure (Effect of CYP 3A4 Inhibitors on MIFEPREX)
7.3 Effects of MIFEPREX on Other Drugs (Effect of MIFEPREX on CYP 3A4 Substrates)
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation
8.4 Pediatric Use
10 OVERDOSAGE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
14 CLINICAL STUDIES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.

Reference ID: 5103833

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For current labeling information, please visit https://www.fda.gov/drugsatfda

FULL PRESCRIBING INFORMATION

WARNING: SERIOUS AND SOMETIMES FATAL INFECTIONS OR BLEEDING

Serious and sometimes fatal infections and bleeding occur very rarely following spontaneous, surgical, and medical abortions, including following MIFEPREX use. No causal relationship between the use of MIFEPREX and misoprostol and these events has been established.

- **Atypical Presentation of Infection. Patients with serious bacterial infections (e.g., *Clostridium sordellii*) and sepsis can present without fever, bacteremia, or significant findings on pelvic examination following an abortion. Very rarely, deaths have been reported in patients who presented without fever, with or without abdominal pain, but with leukocytosis with a marked left shift, tachycardia, hemoconcentration, and general malaise. A high index of suspicion is needed to rule out serious infection and sepsis *[see Warnings and Precautions (5.1)]*.**
- **Bleeding. Prolonged heavy bleeding may be a sign of incomplete abortion or other complications and prompt medical or surgical intervention may be needed. Advise patients to seek immediate medical attention if they experience prolonged heavy vaginal bleeding *[see Warnings and Precautions (5.2)]*.**

Because of the risks of serious complications described above, MIFEPREX is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the mifepristone REMS Program *[see Warnings and Precautions (5.3)]*.

Before prescribing MIFEPREX, inform the patient about the risk of these serious events. Ensure that the patient knows whom to call and what to do, including going to an Emergency Room if none of the provided contacts are reachable, if they experience sustained fever, severe abdominal pain, prolonged heavy bleeding, or syncope, or if they experience abdominal pain or discomfort, or general malaise (including weakness, nausea, vomiting, or diarrhea) for more than 24 hours after taking misoprostol.

1 INDICATIONS AND USAGE

MIFEPREX is indicated, in a regimen with misoprostol, for the medical termination of intrauterine pregnancy through 70 days gestation.

2 DOSAGE AND ADMINISTRATION

2.1 Dosing Regimen

For purposes of this treatment, pregnancy is dated from the first day of the last menstrual period. The duration of pregnancy may be determined from menstrual history and clinical examination. Assess the pregnancy by ultrasonographic scan if the duration of pregnancy is uncertain or if ectopic pregnancy is suspected.

Remove any intrauterine device (“IUD”) before treatment with MIFEPREX begins [*see Contraindications (4)*].

The dosing regimen for MIFEPREX and misoprostol is:

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- MIFEPREX 200 mg orally + misoprostol 800 mcg buccally
  - *Day One:* MIFEPREX Administration
    One 200 mg tablet of MIFEPREX is taken in a single oral dose.
  - *Day Two or Three:* Misoprostol Administration (minimum 24-hour interval between MIFEPREX and misoprostol)
    Four 200 mcg tablets (total dose 800 mcg) of misoprostol are taken by the buccal route.

    Tell the patient to place two 200 mcg misoprostol tablets in each cheek pouch (the area between the cheek and gums) for 30 minutes and then swallow any remnants with water or another liquid (see Figure 1).

    Figure 1

    2 pills between cheek and gum on left side + 2 pills between cheek and gum on right side

Patients taking MIFEPREX must take misoprostol within 24 to 48 hours after taking MIFEPREX. The effectiveness of the regimen may be lower if misoprostol is administered less than 24 hours or more than 48 hours after mifepristone administration.

Because most women will expel the pregnancy within 2 to 24 hours of taking misoprostol *[see Clinical Studies (14)]*, discuss with the patient an appropriate location for them to be when taking the misoprostol, taking into account that expulsion could begin within 2 hours of administration.

2.2 Patient Management Following Misoprostol Administration

During the period immediately following the administration of misoprostol, the patient may need medication for cramps or gastrointestinal symptoms *[see Adverse Reactions (6)].*

Give the patient:

- Instructions on what to do if significant discomfort, excessive vaginal bleeding or other adverse reactions occur
- A phone number to call if the patient has questions following the administration of the misoprostol
- The name and phone number of the healthcare provider who will be handling emergencies.

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2.3 Post-treatment Assessment: Day 7 to 14

Patients should follow-up with their healthcare provider approximately 7 to 14 days after the administration of MIFEPREX. This assessment is very important to confirm that complete termination of pregnancy has occurred and to evaluate the degree of bleeding. Termination can be confirmed by medical history, clinical examination, human Chorionic Gonadotropin (hCG) testing, or ultrasonographic scan. Lack of bleeding following treatment usually indicates failure; however, prolonged or heavy bleeding is not proof of a complete abortion.

The existence of debris in the uterus (e.g., if seen on ultrasonography) following the treatment procedure will not necessarily require surgery for its removal.

Patients should expect to experience vaginal bleeding or spotting for an average of 9 to 16 days. Women report experiencing heavy bleeding for a median duration of 2 days. Up to 8% of women may experience some type of bleeding for more than 30 days. Persistence of heavy or moderate vaginal bleeding at the time of follow-up, however, could indicate an incomplete abortion.

If complete expulsion has not occurred, but the pregnancy is not ongoing, patients may be treated with another dose of misoprostol 800 mcg buccally. There have been rare reports of uterine rupture in women who took MIFEPREX and misoprostol, including women with prior uterine rupture or uterine scar and women who received multiple doses of misoprostol within 24 hours. Patients who choose to use a repeat dose of misoprostol should have a follow-up visit with their healthcare provider in approximately 7 days to assess for complete termination.

Surgical evacuation is recommended to manage ongoing pregnancies after medical abortion *[see Use in Specific Populations (8.1)]*. Advise the patient whether you will provide such care or will refer them to another provider as part of counseling prior to prescribing MIFEPREX.

2.4 Contact for Consultation

For consultation 24 hours a day, 7 days a week with an expert in mifepristone, call Danco Laboratories at 1-877-4 Early Option (1-877-432-7596).

3 DOSAGE FORMS AND STRENGTHS

Tablets containing 200 mg of mifepristone each, supplied as 1 tablet on one blister card. MIFEPREX tablets are light yellow, cylindrical, and bi-convex tablets, approximately 11 mm in diameter and imprinted on one side with “MF.”

4 CONTRAINDICATIONS

- Administration of MIFEPREX and misoprostol for the termination of pregnancy (the “treatment procedure”) is contraindicated in patients with any of the following conditions:
  - Confirmed or suspected ectopic pregnancy or undiagnosed adnexal mass (the treatment procedure will not be effective to terminate an ectopic pregnancy) *[see Warnings and Precautions (5.4)]*
  - Chronic adrenal failure (risk of acute adrenal insufficiency)
  - Concurrent long-term corticosteroid therapy (risk of acute adrenal insufficiency)
  - History of allergy to mifepristone, misoprostol, or other prostaglandins (allergic reactions including anaphylaxis, angioedema, rash, hives, and itching have been reported *[see Adverse Reactions (6.2)]*)
  - Hemorrhagic disorders or concurrent anticoagulant therapy (risk of heavy bleeding)

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- Inherited porphyrias (risk of worsening or of precipitation of attacks)

- Use of MIFEPREX and misoprostol for termination of intrauterine pregnancy is contraindicated in patients with an intrauterine device ("IUD") in place (the IUD might interfere with pregnancy termination). If the IUD is removed, MIFEPREX may be used.

5 WARNINGS AND PRECAUTIONS

5.1 Infection and Sepsis

As with other types of abortion, cases of serious bacterial infection, including very rare cases of fatal septic shock, have been reported following the use of MIFEPREX *[see Boxed Warning]*. Healthcare providers evaluating a patient who is undergoing a medical abortion should be alert to the possibility of this rare event. A sustained (> 4 hours) fever of 100.4°F or higher, severe abdominal pain, or pelvic tenderness in the days after a medical abortion may be an indication of infection.

A high index of suspicion is needed to rule out sepsis (e.g., from *Clostridium sordellii*) if a patient reports abdominal pain or discomfort or general malaise (including weakness, nausea, vomiting, or diarrhea) more than 24 hours after taking misoprostol. Very rarely, deaths have been reported in patients who presented without fever, with or without abdominal pain, but with leukocytosis with a marked left shift, tachycardia, hemoconcentration, and general malaise. No causal relationship between MIFEPREX and misoprostol use and an increased risk of infection or death has been established. *Clostridium sordellii* infections have also been reported very rarely following childbirth (vaginal delivery and caesarian section), and in other gynecologic and non-gynecologic conditions.

5.2 Uterine Bleeding

Uterine bleeding occurs in almost all patients during a medical abortion. Prolonged heavy bleeding (soaking through two thick full-size sanitary pads per hour for two consecutive hours) may be a sign of incomplete abortion or other complications, and prompt medical or surgical intervention may be needed to prevent the development of hypovolemic shock. Counsel patients to seek immediate medical attention if they experience prolonged heavy vaginal bleeding following a medical abortion *[see Boxed Warning]*.

Women should expect to experience vaginal bleeding or spotting for an average of 9 to 16 days. Women report experiencing heavy bleeding for a median duration of 2 days. Up to 8% of all subjects may experience some type of bleeding for 30 days or more. In general, the duration of bleeding and spotting increased as the duration of the pregnancy increased.

Decreases in hemoglobin concentration, hematocrit, and red blood cell count may occur in patients who bleed heavily.

Excessive uterine bleeding usually requires treatment by uterotonics, vasoconstrictor drugs, surgical uterine evacuation, administration of saline infusions, and/or blood transfusions. Based on data from several large clinical trials, vasoconstrictor drugs were used in 4.3% of all subjects, there was a decrease in hemoglobin of more than 2 g/dL in 5.5% of subjects, and blood transfusions were administered to ≤ 0.1% of subjects. Because heavy bleeding requiring surgical uterine evacuation occurs in about 1% of patients, special care should be given to patients with hemostatic disorders, hypocoagulability, or severe anemia.

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

5.3 Mifepristone REMS Program

MIFEPREX is available only through a restricted program under a REMS called the mifepristone REMS Program, because of the risks of serious complications *[see Warnings and Precautions (5.1, 5.2)]*.

Notable requirements of the mifepristone REMS Program include the following:

- Prescribers must be certified with the program by completing the Prescriber Agreement Form.
- Patients must sign a Patient Agreement Form.
- MIFEPREX must only be dispensed to patients by or under the supervision of a certified prescriber, or by certified pharmacies on prescriptions issued by certified prescribers.

Further information is available at 1-877-4 Early Option (1-877-432-7596).

5.4 Ectopic Pregnancy

MIFEPREX is contraindicated in patients with a confirmed or suspected ectopic pregnancy because MIFEPREX is not effective for terminating ectopic pregnancies *[see Contraindications (4)].* Healthcare providers should remain alert to the possibility that a patient who is undergoing a medical abortion could have an undiagnosed ectopic pregnancy because some of the expected symptoms experienced with a medical abortion (abdominal pain, uterine bleeding) may be similar to those of a ruptured ectopic pregnancy. The presence of an ectopic pregnancy may have been missed even if the patient underwent ultrasonography prior to being prescribed MIFEPREX.

Patients who became pregnant with an IUD in place should be assessed for ectopic pregnancy.

5.5 Rhesus Immunization

The use of MIFEPREX is assumed to require the same preventive measures as those taken prior to and during surgical abortion to prevent rhesus immunization.

6 ADVERSE REACTIONS

The following adverse reactions are described in greater detail in other sections:

- Infection and sepsis *[see Warnings and Precautions (5.1)]*
- Uterine bleeding *[see Warnings and Precautions (5.2)]*

6.1 Clinical Trials Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

Information presented on common adverse reactions relies solely on data from U.S. studies, because rates reported in non-U.S. studies were markedly lower and are not likely generalizable to the U.S. population. In three U.S. clinical studies totaling 1,248 women through 70 days gestation who used mifepristone 200 mg orally followed 24-48 hours later by misoprostol 800 mcg buccally, women reported adverse reactions in diaries and in interviews at the follow-up visit. These studies enrolled generally healthy women of reproductive age without contraindications to mifepristone or misoprostol use according to the MIFEPREX product label. Gestational age was assessed prior to study enrollment using the date of the woman's last menstrual period, clinical evaluation, and/or ultrasound examination.

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About 85% of patients report at least one adverse reaction following administration of MIFEPREX and misoprostol, and many can be expected to report more than one such reaction. The most commonly reported adverse reactions (>15%) were nausea, weakness, fever/chills, vomiting, headache, diarrhea, and dizziness (see Table 1). The frequency of adverse reactions varies between studies and may be dependent on many factors, including the patient population and gestational age.

Abdominal pain/cramping is expected in all medical abortion patients and its incidence is not reported in clinical studies. Treatment with MIFEPREX and misoprostol is designed to induce uterine bleeding and cramping to cause termination of an intrauterine pregnancy. Uterine bleeding and cramping are expected consequences of the action of MIFEPREX and misoprostol as used in the treatment procedure. Most patients can expect bleeding more heavily than they do during a heavy menstrual period *[see Warnings and Precautions (5.2)]*.

Table 1 lists the adverse reactions reported in U.S. clinical studies with incidence >15% of women.

Table 1
Adverse Reactions Reported in Women Following Administration of Mifepristone (oral) and Misoprostol (buccal) in U.S. Clinical Studies

Adverse Reaction	# U.S. studies	Number of Evaluable Women	Range of frequency (%)	Upper Gestational Age of Studies Reporting Outcome
Nausea	3	1,248	51-75%	70 days
Weakness	2	630	55-58%	63 days
Fever/chills	1	414	48%	63 days
Vomiting	3	1,248	37-48%	70 days
Headache	2	630	41-44%	63 days
Diarrhea	3	1,248	18-43%	70 days
Dizziness	2	630	39-41%	63 days

One study provided gestational-age stratified adverse reaction rates for women who were 57-63 and 64-70 days; there was little difference in frequency of the reported common adverse reactions by gestational age.

Information on serious adverse reactions was reported in six U.S. and four non-U.S. clinical studies, totaling 30,966 women through 70 days gestation who used mifepristone 200 mg orally followed 24-48 hours later by misoprostol 800 mcg buccally. Serious adverse reaction rates were similar between U.S. and non-U.S. studies, so rates from both U.S. and non-U.S. studies are presented. In the U.S. studies, one studied women through 56 days gestation, four through 63 days gestation, and one through 70 days gestation, while in the non-U.S. studies, two studied women through 63 days gestation, and two through 70 days gestation. Serious adverse reactions were reported in <0.5% of women. Information from the U.S. and non-U.S. studies is presented in Table 2.

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Table 2
Serious Adverse Reactions Reported in Women Following Administration of Mifepristone (oral) and Misoprostol (buccal) in U.S. and Non-U.S. Clinical Studies

Adverse Reaction	U.S.			Non-U.S.		
	# of studies	Number of Evaluable Women	Range of frequency (%)	# of studies	Number of Evaluable Women	Range of frequency (%)
Transfusion	4	17,774	0.03-0.5%	3	12,134	0-0.1%
Sepsis	1	629	0.2%	1	11,155	<0.01%*
ER visit	2	1,043	2.9-4.6%	1	95	0
Hospitalization Related to Medical Abortion	3	14,339	0.04-0.6%	3	1,286	0-0.7%
Infection without sepsis	1	216	0	1	11,155	0.2%
Hemorrhage	NR	NR	NR	1	11,155	0.1%

NR= Not reported
* This outcome represents a single patient who experienced death related to sepsis.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of MIFEPREX and misoprostol. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Infections and infestations: post-abortal infection (including endometritis, endomyometritis, parametritis, pelvic infection, pelvic inflammatory disease, salpingitis)
Blood and the lymphatic system disorders: anemia
Immune system disorders: allergic reaction (including anaphylaxis, angioedema, hives, rash, itching)
Psychiatric disorders: anxiety
Cardiac disorders: tachycardia (including racing pulse, heart palpitations, heart pounding)
Vascular disorders: syncope, fainting, loss of consciousness, hypotension (including orthostatic), light-headedness
Respiratory, thoracic and mediastinal disorders: shortness of breath
Gastrointestinal disorders: dyspepsia
Musculoskeletal, connective tissue and bone disorders: back pain, leg pain
Reproductive system and breast disorders: uterine rupture, ruptured ectopic pregnancy, hematometra, leukorrhea
General disorders and administration site conditions: pain

7 DRUG INTERACTIONS

7.1 Drugs that May Reduce MIFEPREX Exposure (Effect of CYP 3A4 Inducers on MIFEPREX)

CYP450 3A4 is primarily responsible for the metabolism of mifepristone. CYP3A4 inducers such as rifampin, dexamethasone, St. John's Wort, and certain anticonvulsants (such as phenytoin, phenobarbital, carbamazepine) may induce mifepristone metabolism (lowering serum concentrations of mifepristone). Whether this action has an impact on the efficacy of the dose

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regimen is unknown. Refer to the follow-up assessment *[see Dosage and Administration (2.3)]* to verify that treatment has been successful.

7.2 Drugs that May Increase MIFEPREX Exposure (Effect of CYP 3A4 Inhibitors on MIFEPREX)

Although specific drug or food interactions with mifepristone have not been studied, on the basis of this drug's metabolism by CYP 3A4, it is possible that ketoconazole, itraconazole, erythromycin, and grapefruit juice may inhibit its metabolism (increasing serum concentrations of mifepristone). MIFEPREX should be used with caution in patients currently or recently treated with CYP 3A4 inhibitors.

7.3 Effects of MIFEPREX on Other Drugs (Effect of MIFEPREX on CYP 3A4 Substrates)

Based on *in vitro* inhibition information, coadministration of mifepristone may lead to an increase in serum concentrations of drugs that are CYP 3A4 substrates. Due to the slow elimination of mifepristone from the body, such interaction may be observed for a prolonged period after its administration. Therefore, caution should be exercised when mifepristone is administered with drugs that are CYP 3A4 substrates and have narrow therapeutic range.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

MIFEPREX is indicated, in a regimen with misoprostol, for the medical termination of intrauterine pregnancy through 70 days gestation. Risks to pregnant patients are discussed throughout the labeling.

Refer to misoprostol labeling for risks to pregnant patients with the use of misoprostol.

The risk of adverse developmental outcomes with a continued pregnancy after a failed pregnancy termination with MIFEPREX in a regimen with misoprostol is unknown; however, the process of a failed pregnancy termination could disrupt normal embryo-fetal development and result in adverse developmental effects. Birth defects have been reported with a continued pregnancy after a failed pregnancy termination with MIFEPREX in a regimen with misoprostol. In animal reproduction studies, increased fetal losses were observed in mice, rats, and rabbits and skull deformities were observed in rabbits with administration of mifepristone at doses lower than the human exposure level based on body surface area.

Data

Animal Data

In teratology studies in mice, rats and rabbits at doses of 0.25 to 4.0 mg/kg (less than 1/100 to approximately 1/3 the human exposure based on body surface area), because of the antiprogestational activity of mifepristone,fetal losses were much higher than in control animals. Skull deformities were detected in rabbit studies at approximately 1/6 the human exposure, although no teratogenic effects of mifepristone have been observed to date in rats or mice. These deformities were most likely due to the mechanical effects of uterine contractions resulting from inhibition of progesterone action.

8.2 Lactation

MIFEPREX is present in human milk. Limited data demonstrate undetectable to low levels of the drug in human milk with the relative (weight-adjusted) infant dose 0.5% or less as compared to maternal dosing. There is no information on the effects of MIFEPREX in a regimen with

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misoprostol in a breastfed infant or on milk production. Refer to misoprostol labeling for lactation information with the use of misoprostol. The developmental and health benefits of breast-feeding should be considered along with any potential adverse effects on the breast-fed child from MIFEPREX in a regimen with misoprostol.

8.4 Pediatric Use

Safety and efficacy of MIFEPREX have been established in pregnant females. Data from a clinical study of MIFEPREX that included a subset of 322 females under age 17 demonstrated a safety and efficacy profile similar to that observed in adults.

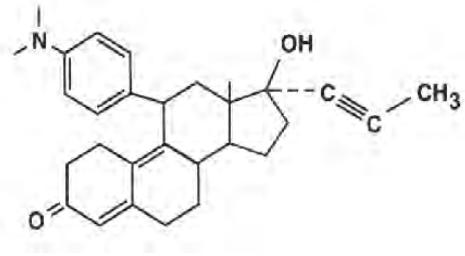
10 OVERDOSAGE

No serious adverse reactions were reported in tolerance studies in healthy non-pregnant female and healthy male subjects where mifepristone was administered in single doses greater than 1800 mg (ninefold the recommended dose for medical abortion). If a patient ingests a massive overdose, the patient should be observed closely for signs of adrenal failure.

11 DESCRIPTION

MIFEPREX tablets each contain 200 mg of mifepristone, a synthetic steroid with antiprogestational effects. The tablets are light yellow in color, cylindrical, and bi-convex, and are intended for oral administration only. The tablets include the inactive ingredients colloidal silica anhydrous, corn starch, povidone, microcrystalline cellulose, and magnesium stearate.

Mifepristone is a substituted 19-nor steroid compound chemically designated as 11ß-[*p*-(Dimethylamino)phenyl]-17ß-hydroxy-17-(1-propynyl)estra-4,9-dien-3-one. Its empirical formula is $C_{29}H_{35}NO_2$. Its structural formula is:



The compound is a yellow powder with a molecular weight of 429.6 and a melting point of 192-196°C. It is very soluble in methanol, chloroform and acetone and poorly soluble in water, hexane and isopropyl ether.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The anti-progestational activity of mifepristone results from competitive interaction with progesterone at progesterone-receptor sites. Based on studies with various oral doses in several animal species (mouse, rat, rabbit, and monkey), the compound inhibits the activity of endogenous or exogenous progesterone, resulting in effects on the uterus and cervix that, when combined with misoprostol, result in termination of an intrauterine pregnancy.

During pregnancy, the compound sensitizes the myometrium to the contraction-inducing activity

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of prostaglandins.

12.2 Pharmacodynamics

Use of MIFEPREX in a regimen with misoprostol disrupts pregnancy by causing decidual necrosis, myometrial contractions, and cervical softening, leading to the expulsion of the products of conception.

Doses of 1 mg/kg or greater of mifepristone have been shown to antagonize the endometrial and myometrial effects of progesterone in women.

Antiglucocorticoid and antiandrogenic activity: Mifepristone also exhibits antiglucocorticoid and weak antiandrogenic activity. The activity of the glucocorticoid dexamethasone in rats was inhibited following doses of 10 to 25 mg/kg of mifepristone. Doses of 4.5 mg/kg or greater in human beings resulted in a compensatory elevation of adrenocorticotropic hormone (ACTH) and cortisol. Antiandrogenic activity was observed in rats following repeated administration of doses from 10 to 100 mg/kg.

12.3 Pharmacokinetics

Mifepristone is rapidly absorbed after oral ingestion with non-linear pharmacokinetics for Cmax after single oral doses of 200 mg and 600 mg in healthy subjects.

Absorption

The absolute bioavailability of a 20 mg mifepristone oral dose in females of childbearing age is 69%. Following oral administration of a single dose of 600 mg, mifepristone is rapidly absorbed, with a peak plasma concentration of 1.98 ± 1.0 mg/L occurring approximately 90 minutes after ingestion.

Following oral administration of a single dose of 200 mg in healthy men (n=8), mean Cmax was 1.77 ± 0.7 mg/L occurring approximately 45 minutes after ingestion. Mean $AUC_{0-\infty}$ was 25.8 ± 6.2 mg*hr/L.

Distribution

Mifepristone is 98% bound to plasma proteins, albumin, and α_1-acid glycoprotein. Binding to the latter protein is saturable, and the drug displays nonlinear kinetics with respect to plasma concentration and clearance.

Elimination

Following a distribution phase, elimination of mifepristone is slow at first (50% eliminated between 12 and 72 hours) and then becomes more rapid with a terminal elimination half-life of 18 hours.

Metabolism

Metabolism of mifepristone is primarily via pathways involving N-demethylation and terminal hydroxylation of the 17-propynyl chain. *In vitro* studies have shown that CYP450 3A4 is primarily responsible for the metabolism. The three major metabolites identified in humans are: (1) RU 42 633, the most widely found in plasma, is the N-monodemethylated metabolite; (2) RU 42 848, which results from the loss of two methyl groups from the 4-dimethylaminophenyl in position 11ß; and (3) RU 42 698, which results from terminal hydroxylation of the 17-propynyl chain.

Excretion

By 11 days after a 600 mg dose of tritiated compound, 83% of the drug has been accounted for by the feces and 9% by the urine. Serum concentrations are undetectable by 11 days.

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Specific Populations

The effects of age, hepatic disease and renal disease on the safety, efficacy and pharmacokinetics of mifepristone have not been investigated.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

No long-term studies to evaluate the carcinogenic potential of mifepristone have been performed.

Mutagenesis

Results from studies conducted *in vitro* and in animals have revealed no genotoxic potential for mifepristone. Among the tests carried out were: Ames test with and without metabolic activation; gene conversion test in *Saccharomyces cerevisiae* D4 cells; forward mutation in *Schizosaccharomyces pompe* P1 cells; induction of unscheduled DNA synthesis in cultured HeLa cells; induction of chromosome aberrations in CHO cells; *in vitro* test for gene mutation in V79 Chinese hamster lung cells; and micronucleus test in mice.

Impairment of Fertility

In rats, administration of 0.3 mg/kg mifepristone per day caused severe disruption of the estrus cycles for the three weeks of the treatment period. Following resumption of the estrus cycle, animals were mated and no effects on reproductive performance were observed.

14 CLINICAL STUDIES

Safety and efficacy data from clinical studies of mifepristone 200 mg orally followed 24-48 hours later by misoprostol 800 mcg buccally through 70 days gestation are reported below. Success was defined as the complete expulsion of the products of conception without the need for surgical intervention. The overall rates of success and failure, shown by reason for failure based on 22 worldwide clinical studies (including 7 U.S. studies) appear in Table 3.

The demographics of women who participated in the U.S. clinical studies varied depending on study location and represent the racial and ethnic variety of American females. Females of all reproductive ages were represented, including females less than 18 and more than 40 years of age; most were 27 years or younger.

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Table 3
Outcome Following Treatment with Mifepristone (oral) and Misoprostol (buccal) Through 70 Days Gestation

	U.S. Trials	Non-U.S. Trials
N	16,794	18,425
Complete Medical Abortion	97.4%	96.2%
Surgical Intervention*	2.6%	3.8%
Ongoing Pregnancy**	0.7%	0.9%

* Reasons for surgical intervention include ongoing pregnancy, medical necessity, persistent or heavy bleeding after treatment, patient request, or incomplete expulsion.
** Ongoing pregnancy is a subcategory of surgical intervention, indicating the percent of women who have surgical intervention due to an ongoing pregnancy.

The results for clinical studies that reported outcomes, including failure rates for ongoing pregnancy, by gestational age are presented in Table 4.

Table 4
Outcome by Gestational Age Following Treatment with Mifepristone and Misoprostol (buccal) for U.S. and Non-U.S. Clinical Studies

	≤49 days			50-56 days			57-63 days			64-70 days		
	N	**%**	**Number of Evaluable Studies**	**N**	**%**	**Number of Evaluable Studies**	**N**	**%**	**Number of Evaluable Studies**	**N**	**%**	**Number of Evaluable Studies**
Complete medical abortion	12,046	98.1	10	3,941	96.8	7	2,294	94.7	9	479	92.7	4
Surgical intervention for ongoing pregnancy	10,272	0.3	6	3,788	0.8	6	2,211	2	8	453	3.1	3

One clinical study asked subjects through 70 days gestation to estimate when they expelled the pregnancy, with 70% providing data. Of these, 23-38% reported expulsion within 3 hours and over 90% within 24 hours of using misoprostol.

16 HOW SUPPLIED/STORAGE AND HANDLING

is only available through a restricted program called the Mifepristone REMS Program *[see Warnings and Precautions (5.3)].*

MIFEPREX is supplied as light yellow, cylindrical, and bi-convex tablets imprinted on one side with “MF.” Each tablet contains 200 mg of mifepristone. One tablet is individually blistered on one blister card that is packaged in an individual package (National Drug Code 64875-001-01).

Store at 25°C (77°F); excursions permitted to 15 to 30°C (59 to 86°F) [see USP Controlled Room Temperature].

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17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide), included with each package of MIFEPREX. Additional copies of the Medication Guide are available by contacting Danco Laboratories at 1-877-4 Early Option (1-877-432-7596) or from www.earlyoptionpill.com.

Serious Infections and Bleeding

- Inform the patient that uterine bleeding and uterine cramping will occur [*see Warnings and Precautions (5.2)*].
- Advise the patient that serious and sometimes fatal infections and bleeding can occur very rarely [*see Warnings and Precautions (5.1, 5.2)*].
- MIFEPREX is only available through a restricted program called the Mifepristone REMS Program [*see Warnings and Precautions (5.3)*]. Under the mifepristone REMS Program:
    - Patients must sign a Patient Agreement Form.
    - MIFEPREX is only dispensed by or under the supervision of certified prescribers or by certified pharmacies on prescriptions issued by certified prescribers.

Provider Contacts and Actions in Case of Complications

- Ensure that the patient knows whom to call and what to do, including going to an Emergency Room if none of the provided contacts are reachable, or if the patient experiences complications including prolonged heavy bleeding, severe abdominal pain, or sustained fever *[see Boxed Warning]*.
-

Compliance with Treatment Schedule and Follow-up Assessment

- Advise the patient that it is necessary to complete the treatment schedule, including a follow-up assessment approximately 7 to14 days after taking MIFEPREX *[see Dosage and Administration (2.3)]*.
- Explain that
    - prolonged heavy vaginal bleeding is not proof of a complete abortion,
    - if the treatment fails and the pregnancy continues, the risk of fetal malformation is unknown,
    - it is recommended that ongoing pregnancy be managed by surgical termination *[see Dosage and Administration (2.3)]*. Advise the patient whether you will provide such care or will refer them to another provider.

Subsequent Fertility

- Inform the patient that another pregnancy can occur following medical abortion and before resumption of normal menses.
- Inform the patient that contraception can be initiated as soon as pregnancy expulsion has been confirmed, or before resuming sexual intercourse.

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Manufactured for:
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MEDICATION GUIDE

Mifeprex (MIF-eh-prex) (mifepristone tablets, for oral use

Read this information carefully before taking Mifeprex and misoprostol. It will help you understand how the treatment works. This Medication Guide does not take the place of talking with your healthcare provider.

What is the most important information I should know about Mifeprex?

What symptoms should I be concerned with? Although cramping and bleeding are an expected part of ending a pregnancy, rarely, serious and potentially life-threatening bleeding, infections, or other problems can occur following a miscarriage, surgical abortion, medical abortion, or childbirth. Seeking medical attention as soon as possible is needed in these circumstances. Serious infection has resulted in death in a very small number of cases. There is no information that use of Mifeprex and misoprostol caused these deaths. If you have any questions, concerns, or problems, or if you are worried about any side effects or symptoms, you should contact your healthcare provider. You can write down your healthcare provider's telephone number here _____.

Be sure to contact your healthcare provider promptly if you have any of the following:

- **Heavy Bleeding.** Contact your healthcare provider right away if you bleed enough to soak through two thick full-size sanitary pads per hour for two consecutive hours or if you are concerned about heavy bleeding. In about 1 out of 100 women, bleeding can be so heavy that it requires a surgical procedure (surgical aspiration or D&C).
- **Abdominal Pain or "Feeling Sick."** If you have abdominal pain or discomfort, or you are "feeling sick," including weakness, nausea, vomiting, or diarrhea, with or without fever, more than 24 hours after taking misoprostol, you should contact your healthcare provider without delay. These symptoms may be a sign of a serious infection or another problem (including an ectopic pregnancy, a pregnancy outside the womb).
- **Fever.** In the days after treatment, if you have a fever of 100.4°F or higher that lasts for more than 4 hours, you should contact your healthcare provider right away. Fever may be a symptom of a serious infection or another problem.

If you cannot reach your healthcare provider, go to the nearest hospital emergency room.

What to do if you are still pregnant after Mifeprex with misoprostol treatment. If you are still pregnant, your healthcare provider will talk with you about a surgical procedure to end your pregnancy. In many cases, this surgical procedure can be done in the office/clinic. The chance of birth defects if the pregnancy is not ended is unknown.

Talk with your healthcare provider. Before you take Mifeprex, you should read this Medication Guide and you and your healthcare provider should discuss the benefits and risks of your using Mifeprex.

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What is Mifeprex?

Mifeprex is used in a regimen with another prescription medicine called misoprostol, to end an early pregnancy. Early pregnancy means it is 70 days (10 weeks) or less since your last menstrual period began. Mifeprex is not approved for ending pregnancies that are further along. Mifeprex blocks a hormone needed for your pregnancy to continue. When you use Mifeprex on Day 1, you also need to take another medicine called misoprostol 24 to 48 hours after you take Mifeprex, to cause the pregnancy to be passed from your uterus.

The pregnancy is likely to be passed from your uterus within 2 to 24 hours after taking Mifeprex and misoprostol. When the pregnancy is passed from the uterus, you will have bleeding and cramping that will likely be heavier than your usual period. About 2 to 7 out of 100 women taking Mifeprex will need a surgical procedure because the pregnancy did not completely pass from the uterus or to stop bleeding.

Who should not take Mifeprex?

Some patients should not take Mifeprex. Do not take Mifeprex if you:

- Have a pregnancy that is more than 70 days (10 weeks). Your healthcare provider may do a clinical examination, an ultrasound examination, or other testing to determine how far along you are in pregnancy.
- Are using an IUD (intrauterine device or system). It must be taken out before you take Mifeprex.
- Have been told by your healthcare provider that you have a pregnancy outside the uterus (ectopic pregnancy).
- Have problems with your adrenal glands (chronic adrenal failure).
- Take a medicine to thin your blood.
- Have a bleeding problem.
- Have porphyria.
- Take certain steroid medicines.
- Are allergic to mifepristone, misoprostol, or medicines that contain misoprostol, such as Cytotec or Arthrotec.

Ask your healthcare provider if you are not sure about all your medical conditions before taking this medicine to find out if you can take Mifeprex.

What should I tell my healthcare provider before taking Mifeprex?

Before you take Mifeprex, tell your healthcare provider if you:

- cannot follow-up within approximately 7 to 14 days of your first visit
- are breastfeeding. Mifeprex can pass into your breast milk. The effect of the Mifeprex and misoprostol regimen on the breastfed infant or on milk production is unknown.
- are taking medicines, including prescription and over-the-counter medicines, vitamins, and herbal supplements.
  Mifeprex and certain other medicines may affect each other if they are used together. This can cause side effects.

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How should I take Mifeprex?

- Mifeprex will be given to you by a healthcare provider or pharmacy.
- You and your healthcare provider will plan the most appropriate location for you to take the misoprostol, because it may cause bleeding, cramps, nausea, diarrhea, and other symptoms that usually begin within 2 to 24 hours after taking it.
- Most women will pass the pregnancy within 2 to 24 hours after taking the misoprostol tablets.

Follow the instruction below on how to take Mifeprex and misoprostol:

Mifeprex (1 tablet) orally + misoprostol (4 tablets) buccally

Day 1:

- Take 1 Mifeprex tablet by mouth.

24 to 48 hours after taking Mifeprex:

- Take 4 misoprostol tablets by placing 2 tablets in each cheek pouch (the area between your teeth and cheek - see Figure A) for 30 minutes and then swallow anything left over with a drink of water or another liquid.
- The medicines may not work as well if you take misoprostol sooner than 24 hours after Mifeprex or later than 48 hours after Mifeprex.
- Misoprostol often causes cramps, nausea, diarrhea, and other symptoms. Your healthcare provider may send you home with medicines for these symptoms.

Figure A (2 tablets between your left cheek and gum and 2 tablets between your right cheek and gum).

Follow-up Assessment at Day 7 to 14:

- This follow-up assessment is very important. You must follow-up with your healthcare provider about 7 to 14 days after you have taken Mifeprex to be sure you are well and that you have had bleeding and the pregnancy has passed from your uterus.
- Your healthcare provider will assess whether your pregnancy has passed from your uterus. If your pregnancy continues, the chance that there may be birth defects is unknown. If you are still pregnant, your healthcare provider will talk with you about a surgical procedure to end your pregnancy.
- If your pregnancy has ended, but has not yet completely passed from your uterus, your provider will talk with you about other choices you have, including waiting, taking another dose of misoprostol, or having a surgical procedure to empty your uterus.

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When should I begin birth control?

You can become pregnant again right after your pregnancy ends. If you do not want to become pregnant again, start using birth control as soon as your pregnancy ends or before you start having sexual intercourse again.

What should I avoid while taking Mifeprex and misoprostol?

Do not take any other prescription or over-the-counter medicines (including herbal medicines or supplements) at any time during the treatment period without first asking your healthcare provider about them because they may interfere with the treatment. Ask your healthcare provider about what medicines you can take for pain and other side effects.

What are the possible side effects of Mifeprex and misoprostol?

Mifeprex may cause serious side effects. See "What is the most important information I should know about Mifeprex?"

Cramping and bleeding. Cramping and vaginal bleeding are expected with this treatment. Usually, these symptoms mean that the treatment is working. But sometimes you can get cramping and bleeding and still be pregnant. This is why you must follow-up with your healthcare provider approximately 7 to 14 days after taking Mifeprex. See "How should I take Mifeprex?" for more information on your follow-up assessment. If you are not already bleeding after taking Mifeprex, you probably will begin to bleed once you take misoprostol, the medicine you take 24 to 48 hours after Mifeprex. Bleeding or spotting can be expected for an average of 9 to16 days and may last for up to 30 days. Your bleeding may be similar to, or greater than, a normal heavy period. You may see blood clots and tissue. This is an expected part of passing the pregnancy.

The most common side effects of Mifeprex treatment include: nausea, weakness, fever/chills, vomiting, headache, diarrhea and dizziness. Your provider will tell you how to manage any pain or other side effects. These are not all the possible side effects of Mifeprex.

Call your healthcare provider for medical advice about any side effects that bother you or do not go away. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of Mifeprex.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. This Medication Guide summarizes the most important information about Mifeprex. If you would like more information, talk with your healthcare provider. You may ask your healthcare provider for information about Mifeprex that is written for healthcare professionals.

For more information about Mifeprex, go to www.earlyoptionpill.com or call 1-877-4 Early Option (1-877-432-7596).

Manufactured for: *Danco Laboratories, LLC*
P.O. Box 4816
New York, NY 10185
1-877-4 Early Option (1-877-432-7596) www.earlyoptionpill.com

This Medication Guide has been approved by the U.S. Food and Drug Administration. Approval 01/2023

EXHIBIT

202 FDA etter to AAP and Am. Coll.
of Pediatrician denying in part and granting
in part 20 Citi en Petition,
Doc et o. FDA 20 P 534
(Dec. , 202)

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December 16, 2021

Re: Docket No. FDA-2019-P-1534

Dear Drs. Harrison and Van Meter:

This letter responds to your citizen petition submitted to the Food and Drug Administration (FDA or Agency) on March 29, 2019, on behalf of the American Association of Pro-Life Obstetricians and Gynecologists and the American College of Pediatricians (Petition). In the Petition, you request that FDA: (1) restore and strengthen elements of the Mifeprex regimen and prescriber requirements approved in 2000, and (2) retain the Mifeprex Risk Evaluation and Mitigation Strategy (REMS) and continue limiting the dispensing of Mifeprex to patients in clinics, medical offices, and hospitals, by or under the supervision of a certified prescriber.

Specifically, in your Petition you request that the Agency:

(1) Restore and strengthen elements of the Mifeprex regimen and prescriber requirements approved in 2000, to include the following:

- Indications and Usage - Mifeprex, in a regimen with misoprostol, for the termination of intrauterine pregnancy, should be limited to 49 days gestation.

- Dosage and Administration:
  - Mifeprex should be administered by or under the supervision of a physically present and certified physician who has ruled out ectopic pregnancy.

  - The use of Mifeprex and misoprostol for the termination of pregnancy should require three office visits by the patient.

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- Contraindications - Mifeprex use is contraindicated for patients who do not have convenient access to emergency medical care.

- Adverse Event Reporting - Certified prescribers, emergency medical personnel, physicians treating complications, and Danco Laboratories should report to FDA's MedWatch Reporting system any deaths, hospitalizations, blood transfusions, emergency room visits, failures requiring surgical completion, ongoing pregnancy, or other major complications following the use of Mifeprex and misoprostol.

- Additional studies - The Mifeprex REMS should require a formal study of outcomes for at-risk populations, including: patients under the age of 18; patients with repeat Mifeprex abortions; patients who have limited access to emergency room services; and patients who self-administer misoprostol.

(2) Retain the Mifeprex REMS and continue limiting the dispensing of Mifeprex to patients in clinics, medical offices, and hospitals, by or under the supervision of a certified prescriber.

We have carefully considered the information submitted in your Petition and other relevant data available to the Agency. Based on our review of this information, your Petition is granted in part and denied in part.

I. BACKGROUND

A. Mifeprex

On September 28, 2000, FDA approved Mifeprex for the medical termination of intrauterine pregnancy through 49 days' pregnancy (new drug application (NDA) 020687). The application was approved under part 314, subpart H (21 CFR part 314, subpart H), "Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses" (subpart H). Specifically, § 314.520 of subpart H provides for approval with restrictions that are needed to assure the safe use of the drug product. In accordance with § 314.520, FDA restricted the distribution of Mifeprex as specified in the September 2000 approval letter.[1]

Subsequently, Mifeprex was identified as one of the products that was deemed to have in effect an approved REMS under the Food and Drug Administration Amendments Act of 2007 (FDAAA) because on the effective date of Title IX, subtitle A of FDAAA (March 28, 2008), Mifeprex had in effect elements to assure safe use.[2] Accordingly, in June 2011, we approved a REMS for Mifeprex, consisting of a Medication Guide, elements to assure safe use (ETASU), an implementation system, and a timetable for submission of assessments of the REMS.

Elements to assure safe use included: (1) prescriber certification (ETASU A); (2) that Mifeprex is dispensed only in certain healthcare settings by or under the supervision of a certified prescriber

[1] See https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2000/20687appltr.pdf.
[2] 73 FR 16313 (Mar. 27, 2008).

(ETASU C); and (3) that Mifeprex is dispensed only with documentation of safe use conditions (ETASU D). Documentation of safe use conditions consists of a Patient Agreement Form between the prescriber and the patient indicating that the patient has received counseling from the prescriber regarding the risk of serious complications associated with Mifeprex.

On March 29, 2016, we approved an efficacy supplement (S-020) to NDA 020687 for Mifeprex submitted by the applicant Danco Laboratories, LLC (S-020 efficacy supplement). The approval included changes in the dose of Mifeprex and the dosing regimen for taking Mifeprex and misoprostol (including the dose of misoprostol and a change in the route of misoprostol administration from oral to buccal (in the cheek pouch); the interval between taking Mifeprex and misoprostol; and the location at which the patient may take misoprostol). The approval also modified the gestational age up to which Mifeprex has been shown to be safe and effective, as well as the process for follow-up after administration of the drug.

Specifically, the following changes, among others, were made as part of the 2016 approval:[3]

- Revised the dosing regimen to consist of 200 mg of Mifeprex taken by mouth, followed in 24-48 hours by 800 mcg of misoprostol taken buccally (in the cheek pouch). This differs from the originally approved dosing regimen of 600 mg of oral Mifeprex followed 48 hours later by 400 mcg of oral misoprostol.

- Revised the indication for use of Mifeprex, in a regimen with misoprostol, to extend the maximum gestational age for the medical termination of intrauterine pregnancy from 49 days to 70 days.

- Reduced the number of office visits by the patient under the approved regimen from three to one.

- Replaced the term "physician" with the term "healthcare provider."

In addition, after reviewing the data and information submitted by the applicant in the S-020 efficacy supplement, and after taking into consideration the safety data that had become available since the initial approval of Mifeprex in 2000, we determined the Mifeprex REMS continued to be necessary to ensure the benefits of the product outweigh the risks. However, we approved modifications to the Mifeprex REMS that reflected the changes approved in the efficacy supplement. These changes to the REMS included, among others:[4]

- Updating the Prescriber Agreement Form to reflect the revised indication and dosing regimen.

- Removing the Medication Guide as a REMS element (but retaining the Medication Guide as labeling).

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[3] See https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2016/020687Orig1s020ltr.pdf and https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/020687s020lbl.pdf.

[4] See https://www.accessdata.fda.gov/drugsatfda_docs/nda/2016/020687Orig1s020RemsR.pdf.

- Removing the requirement that certified prescribers report certain enumerated adverse events to the applicant (specifically, any hospitalization, transfusion or other serious adverse events), but retaining the requirement that certified prescribers report all deaths to the sponsor.

Under the March 2016 approval, the Mifeprex REMS also continued to require that Mifeprex be dispensed to patients only in certain healthcare settings, specifically, clinics, medical offices, and hospitals, by or under the supervision of a certified prescriber.[5]

B. Generic Version of Mifeprex

On April 11, 2019, we approved GenBioPro, Inc.'s generic version of Mifeprex, Mifepristone Tablets, 200 mg (abbreviated new drug application (ANDA) 091178). This action took place after this Petition was submitted to the Agency. As required by 21 CFR 314.94(a)(8), GenBioPro's approved generic version of Mifeprex, Mifepristone Tablets, 200 mg, has the same labeling (with certain permissible differences) as the brand product it references, Mifeprex. Accordingly, although we refer to the Mifeprex labeling in several sections of this response, our discussions in this response apply equally to both the NDA and the generic product labeling, unless otherwise specifically noted.[6]

GenBioPro's generic version of Mifeprex is subject to the same ETASU as its listed drug (21 U.S.C. -1(i)). At the time we approved GenBioPro's generic version of Mifeprex, that ANDA product was required to use a single, shared system for the ETASU with the brand drug product, Mifeprex, unless the requirement was waived by FDA (21 U.S.C. 355-1(i)). FDA did not waive this requirement. Accordingly, at the same time that FDA approved GenBioPro's generic version of Mifeprex in 2019, FDA approved a supplemental new drug application (sNDA) for Mifeprex, approving modifications to the existing, approved REMS for Mifeprex to establish a single, shared system REMS for mifepristone products for the medical termination of intrauterine pregnancy through 70 days gestation (referred to as the Mifepristone REMS Program). In establishing the single, shared system REMS in 2019, no substantive changes were made to the ETASU in the March 2016 Mifeprex REMS. References to the REMS in this response refer to the Mifepristone REMS Program established in 2019, unless otherwise noted.

C. In-Person Dispensing Requirement During the COVID-19 PHE

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[5] See https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2016/020687Orig1s020ltr.pdf.

[6] We note that Korlym and the generic version of Korlym (Mifepristone Tablets, 300 mg) contain the same active ingredient – mifepristone - as Mifeprex and the generic version of Mifeprex (Mifepristone Tablets, 200 mg). Although these drug products contain the same active ingredient, their intended uses target different receptors, and the products have different strengths and use different dosing regimens. Korlym and the generic version of Korlym are approved for the control of hyperglycemia (high blood sugar levels) due to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes or glucose intolerance, and have failed surgery or are not candidates for surgery. References to mifepristone in this response refer to the use of mifepristone for the medical termination of intrauterine pregnancy through 70 days gestation, unless otherwise noted.

FDA has recognized that during the COVID-19[7] public health emergency (PHE),[8] certain REMS requirements for various products may be difficult to comply with because patients may need to avoid public places and patients suspected of having COVID-19 may be self-isolating and/or subject to quarantine. The Agency has also received queries concerning products with REMS that have ETASUs, including REMS with ETASUs that restrict distribution, and the impact of such ETASUs on patient access when patients self-isolate or are subject to quarantine.

In April 2021, FDA communicated its intent to exercise enforcement discretion during the COVID-19 PHE regarding the requirement in the Mifepristone REMS Program that mifepristone used for medical termination of intrauterine pregnancy through 70 days gestation be dispensed to patients by or under the supervision of a certified prescriber only in certain healthcare settings, specifically clinics, medical offices, and hospitals (referred to as the "in-person dispensing requirement").

Specifically, FDA communicated that provided all other requirements of the Mifepristone REMS Program are met, the Agency intends to exercise enforcement discretion with respect to the in-person dispensing requirement of the Mifepristone REMS Program, including any in-person requirements that may be related to the Patient Agreement Form, during the COVID-19 PHE. This determination, which FDA made on April 12, 2021, was effective immediately. We also note that from July 13, 2020 to January 12, 2021, per a court order, FDA was enjoined from enforcing the in-person dispensing requirement of the Mifepristone REMS Program.[9]

Further, and as we also communicated on April 12, 2021, to the extent all of the other requirements of the Mifepristone REMS Program are met, the Agency intends to exercise enforcement discretion during the COVID-19 PHE with respect to the dispensing of Mifeprex or the approved generic version of Mifeprex, Mifepristone Tablets, 200 mg, through the mail, either by or under the supervision of a certified prescriber, or through a mail-order pharmacy when such dispensing is done under the supervision of a certified prescriber.

FDA's intent to exercise enforcement discretion with respect to these requirements during the COVID-19 PHE was the result of a thorough scientific review by experts within FDA's Center for Drug Evaluation and Research (CDER), who evaluated relevant information, including available clinical outcomes data and adverse event reports.

D. Minor Modification

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[7] The virus has been named "SARS-CoV-2" and the disease it causes has been named "Coronavirus Disease 2019" (COVID-19).

[8] Secretary of Health and Human Services, Determination that a Public Health Emergency Exists (originally issued Jan. 31, 2020, and subsequently renewed), *available at* https://www.phe.gov/emergency/news/healthactions/phe/Pages/default.aspx.

[9] *Am. Coll. of Obstetricians & Gynecologists v. FDA*, 472 F. Supp. 3d 183, 233 (D. Md. July 13, 2020), order clarified, 2020 WL 8167535 (D. Md. Aug. 19, 2020) (preliminarily enjoining FDA from enforcing the in-person dispensing requirement and any other in-person requirements of the Mifepristone SSS REMS); *FDA v. Am. Coll. of Obstetricians & Gynecologists*, 141 S. Ct. 578 (Jan. 12, 2021) (staying the preliminary injunction imposed by the District Court).

In response to a request submitted by the applicants, FDA approved a minor modification to the Mifepristone REMS Program on May 14, 2021. This minor modification revised the Patient Agreement Form to use gender neutral language. Specifically, the pronouns "she" and "her" in the Patient Agreement Form were replaced with "the patient." The minor modification also included revisions to the REMS document to be consistent with the revisions to the Patient Agreement Form. These changes did not affect the substance of the Patient Agreement Form, the REMS document, or the Mifepristone REMS Program.

E. Review of the Mifepristone REMS Program

In 2021, FDA also undertook a full review of the Mifepristone REMS Program.[10] In conducting this review, FDA reviewed multiple different sources of information, including published literature, safety information submitted to the Agency during the COVID-19 PHE, FDA Adverse Event Reporting System (FAERS) reports, the first REMS assessment report for the Mifepristone REMS Program, and information provided by advocacy groups, individuals, and the Plaintiffs in ongoing litigation, as well as information submitted by the sponsors of the NDA and the ANDA (together, the Applicants). As discussed in more detail below, based on our review of this information, FDA has determined that certain elements of the Mifepristone REMS Program remain necessary to assure the safe use of mifepristone for medical termination of intrauterine pregnancy through 70 days gestation; and therefore, the Mifepristone REMS Program continues to be necessary to ensure the benefits outweigh the risk. Specifically, we find that the healthcare provider certification and dispensing of mifepristone to patients with evidence or other documentation of safe use conditions continue to be necessary components of the REMS to ensure the benefits of mifepristone outweigh the risks for this indication.

We also find that the in-person dispensing requirement is no longer necessary to assure the safe use of mifepristone for medical termination of intrauterine pregnancy through 70 days gestation. We have concluded that mifepristone will remain safe and effective for medical abortion if the in-person dispensing requirement is removed, provided all the other requirements of the REMS are met and pharmacy certification is added.[11] Removing the in-person dispensing requirement will render the REMS less burdensome to healthcare providers and patients, and provided all other requirements of the REMS are met, including the additional requirement for pharmacy certification, the REMS will continue to ensure that the benefits of mifepristone for medical abortion outweigh the risks. Accordingly, today we are sending a REMS Modification Notification letter to both Applicants in the Mifepristone REMS Program. As stated in that letter, FDA has concluded that a modification is necessary and must include the following changes:

- Removing the requirement that mifepristone be dispensed only in certain healthcare settings, specifically clinics, medical offices, and hospitals.

[10] We note that the Agency is in litigation regarding the Mifepristone REMS Program and committed to conducting a full review of the Mifepristone REMS Program, including reviewing any relevant data and evidence submitted to the Agency by the Plaintiffs in that litigation (*Chelius et al v. Becerra*, Joint Mot. to Stay Case Pending Agency Review, ECF No. 148, May 7, 2021, Civ. No. 1:17-00493 (D. Haw.)).

[11] Although we have determined that the Mifepristone REMS Program must be modified to add a requirement for pharmacy certification, this was not raised in your Petition and therefore is not discussed further in this response.

- Adding a requirement that pharmacies that dispense the drug be specially certified.

II. DISCUSSION OF ISSUES RAISED

A. Mifeprex Regimen

1. Indications and Usage

In the Petition, you ask FDA to restore and strengthen elements of the Mifeprex regimen and prescriber requirements approved in 2000, to limit Mifeprex, in a regimen with misoprostol, for the termination of intrauterine pregnancy, to 49 days gestation (Petition at 1 and 3). For the reasons explained below, we deny this request.

Citing to a 2011 study and a practice bulletin issued by the American College of Obstetricians and Gynecologists (ACOG), you state that medical abortion[12] regimens demonstrate an increase in complications and failures, including serious risks of hemorrhage, infection, and ongoing pregnancy, after 49 days gestation (Petition at 3-4).

Our review of the S-020 efficacy supplement in 2016 concluded that Mifeprex, in a regimen with misoprostol, is safe and effective for medical termination of intrauterine pregnancy through 70 days gestation.[13] Complete medical abortion rates from the pivotal clinical trials relied on for the initial approval of Mifeprex (with an indication for medical termination of intrauterine pregnancy through 49 days gestation) were 92.1 percent and 95.5 percent in the United States and French trials, respectively.[14] The studies reviewed in support of the 2016 approval for Mifeprex (with an indication for medical termination of intrauterine pregnancy through 70 days gestation) showed comparable efficacy. The 2016 Clinical Review of the S-020 efficacy supplement summarized clinical outcomes and adverse effects from 22 studies (7 in the United States and 15 from outside the United States) through 70 days gestation, using the currently approved regimen of 200 mg oral mifepristone with 800 mcg buccal misoprostol. The ranges of complete medical abortion rates calculated by the clinical reviewer were 93.2 percent to 98.7 percent in the United States studies, and 92 percent to 98 percent in the non-United States studies.[15]

Serious adverse events associated with the use of mifepristone through 70 days gestational age are rare. Per the current mifepristone labeling, the rates of serious adverse events are low: transfusions are 0-0.1 percent, sepsis is less than 0.01 percent, hospitalization related to medical abortion is 0-0.7 percent, and hemorrhage is 0.1 percent.[16] As discussed

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[12] In this response, the terms "medical abortion" and "medication abortion" both refer to the use of mifepristone, in a regimen with misoprostol, for the medical termination of intrauterine pregnancy.
[13] See 2016 Clinical Review available at https://www.accessdata.fda.gov/drugsatfda_docs/nda/2016/020687Orig1s020MedR.pdf, at 32-38 and 47-47.
[14] See 1999 Medical Officer's Review, available at http://www.accessdata.fda.gov/drugsatfda_docs/nda/2000/20687_Mifepristone_medr_P1.pdf, at 11 (Table 1) and 16.
[15] See 2016 Clinical Review, supra n. 13, at 28-31.
[16] See https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/020687s022lbl.pdf.

throughout this response, the benefit/risk assessment supported our 2016 conclusion that the product is safe and effective through 70 days gestation.

In support of your assertion that medical abortion demonstrates an increase in complications after 49 days gestation, you cite to Mentula, et al.,[17] a register-based, retrospective cohort study that included 18,248 women in Finland who underwent medical abortion between January 1, 2003, and December 31, 2006 (Petition at 3). As an initial matter, we note that the Mentula study was primarily designed to assess the immediate adverse events following medical abortion in the second trimester (13 to 24 gestational weeks as defined by the authors) and then compare those events to those identified with medical abortion in the first trimester (up to 12 gestational weeks as defined by the authors). The study was not designed to compare rates of complications across gestational weeks within the first trimester. It is true that the Mentula publication includes information on the percentages of women who had surgical evacuation following medical abortion and the percentages of women who had infection following medical abortion, based on weekly gestational age, from 5 weeks to 20 weeks gestation.[18] However, the data in the Mentula study are relatively old (2003-2006); in our 2016 review of the S-020 efficacy supplement, we conducted an extensive review of more recent data[19] and concluded that Mifeprex, in a regimen with misoprostol, is safe and effective for medical termination of intrauterine pregnancy through 70 days gestation.

You also cite to ACOG Practice Bulletin No. 143, which states: "the risk of clinically significant bleeding and transfusion may be lower in women who undergo medical abortion of gestations up to 49 days compared with those who undergo medical abortion of gestations of more than 49 days."[20] This statement is based on a 1998 publication which evaluated patients undergoing medical abortion with mifepristone 600 mg and then oral misoprostol 400 mcg two days later.[21] The regimen studied in this 1998 publication is not the currently approved regimen for mifepristone in the United States. Further, ACOG Practice Bulletin No. 143 has been withdrawn and replaced by Practice Bulletin No. 225, which was published in October 2020 and no longer contains this statement.[22]

You also state that the failure rate of the approved regimen (which you refer to as the "buccal misoprostol regimen") increases as the gestational age increases, especially at

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[17] Mentula MJ, Niinimake M, Suhonen S, et al. Immediate Adverse Events After Second Trimester Medical Termination of Pregnancy: Results of a nationwide registry study, Human Reproduction. 2011;26(4):927-932.
[18] Id. at Fig. 2 and Fig. 3. Surgical intervention after medical abortion and infection after medical abortion are two distinct adverse events. The calculation of abortion completion rates accounts for the need for surgical intervention. In clinical studies we reviewed, success of medical abortion was defined as the complete expulsion of the products of conception without the need for surgical intervention.
[19] See 2016 Cross-Discipline Team Leader Review, available at https://www.accessdata.fda.gov/drugsatfda_docs/nda/2016/020687Orig1s020CrossR.pdf, at 37 (Table 4).
[20] Petition at 3. See Medical Management of First-Trimester Abortion. ACOG Practice Bulletin Number 143. March 2014 (Reaffirmed 2016. Replaces Practice Bulletin Number 67, October 2005); Obstet Gynecol. 2014 Mar;123(3):676-692 at 680.
[21] Spitz I, Bardin CW, Benton L, Robbins A. Early pregnancy termination with mifepristone and misoprostol in the United Sates, NEJM. 1998;338 (18):1241-1247.
[22] See ACOG Practice Bulletin No. 225. Medication Abortion Up to 70 Days of Gestation. Obstetrics and Gynecology 2020; 136(4); e31 to e47.

gestational ages greater than 49 days, relying on a 2015 meta-analysis,[23] and that the gestational limit should not have been increased (Petition at 3-4). We agree that the failure rate of medical abortion regimens, including the currently approved regimen, generally increases with increasing gestational age. However, the increase in failure rate with each incremental week of gestation, as described in approved mifepristone labeling and in this 2015 meta-analysis, is small, and we believe that the benefit/risk profile for medical termination of intrauterine pregnancy between 49 and 70 days gestation remains acceptable.

For these reasons, we deny your request that FDA limit mifepristone, in a regimen with misoprostol for the termination of intrauterine pregnancy, to 49 days gestation.

2. Dosage and Administration

a. Prescriber Qualifications

You state that FDA should limit the "ability" to prescribe and dispense Mifeprex to qualified, licensed physicians, rather than permitting non-physicians to apply to be certified prescribers, because of the regimen's serious risks and because physicians are better trained to diagnose patients who have contraindications to Mifeprex and to verify gestational age (Petition at 4). We do not agree.

Healthcare providers who are licensed to prescribe can become certified in REMS programs if they are able to meet the applicable REMS requirements. To become certified to prescribe mifepristone under the Mifepristone REMS Program, the prescriber must review the prescribing information for mifepristone and complete a Prescriber Agreement Form. By signing the form, the prescriber agrees that they meet certain qualifications, including the ability to date pregnancies accurately and to diagnose ectopic pregnancies. These healthcare providers must also: (1) be able to provide any necessary surgical intervention or have made arrangements for others to provide for such care; or (2) be able to assure patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary.[24]

In our review of the S-020 efficacy supplement in 2016, we determined that available data support that Mifeprex is safe and effective when prescribed by midlevel providers, such as physician assistants and nurse practitioners, as well as by physicians.[25] Our 2016 review included four studies that evaluated the safety and efficacy of medical abortion when performed by non-physician healthcare providers. Two trials evaluated the currently

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[23] Petition at 4, fn. 6 (citing Chen MJ, Creinin MD, *Mifepristone with Buccal Misoprostol for Medical Abortion*, Obstet. Gynecol 126 (1) July 2015 12-21).

[24] See https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/020687s022lbl.pdf; see also https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=RemsDetails.page&REMS=390.

[25] See 2016 Clinical Review, supra n. 13, at 79; see also 2016 Cross-Discipline Team Leader Review, supra n. 19, at 17-18. We also note that in most states, midlevel clinicians, such as physician assistants and nurse practitioners, are licensed to prescribe medications.

approved Mifeprex and buccal misoprostol regimen (Olavarrieta and Kopp Kallner);[26,27] one trial studied a regimen using vaginal misoprostol (Warringer);[28] a fourth study did not specify the route of misoprostol administered (Puri).[29] Olavarrieta reported a completion rate of 97.9 percent when medical abortion was provided by nurses as compared with 98.4 percent with physicians. Kopp Kallner reported a completion rate of 99 percent with certified nurse midwives versus 97.4 percent with physicians. Warriner reported an abortion completion rate of 97.4 percent with nurses as compared with 96.3 percent with physicians. Puri reported an abortion completion rate of 96.8 percent when the service was provided by nurse-midwives as compared with 97.4 percent in the "standard care" group.[30] Our 2016 review also included a systematic review of six controlled clinical studies by Renner;[31] the authors concluded that the evidence "indicates that trained mid-level providers may effectively and safely provide first trimester surgical and medical termination of pregnancy services." Additionally, Barnard et al., in a Cochrane systematic review, assessed the safety and effectiveness of abortion procedures administered by mid-level providers (nurse practitioners, midwives, other non-physician healthcare providers) compared to doctors.[32] The authors concluded, based in part on two of the studies that we had reviewed in 2016,[33] that there was no statistically significant difference in the risk of failure for medical abortions performed by mid-level providers compared with doctors.

We also believe that the identification of patients for whom the use of mifepristone is contraindicated can be done by mid-level healthcare providers, as well as physicians. Mifepristone in a regimen with misoprostol for medical termination of intrauterine pregnancy through 70 days gestation is contraindicated in patients with any of the following conditions:[34]

- Confirmed or suspected ectopic pregnancy or undiagnosed adnexal mass

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[26] Olavarrieta CD, Ganatra B, Sorhaindo A, et al. Nurse versus Physician-provision of Early Medical Abortion in Mexico: A Randomized Controlled Non-Inferiority Trial. Bull World Health Organ. 2015;93:249-258.

[27] Kopp Kallner H, Gomperts R, Salomonsson E, et al. The efficacy, safety and acceptability of medical termination of pregnancy provided by standard care by doctors or by nurse-midwives: a randomised controlled equivalence trial. BJOG. 2015; 122: 510-517.

[28] Warriner IK, Wang D, et al. Can midlevel health-care providers administer early medical abortion as safely and effectively as doctors? A randomized controlled equivalence trial in Nepal. Lancet. 2011; 377: 1155-61.

[29] Puri M, Tamang A, Shrestha P, et al. The role of auxiliary nurse-midwives and community health volunteers in expanding access to medical abortion in rural Nepal. Reproductive Health Matters. 2015; 22(44) 94-103.

[30] 2016 Clinical Review, supra n. 13, at 43.

[31] Renner RM, Brahmi D, Kapp N. Who can provide effective and safe termination of pregnancy care? A systematic review. BJOG 2013 Jan;120(1):23-31.

[32] Barnard S, Kim C, Park MN, Ngo TD. Doctors or mid-level providers for abortion (Review). Cochran Database of Systematic Reviews. 2015, Issue 7.

[33] Of the medical abortion studies reviewed by Barnard et al (Id.), two were reviewed by the Agency as part of the review of the S-020 supplement in 2016. See Warriner et al (supra n. 28) and Kopp Kallner et al (supra n. 27). The third used a different dose of misoprostol than the currently approved regimen. See Jejeebhoy SJ, Kalyanwalaa S, Zaviera AJF, Kumara R, Mundleb S, Tankc J, et al. Feasibility of expanding the medication abortion provider based in India to include avurvedic physicians and nurses. International Perspectives on Sexual and Reproductive Health 2012;38(3)133-42)

[34] See https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/020687s022lbl.pdf.

- An intrauterine device in place
- Chronic adrenal failure
- Concurrent long-term corticosteroid therapy
- History of allergy to mifepristone, misoprostol, or other prostaglandins
- Hemorrhagic disorder or concurrent anticoagulant therapy
- Inherited porphyrias

These contraindications can be assessed by trained healthcare providers who prescribe mifepristone by obtaining a medical history, from medical records, and/or from physical examination or ultrasound if appropriate. We continue to believe that available data support the conclusion that mid-level healthcare providers, as well as physicians, possess the clinical and counseling skills necessary to provide medical abortion. We note this is consistent with ACOG's statement in its current practice bulletin that "[i]n addition to physicians, advanced practice clinicians, such as nurse-midwives, physician assistants, and nurse practitioners, possess the clinical and counseling skills necessary to provide first-trimester medical abortion."[35] Further, if necessary, ultrasound training and certification is available to nurse practitioners and physician assistants, as well as physicians.[36] In sum, available information supports that mid-level healthcare providers as well as physicians can determine whether mifepristone is an appropriate treatment for a particular patient and dispense it.

You also assert that FDA should strengthen the requirement that providers accurately assess the duration of the pregnancy by mandating that gestational age be assessed by ultrasound (Petition at 5). We refer you to FDA's 2016 Response to the citizen petition submitted to Docket No. FDA-2002-P-0364 (the "2016 CP Response"), where FDA stated that the determination of gestational age does not always require an ultrasound. In the 2016 CP Response, FDA stated it had "determined that it was inappropriate for us to mandate how providers clinically assess women for duration of pregnancy and for ectopic pregnancy. These decisions should be left to the professional judgment of each provider, as no method (including TVS [transvaginal ultrasound]) provides complete accuracy. The approved labeling for Mifeprex recommended ultrasound evaluation as needed, leaving this decision to the judgment of the provider."[37]

In the Petition, you reference the Prescriber Agreement Form, in which the provider must attest they have the ability to: (1) accurately assess the duration of the pregnancy; (2) diagnose ectopic pregnancies; and (3) provide surgical intervention if needed (or have made plans to provide such care through others), and you state that a provider who does not physically meet with and examine a patient, but simply consults with the patient over the Internet, is not capable of fulfilling these requirements, or of ruling out additional

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[35] ACOG Practice Bulletin No. 225, supra n. 22.

[36] American Institute of Ultrasound in Medicine. Accessed November 26, 2021. https://www.aium.org/officialStatements/70.

[37] FDA's citizen petition response dated March 29, 2016, to the citizen petition submitted by the American Association of Pro-Life Obstetricians and Gynecologists, the Christian Medical and Dental Association, and Concerned Women for America on August 20, 2002, Docket No. FDA-2002-P-0364 at 18. See https://www.regulations.gov/document/FDA-2002-P-0364-0002.

contraindications (Petition at 5-6). You state that FDA should require certified prescribers to be physically present when Mifeprex is dispensed so that they can appropriately examine patients and rule out contraindications to the use of Mifeprex (Petition at 4).

Certified prescribers do not have to be physically present with the patient as long as they have confirmed the patient's gestational age and intrauterine pregnancy. As noted above, in the 2016 CP response, FDA "determined that it was inappropriate for us to mandate how providers clinically assess women for duration of pregnancy and for ectopic pregnancy."[38] Moreover, the evaluation of patients for contraindications to medical abortion does not necessarily require direct physical contact with the certified prescriber and can be done in different types of healthcare settings. A certified prescriber can also review the Patient Agreement Form[39] with the patient, fully explain the risks of the mifepristone treatment regimen, and answer any questions, as in any consent process, without physical proximity. See also section II.B.1.c (ETASU C – In-person Dispensing).

With respect to providing surgical intervention in cases of incomplete abortion or severe bleeding and assuring patient access to medical facilities equipped to provide blood transfusions and resuscitation (if necessary), the Prescriber Agreement Form does not reflect a requirement that the certified prescriber must provide such care personally; rather, the prescriber must agree that they have the ability to provide such care or that they have made plans to provide such care through others, and that they have the ability to assure the patient has access to appropriate medical facilities. It is common practice for healthcare providers to provide emergency care coverage for other healthcare providers' patients, and in many places, hospitals employ "hospitalists" to provide care to all hospitalized patients. We also note ACOG's statement that "[i]n rare cases, a patient who undergoes a medication abortion may need to obtain an additional intervention, such as uterine aspiration. If the prescribing clinician does not perform the intervention, it is medically appropriate to provide a referral."[40]

For these reasons, we deny your request that FDA limit the "ability" to prescribe and dispense mifepristone to licensed physicians, and we deny your request that FDA require certified providers to physically meet with and examine the patient.

b. Office Visits and Administration of Mifepristone/Misoprostol

In the Petition, you state that the use of mifepristone and misoprostol should require three office visits by the patient (Petition at 7). In support of this position, you state the following:

- Drug-induced abortion is contraindicated for patients who are not available for follow-up contact or evaluation (Petition at 10).

[38] Id.
[39] See https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=RemsDetails.page&REMS=390.
[40] ACOG Practice Bulletin Number 225 supra n. 22.

- Abortion complications are more frequent when women abort at home and more healthcare oversight is needed (Petition at 8).

- Home administration of misoprostol does not permit healthcare providers to control when their patients take misoprostol and without monitoring:

    - a patient may take buccal misoprostol before the minimum 24-hour period after taking Mifeprex, which leads to a significantly increased failure rate (Petition at 7).

    - a patient may swallow misoprostol rather than administer it buccally, and oral administration is not as effective as buccal administration in ending the pregnancy (Petition at 7).

- Because providers may now "confirm" that a patient's drug-induced abortion was successful without a clinic visit, this increases the threat that Rh-negative patients will not receive Rhogam, which is necessary to prevent serious risks in subsequent pregnancies (Petition at 7 and 9).

We address each of these points below.

i. Follow-up Care

The safe use of mifepristone when used in the approved regimen with misoprostol is not contingent on a specific number of office visits being made by the patient undergoing a medical termination of pregnancy. The 2016 labeling change for Mifeprex regarding post-treatment assessment, including the change to the approved regimen to reduce the number of offices visits from three to one, was based on evidence reviewed in the S-020 efficacy supplement. We concluded, upon reviewing the data, that three office visits were not necessary to assure the safe use of Mifeprex.[41]

In your Petition, you point to statements by ACOG that medical abortion is contraindicated for patients who are not available for follow-up contact or evaluation (Petition at 8, 10). The ACOG statements you point to are from ACOG Practice Bulletin No. 143, which has been withdrawn and replaced by Practice Bulletin No. 225.[42] Neither of the statements from the withdrawn Practice Bulletin nor Practice Bulletin No. 225 contraindicate medical abortion in women who are not available for an in-clinic follow-up visit. The current ACOG recommendations indicate that for medical abortion, "[f]ollow-up can be performed by telephone at 1 week, with subsequent at-home urine pregnancy testing at 4 weeks after treatment, which avoids the need for the patient to go to a facility."[43] The patient and their healthcare provider should determine the best option for follow-up as part of the consultation and consent process.[44] As reflected in ACOG's guidance, appropriate follow-

[41] See 2016 Clinical Review, supra n. 13, at 44 and 64-67.
[42] ACOG Practice Bulletin Number 225, supra n. 22.
[43] Id.
[44] Id.

up after medical termination of a pregnancy may be accomplished in multiple ways and not all require an in-clinic visit.

You also question findings in multiple studies that evaluated the effectiveness of semiquantitative urine pregnancy tests (multi-level pregnancy tests, or MLPT) and low sensitivity urine pregnancy tests (LSPT) to rule out on-going pregnancies and assessed the ability of patients to self-administer these tests and interpret the test results (Petition at 9-10). Overall, these studies concluded that in the majority of women, it is feasible to use a simplified test to determine if further follow-up is necessary. A recent systematic review and meta-analysis by Baiju assessed the effectiveness and safety of self-assessment of the outcome of medical abortion completed at home versus routine clinic follow-up after medical abortion, concluding self-assessment was not inferior to routine clinic follow-up.[45] We note that this is consistent with current ACOG recommendations, which state that "follow-up can be performed by telephone at 1 week, with subsequent at-home urine pregnancy testing at 4 weeks after treatment, which avoids the need for the patient to go to a facility."[46]

You also assert that it is important for a patient to be under observation after taking misoprostol to ensure that they are appropriately monitored and provided sufficient pain medication (Petition at 8). You cite the World Health Organization (WHO)'s statement in guidance that up to 90 percent of women will abort within 4-6 hours after taking misoprostol; you further state that the 2000 regimen permitted patients to be in the clinic during this time period (Petition at 8). Your reference to the WHO guidance document[47] appears to be out of context. The WHO guidance takes no position on whether women should return to and remain in the clinic during a follow-up visit for purposes of taking misoprostol; in fact, it explicitly recognizes that post-abortion care may not require a follow-up visit if the patient is adequately counseled.[48] In the United States, and as reflected in the approved labeling, medical termination of pregnancy usually involves patients terminating the pregnancy at home, with appropriate follow-up that may not include a return visit.

ii. At Home Medical Abortion and Healthcare Oversight

In addition, you cite a 2018 study to support your statement that abortion complications are more frequent when women abort at home (Petition at 8). The study evaluated complications following medical abortion (both less than 12 weeks and more than 12 weeks gestation) as well as following surgical abortion, at one hospital in Sweden between 2008 and 2015.[49] For the years 2008 to 2010, data were collected retrospectively; for the years

[45] Baiju, N, Acharya, G, D'Antonio, F, et al. 2019. Effectiveness, safety and acceptability of self-assessment of the outcome of first-trimester medical abortion: a systematic review and meta-analysis. BJOG; 126:1536-1544.
[46] ACOG Practice Bulletin Number 225, supra n. 22.
[47] World Health Organization, Safe Abortion: technical and policy guidance for health systems – 2nd edition. 2012. Page 45 and Section 2.2.2.1 Medication for pain.
[48] Id. at Section 2.3 Post-abortion care and follow-up, at 52.
[49] Carlsson I, Breding K, Larsson PG, 2018, Complications Related to Induced Abortion: A Combined Retrospective and Longitudinal Follow-up Study, BMC Women's Health 18:158.

2011 to 2015, data were collected prospectively. In this study, medical abortions after 12 gestational weeks all occurred at the hospital. The authors report that, among medical abortions less than 12 weeks, the complication frequency increased from 5.4 percent (2008 to 2010) to 8.2 percent (2015). However, the authors also compared the complications related to medical abortions that occurred at less than 12 gestational weeks between "at home" abortions (managed as an outpatient) and "at the hospital" abortions, in 2015 and found no statistically significant difference (8.2 percent "at home" versus 8.0 percent at the hospital). For pregnancies less than or equal to 9 gestational weeks, the rates are similar for the "at home" group (10.0 percent) and the "at the hospital" group (9.3 percent). Notably, as part of our review and approval of the S-020 efficacy supplement in 2016, we assessed serious adverse events by gestational age, including hospitalizations, serious infection requiring hospitalization or intravenous antibiotics, bleeding requiring transfusion, and ectopic pregnancy, as reported in the literature submitted by the Applicant. We concluded that these serious adverse events are rarely reported in the literature and that the regimen of mifepristone 200 mg followed by buccal misoprostol 800 mcg in 24-48 hours is safe to approve for use through 70 days gestation.[50]

You also state that medical abortion is a longer process than surgical abortion and that it requires more attention and care from healthcare providers (Petition at 10). We agree that medical abortion can be a longer process than surgical abortion,[51] but we disagree that medical abortion always requires in-person follow-up with a healthcare provider. Not all of the complications associated with medical abortion necessarily require more intensive management from healthcare providers during a follow-up visit. The question of whether to include an in-person follow-up visit should be discussed by the healthcare provider and the patient. We have concluded that medical abortions are safe and effective for patients who are appropriate candidates and reducing the number of clinic visits does not compromise patient safety.

The current approved labeling for mifepristone for medical termination of pregnancy states that complete pregnancy termination "can be confirmed by medical history, clinical examination, human Chorionic Gonadotropin (hCG) testing, or ultrasonographic scan." Not all these modalities require an in-clinic assessment during a follow-up visit. Our review of the S-020 efficacy supplement concluded that "available data support … that there are a variety of follow-up modalities that can adequately identify the need for additional intervention."[52] We note that these findings are also consistent with ACOG guidelines, which state that "[r]outine in-person follow-up is not necessary after uncomplicated medication abortion" and recommend several methods for post-treatment follow-up, as appropriate, including serial serum hCG testing alone or telephone follow-up at one week after treatment followed by urine pregnancy testing at four weeks after treatment.[53] Because there is more than one effective method to detect an on-going pregnancy, we conclude that the way in which post-treatment follow-up is performed may be determined by the healthcare provider and the patient.

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[50] 2016 Clinical Review, supra n. 13, at 51-57.
[51] See ACOG Practice Bulletin Number 225, supra note 22.
[52] 2016 Cross Discipline Team Leader Review, supra n. 19, at 17.
[53] ACOG Practice Bulletin Number 225, supra note 22.

iii. Misoprostol

In the Petition, you make a number of assertions regarding the use of misoprostol. We address each in turn.

First, you assert that a patient may take misoprostol before the prescribed minimum 24-hour period after taking Mifeprex, thereby rendering the regimen ineffective, and that home administration of misoprostol does not permit health providers to control when their patients take misoprostol (Petition at 7). You similarly assert that the use of buccal misoprostol sooner than 24 hours after administering mifepristone leads to significantly increased failure rates (Petition at 7).

As an initial matter, our review of the S-020 efficacy supplement in 2016 included data that evaluated the home use of misoprostol in over 30,000 women. The data showed that Mifeprex was safe and effective in a regimen with misoprostol when misoprostol was self-administered at home.[54] Therefore, any incorrect administration resulting in a failed abortion was infrequent and did not significantly affect the safety and efficacy of medical abortion. Furthermore, because the process of expelling the pregnancy may begin as soon as 2 hours after taking misoprostol, there is a benefit in allowing patients to choose when and where to start this process, to maximize the possibility of their being at a safe place at a convenient time to experience cramping and bleeding.[55]

In support of your assertion of significantly increased failure rates, you cite a pilot study by Lohr et al.[56] Lohr et al. assessed the complete abortion rate using simultaneous oral mifepristone and buccal misoprostol in three gestational age groupings (less than or equal to 49 days, 50-56 days, 57-63 days) and compared the rates with those published in previous pilot investigations[57] using simultaneous oral mifepristone and vaginal misoprostol in the same three gestational age groupings. The complete abortion rates reported by Lohr at 24 hours for oral mifepristone and buccal misoprostol were 72.5 percent, 69.2 percent, and 72.5 percent, respectively; the complete abortion rates at two weeks, however, were 97.5 percent, 100 percent, and 94.9 percent, respectively (and are consistent with the completion rates as described in the approved labeling).[58] The published complete abortion rates at 24 hours for simultaneous oral mifepristone and vaginal misoprostol administration were 90 percent, 88 percent, and 83 percent, respectively, for the gestational age groupings and the complete abortion rates at 2 weeks were 98 percent, 93 percent, 90 percent, respectively. Based on the data presented in Lohr,

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[54] See 2016 Clinical Review, supra n. 13, at 41 and 48.
[55] Id. at 38.
[56] Petition at 7 (referencing Lohr PA, Reeves MF, Hayes JL, et al., 2007, Oral Mifepristone and Buccal Misoprostol Administered Simultaneously for Abortion: A Pilot Study, Contraception, 76:215-220).
[57] Schreiber CA, Creinin MD, Harwood B, Murthy AS. A pilot study of mifepristone and misoprostol administered at the same time for abortion in women with gestation from 50 to 63 days. Contraception 2005;71:447–50; Murthy AS, Creinin MD, Harwood B, Schreiber C. A pilot study of mifepristone and misoprostol administered at the same time for abortion up to 49 days gestation. Contraception 2005;71:333–6.
[58] See https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/020687s022lbl.pdf.

the use of buccal misoprostol at the same time as oral mifepristone does not adversely affect efficacy, although expulsion may be delayed. As recommended in Section 2.3 of the approved labeling, follow-up at 7-14 days after administration of mifepristone is more appropriate to evaluate efficacy.[59] It is misleading to only reference the abortion completion rates observed at the 24-hour timepoint from Lohr. Therefore, we do not agree that data from Lohr indicate higher failure rate with misoprostol taken before the prescribed minimum 24-hour period after taking mifepristone.

Although we disagree that Lohr demonstrates a higher failure rate with misoprostol taken before 24-hours after taking mifepristone, we note that our 2016 review of the S-020 efficacy supplement referenced a 2013 systematic review by Raymond, which concluded that if the interval between mifepristone and misoprostol interval is less than or equal to 24 hours, the procedure is less effective compared to an interval of 24-48 hours.[60] As explained above, the data reviewed in 2016 showed that Mifeprex, in a regimen with misoprostol administered at home, was safe and effective. Therefore, incorrect administration, if it occurred, was infrequent and did not significantly affect the safety and efficacy of medical abortion. However, in light of the data reviewed, section 2.1 of the labeling approved in 2016 (as well as the currently approved labeling and Medication Guide) states that there should be a "minimum 24-hour interval between" mifepristone and misoprostol (emphasis included in the labeling).[61] The approved dosing regimen also states that misoprostol is taken within 24 to 48 hours after taking mifepristone and acknowledges that the effectiveness of the regimen may be lower if misoprostol is administered less than 24 hours after mifepristone administration.

In addition to your concerns that a woman may take misoprostol too soon after administering mifepristone, you also state that waiting until 24 hours after administering mifepristone does not guarantee success (Petition at 7-8). In support of this concern, you cite a 2015 review by Chen and Creinin. You state that this review found "women taking misoprostol earlier than 48 hours after Mifeprex are more likely to fail the regimen" (Petition at 8). Chen and Creinin included studies in which the intervals between mifepristone and buccal misoprostol were 24 hours or 24-48 hours and stated that "based on the available literature, the overall efficacy of regimens with a 24-hour interval between mifepristone and buccal misoprostol is significantly lower than those with a 24- to 48-hour interval (94.2 percent compared with 96.8 percent)."[62] The rate differences were statistically significant, but both regimens were more effective than the 92 percent efficacy rate of the original regimen approved in 2000 (administering misoprostol 48 hours after taking mifepristone).

Finally, you also express concern that if misoprostol is self-administered, a woman may swallow it rather than keep the pill between her cheek and gum, and oral administration of

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[59] See https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/020687s022lbl.pdf.
[60] 2016 Clinical Review, supra n. 13, at 31 (citing 8 Raymond EG, et al. First-trimester medical abortion with mifepristone 200 mg and misoprostol: a systematic review. Contraception 2013;87(1):26-37.)
[61] See https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/020687s022lbl.pdf.
[62] See Chen MJ and Creinin MD. Mifepristone with buccal misoprostol for medical abortion. Obstet Gynecol. 2015;126(1):12-21; see also 2016 Clinical Review, supra n. 13, at 21.

misoprostol (i.e., swallowing the pill) following the lower dose of mifepristone in the current regimen is not as effective in ending the pregnancy (Petition at 7). Winikoff et al. specifically studied the use of oral compared to buccal misoprostol 24-36 hours after mifepristone 200 mg with overall success rates of 91.3 percent and 96.2 percent, respectively.[63] Both regimens resulted in a greater than 91 percent successful medical abortion. Although the study showed decreased efficacy with oral versus buccal administration in 57-63 days gestational age, there were no statistical differences in other gestational age groupings. Even assuming there is a small proportion of women who are 57-63 days gestational age and use oral administration of misoprostol (rather than buccal as labeled), a small decrease in the reported efficacy in that population would not justify requiring a clinic visit for all women undergoing medical abortion.

Overall, studies support the efficacy of the mifepristone, in a regimen with misoprostol when taken by the patient at home, Therefore, we do not agree that an in-person visit is necessary to manage administration of misoprostol.

iii. Rh-Negative Patients

In the Petition, you state that a follow-up examination is particularly critical for Rh-negative patients and that without that follow-up examination, women will not receive Rhogam after the abortion, increasing their risk of subsequent Rh isoimmunization, which can endanger future pregnancies (Petition at 9). You suggest that a clinic visit after the administration of Mifeprex is important for Rh-negative women to receive Rhogam and that removing the required follow-up visit puts Rh-negative women at risk for isoimmunization. We do not agree.

Rh testing is standard of care in the United States and RhD immunoglobulin (such as Rhogam) should be administered if indicated. Further, administration of RhD immunoglobulin should be given within 72 hours of a sensitizing event (e.g., medical abortion).[64] However, the facility where the RhD immunoglobulin injection occurs (clinic, hospital or laboratory) is not critical. A shift from medical clinics to hospitals for administration of injections has occurred over the years due to shortages of RhD immunoglobulin and poor reimbursement for RhD immunoglobulin injection from third-party payers.[65] This has resulted in pregnant women frequently obtaining routine 28-week RhD immunoglobulin injections at hospitals/laboratories with a prescription provided by their healthcare providers. This same process of obtaining RhD immunoglobulin via prescription is available to patients after medical termination of pregnancy and does not require a follow-up clinic visit.

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[63] Winikoff B, Dzuba, IG, Creinin MD, et al, 2008, Two Distinct Oral Routes of Misoprostol in Mifepristone Medical Abortion, Obstet Gynecol 112(6):1303-1310.

[64] ACOG Practice Bulletin No. 181. Prevention of Rh D Alloimmunization. August 2017.

[65] See https://www.mdedge.com/obgyn/article/61083/practice-management/rhogam-injections-payment-levels-vary-among-insurers.

In summary, the totality of data on the efficacy and safety of medical abortion at less than 70 days gestation, derived from numerous studies, has characterized the complications and rates of complications for completing medical abortion at home, and the findings show medical abortion at home is both safe and effective without three office visits. We therefore deny your request that the use of mifepristone in a regimen with misoprostol require three office visits by the patient.

c. Contraindications

In the Petition, you assert that critical language contraindicating Mifeprex for patients without access to appropriate emergency medical care was excluded from the 2016 Mifeprex labeling. You cite to a study[66] and ACOG statements as evidence that medical abortions have greater risks and more need for emergency "operation" than a surgical abortion, particularly for patients in rural areas with limited access to emergency medical care (Petition at 11).

Although inadequate access to medical facilities for appropriate care was removed from the list of contraindications in section 4 of the approved labeling when we approved the S-020 efficacy supplement, the 2016 Mifeprex labeling and the currently approved mifepristone labeling, as well as the Mifepristone REMS Program, continue to include appropriate instructions for providers regarding patient access to appropriate medical care.[67] For example, the Boxed Warning includes language directing healthcare providers to ensure that the patient knows whom to call and what to do, including potentially going to an emergency room, if the patient experiences serious events associated with the use of mifepristone. The labeling also directs healthcare providers, as part of the dosing regimen, to give the patient the name and phone number of a healthcare provider who will be handling emergencies.[68] In addition, one of the required qualifications listed in the Prescriber Agreement Form is the "[a]bility to provide surgical intervention in cases of incomplete abortion or severe bleeding, or to have made plans to provide such care through others, and ability to assure patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary."[69] Therefore, although certain language about access to medical facilities was removed from the approved labeling in 2016, we disagree that critical language about access to appropriate emergency medical care is lacking from the approved labeling.

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[66] See Petition Reference Document No. 17 (Harrison Affidavit: Donna Harrison, M.D., Aff. *Okla. Coalition for Reproductive Justice v. Cline*, Case No. CV-2014-1886 (Feb. 24, 2015), ¶115 (referencing M. Niinimaki et al., Immediate Complications after Medical compared with Surgical Termination of Pregnancy, Obstet. Gynecol. 114:795 (Oct. 2009)).

[67] See Mifeprex labeling, approved 2016. https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/020687s020lbl.pdf. See also current labeling at https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/020687s022lbl.pdf.

[68] Id.

[69] Mifepristone REMS Program, https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=RemsDetails.page&REMS=390. Emphasis added.

You also cite information in Box 1, Features of Medical and Surgical Abortion (page 3) in the ACOG Practice Bulletin No. 143.[70] As mentioned above, the ACOG Practice Bulletin No. 143 has been withdrawn and the language you cite is not included in the current Practice Bulletin No. 225.

d. Adverse Event Reporting

In the Petition, you assert that even under the regimen approved in 2000, it was difficult to collect accurate and complete adverse event information for Mifeprex, and that collecting such information is virtually impossible under the regimen approved in 2016 because prescribers only are required to report deaths associated with Mifeprex (Petition at 12). You also assert that FDA cannot adequately assess the safety of the current Mifeprex regimen without comprehensive information on adverse events (Petition at 12). You state that certified prescribers should at a minimum be required to report the following to FDA's MedWatch reporting system and to the sponsor: deaths, hospitalizations, blood transfusions, emergency room visits, failures requiring surgical completion, ongoing pregnancy, or other major complications, including detailed information on these events (Petition at 13).

We acknowledge that there is always a possibility with any drug that some adverse events are not being reported, because reporting to the Agency's MedWatch program by health care professionals and patients is voluntary. We do not agree, however, that the 2016 changes to the prescriber reporting requirements limit our ability to adequately monitor the safety of mifepristone for medical termination of pregnancy. Prior to the 2016 approval of the S-20 efficacy supplement, we assessed approximately 15 years of adverse event reports both from the Applicant and through the MedWatch program and determined that certain ongoing additional reporting requirements under the Mifeprex REMS, such as hospitalization and blood transfusions, were not warranted. This assessment was based on the well-characterized safety profile of Mifeprex, with known risks occurring rarely, along with the essentially unchanged safety profile of Mifeprex during this 15-year period of surveillance. Accordingly, the Prescriber Agreement Form was amended as part of our 2016 approval of the S-20 efficacy supplement to require, with respect to adverse event reporting, only that prescribers report any cases of death to the Applicant.

We also note that the reporting changes to the Prescriber Agreement Form as part of our 2016 approval do not change the adverse event reporting requirements for the Applicants. Like all other holders of approved NDAs and ANDAs, the Applicants are required to report all adverse events, including serious adverse events, to FDA in accordance with the requirements set forth in FDA's regulations (see 21 CFR 314.98, 21 CFR 314.80, and 21 CFR 314.81). FDA also routinely reviews the safety information provided by the Applicants in the Annual Reports. As with all drugs, FDA continues to closely monitor the postmarketing safety data on mifepristone for the medical termination of pregnancy.

[70] Petition at 11. Medical Management of First-Trimester Abortion. ACOG Practice Bulletin Number 143. March 2014 (Reaffirmed 2016. Replaces Practice Bulletin Number 67, October 2005); Obstet Gynecol. 2014 Mar;123(3):676-692 at 680.

You state that FDA should provide guidance to emergency healthcare providers and physicians so that they know how to distinguish complications following drug-induced abortion from complications following spontaneous miscarriage (Petition at 13). We disagree that specific guidance is needed at this time. In the past, when appropriate, FDA has worked with the NDA Applicant to issue communications to healthcare providers and emergency department providers concerning certain serious adverse events.[71] Furthermore, the approved Medication Guide advises patients to take the Medication Guide with them if they need to go to the emergency room or seek care from a healthcare provider other than the one who dispensed the medication to them, so the emergency room or healthcare provider understands the patient is having a medical abortion. We have not identified a change in the safety profile of mifepristone that would warrant additional communications to healthcare providers and emergency department providers concerning complications following medical abortion. If we become aware of safety information that merits further communications with emergency department providers or healthcare providers, or that warrants revisions to the approved labeling, we will act as appropriate.

You also assert that many Mifeprex prescribers "violate FDA protocol," instructing their patients to lie to emergency medical personnel, and that this prevents emergency healthcare providers from appropriately caring for their patients and further decreases the likelihood that adverse events will be reported (Petition at 12). Your only support for this claim is a reference to instructions from the organization Aid Access[72] to patients that they can tell emergency room staff that they had a miscarriage and do not need to tell medical staff that they had a medical abortion. The Petition does not provide any data or additional information establishing "many Mifeprex prescribers violate FDA protocol, instructing their patients to lie," or that these providers thereby prevented appropriate care and decreased the number of adverse events reported.

B. REMS

1. Request to Retain Mifeprex REMS

In your Petition, you request that FDA retain the Mifeprex REMS (Petition at 14). We agree that a REMS is necessary to ensure that the benefits of mifepristone in a regimen with misoprostol outweigh the risks. FDA's determination as to whether a REMS is necessary

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[71] See Historical Information on Mifepristone (Marketed as Mifeprex), available at http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111334.htm. For example, the NDA applicant and FDA agreed that there was a need to issue a Dear Health Care Provider letter in April 2002 and a Dear Emergency Room Director letter in September 2004. The fact that these letters were issued does not imply that the approved mifepristone regimen is unsafe; it is not uncommon for drug sponsors to issue "Dear Health Care Provider" letters, and, as noted in the Mifepristone Q&A document posted on our Web site in April 2002, "[w]hen FDA receives and reviews new information, the agency provides appropriate updates to doctors and their patients so that they have essential information on how to use a drug safely."

[72] We note that Aid Access facilitated the sale of unapproved mifepristone and misoprostol to U.S. consumers and that FDA sent Aid Access a warning letter asking it to promptly cease causing the sale of unapproved and misbranded drugs to U.S. consumers. US FDA Warning Letter to Aidaccess.org, dated March 8, 2019. https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/aidaccessorg-575658-03082019.

to ensure that the benefits of a drug outweigh its risks is a complex, drug-specific inquiry, reflecting an analysis of multiple, interrelated factors and of how those factors apply in a particular case.[73] In conducting this analysis, FDA considers whether (based on premarketing or postmarketing risk assessments) there is a particular risk or risks associated with the use of the drug that, on balance, outweigh its benefits and whether additional interventions beyond FDA-approved labeling are necessary to ensure that the drug's benefits outweigh its risks.[74]

As described in the background section of this response (see section I.A.), FDA determined that interventions in addition to the FDA-approved labeling were necessary to ensure that the benefits of Mifeprex outweighed its risks when the drug was initially approved in 2000, and periodic re-evaluations of the REMS since that time have reached the same conclusion. As further described in the background section of this response (see section I.E.), FDA recently undertook a review of the Mifepristone REMS Program. As explained below, the Mifepristone REMS Program continues to be necessary to ensure the benefits outweigh the risks.

After review of multiple different sources of information, including published literature, safety information submitted to the Agency during the COVID-19 PHE, FAERS reports, the first REMS assessment report for the Mifepristone REMS Program, and information provided by advocacy groups, individuals, and the Plaintiffs in ongoing litigation,[75] as well as information submitted by the Applicants, we have concluded that the REMS can be modified to reduce the burden on the health care delivery system without compromising patient safety. As explained below, we agree that the healthcare provider certification (ETASU A) and dispensing of mifepristone to patients with evidence or other documentation of safe use conditions (ETASU D) continue to be necessary components of the REMS to ensure the benefits outweigh the risks. However, we have concluded that the Mifepristone REMS Program must be modified to remove the requirement under ETASU C that mifepristone be dispensed only in certain healthcare settings, specifically clinics, medical offices, and hospitals.

Below, we discuss each of these elements of the Mifepristone REMS Program.

a. ETASU A – Prescriber Certification/Qualifications

ETASU A under the Mifepristone REMS Program requires healthcare providers who prescribe mifepristone to be certified. In order to become certified, prescribers must: 1) review the prescribing information for mifepristone and 2) complete the Prescriber Agreement Form. In signing the Prescriber Agreement Form, prescribers agree they meet the qualifications listed below:

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[73] See FDA Guidance for Industry, *REMS: FDA's Application of Statutory Factors in Determining When a REMS Is Necessary* (Apr. 2019).
[74] Id.
[75] See supra n. 10.

- Ability to assess the duration of pregnancy accurately
- Ability to diagnose ectopic pregnancies
- Ability to provide surgical intervention in cases of incomplete abortion or severe bleeding, or to have made plans to provide such care through others, and ability to assure patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary.
- Has read and understood the Prescribing Information of mifepristone (which the provider can access by phone or online).

In addition to meeting these qualifications, as a condition of certification the healthcare provider also agrees to follow the guidelines for use below:

- Review the Patient Agreement Form with the patient and fully explain the risks of the mifepristone treatment regimen. Answer any questions the patient may have prior to receiving mifepristone.
- Sign and obtain the patient's signature on the Patient Agreement Form.
- Provide the patient with a copy of the Patient Agreement Form and the Medication Guide.
- Place the signed Patient Agreement Form in the patient's medical record.
- Record the serial number from each package of mifepristone in each patient's record.
- Report deaths to the Applicant, identifying the patient by a non-identifiable patient reference and the serial number from each package of mifepristone.

Our review of the published literature did not identify any studies comparing healthcare providers who met these qualifications with healthcare providers who did not. In the absence of such studies, there is no evidence to contradict our previous finding that prescribers' ability to accurately date pregnancies, diagnose ectopic pregnancies, and provide surgical intervention either personally or through others, is necessary to mitigate the serious risks associated with the use of mifepristone in a regimen with misoprostol. Therefore, our conclusion continues to be that a healthcare provider who prescribes mifepristone in a regimen with misoprostol should meet the above qualifications. Absent these provider qualifications, we are concerned that serious and potentially fatal complications associated with medical abortion, including missed ectopic pregnancy and heavy bleeding from incomplete abortion, may not be detected or appropriately managed.

Accordingly, we have determined that ETASU A must remain an element of the Mifepristone REMS Program to ensure the benefits outweigh the risks. Maintaining the requirement for prescriber certification ensures that providers meet the necessary qualifications and adhere to the guidelines for use listed above. The burden of prescriber certification has been minimized to the extent possible by requiring prescribers to certify only one-time for each applicant.

Although we agree with your request to retain the REMS for mifepristone (now the Mifepristone REMS Program) insofar as it pertains to ETASU A, as discussed in section II.A.2.a of this response, we do not agree with your request that the healthcare provider needs to be a licensed physician to meet this requirement.

b. ETASU D – Requirement For The Drug To Be Dispensed With Evidence Or Other Documentation Of Safe-Use Conditions

ETASU D under the Mifepristone REMS Program requires mifepristone to be dispensed with evidence or other documentation of safe-use conditions. To receive mifepristone for medical termination of intrauterine pregnancy through 70 days gestation, the patient must sign a Patient Agreement Form indicating that the patient has received, read, and been provided a copy of the Patient Agreement Form and received counseling from the prescriber regarding the risk of serious complications associated with mifepristone for this indication. The Patient Agreement Form ensures that patients are informed of the risks of serious complications associated with mifepristone for this indication. In a number of approved REMS, Patient Agreement Forms or Patient Enrollment Forms ensure that patients are counseled about the risks of the product and/or informed of appropriate safe use conditions.[76]

As a condition of certification under the Mifepristone REMS Program, healthcare providers must follow the guidelines for use of mifepristone, including reviewing the Patient Agreement Form with the patient, fully explaining the risks of the treatment regimen and answering any questions the patient may have before receiving the medication. With this form, the patient acknowledges that they have received and read the form, and that they have received the counseling regarding when to take mifepristone, the risk of serious complications associated with mifepristone and what to do if they experience adverse events (e.g., fever, heavy bleeding). Both the healthcare provider and patient must sign the document and the patient must receive a copy of the signed form. In addition to the counseling described in the Patient Agreement Form, patients also receive a copy of the Medication Guide for mifepristone. Ultimately, the Patient Agreement Form serves as an important counseling component, and documentation that the safe use conditions of the Mifepristone REMS Program have been satisfied, as the prescriber is required to place the signed Patient Agreement Form in the patient's medical record.

In addition, we conducted an updated review of published literature since 2016 to assess the utility of maintaining the Patient Agreement Form as part of the Mifepristone REMS Program, and these studies do not provide evidence that would support removing ETASU D. For these reasons, we have determined that ETASU D must remain an element of the Mifepristone REMS Program to ensure the benefits outweigh the risks.

[76] REMS@FDA, https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm, Accessed November 15, 2021.

c. ETASU C – In-Person Dispensing

ETASU C under the Mifepristone REMS Program currently requires mifepristone to be dispensed to patients only in certain healthcare settings, specifically clinics, medical offices, and hospitals, by or under the supervision of a certified prescriber. This creates what we refer to in this response as an in-person dispensing requirement under the REMS; i.e., the patient must be present in person in the clinic, medical office, or hospital when the drug is dispensed. The mifepristone REMS document currently states that mifepristone may not be distributed to or dispensed through retail pharmacies or settings other than a clinic, medical office, or hospital. As explained below, based on a recent review of the REMS, we believe that the Mifepristone REMS Program must be modified to remove the requirement that mifepristone be dispensed only in certain healthcare settings, specifically clinics, medical offices, and hospitals, because this requirement is no longer necessary to ensure that the benefits of the drug outweigh the risks. This conclusion is based on our review of information from the Mifepristone REMS Program one-year (1st) REMS[77] assessment data and postmarketing safety information, and supported by our review of the published literature.

i. Assessment Data

As part of our review of the REMS, we evaluated information included in the 1st REMS assessment report for the Mifepristone REMS Program, which included healthcare provider certification data, program utilization data, and non-compliance data. This 1st REMS assessment report covers a reporting period between April 11, 2019 through February 29, 2020. During this reporting period, a small number of non-compliance events were reported.

As described in section I.C. of this response, during the timeframe from January 27, 2020 through September 30, 2021, there were periods when the in-person dispensing requirement was not enforced. To better understand whether there was any impact on safety or non-compliance during the periods when the in-person dispensing requirement was not enforced, we requested additional information from the Applicants to provide for more comprehensive assessment of the REMS for the time period from January 27, 2020 (the effective date of the COVID-19 PHE) to September 30, 2021. We requested the Applicants provide a summary and analysis of any program deviation or non-compliance events from the REMS requirements and any adverse events that occurred during this time period that had not already been submitted to FDA. The NDA and the ANDA Applicants reported a total of eight cases reporting adverse events between January 27, 2020 and September 30, 2021. These eight cases were also identified in the FAERS database and are described below.

The number of adverse events reported to FDA during the COVID-19 PHE with mifepristone use for medical termination of pregnancy is small, and the data provide no

[77] This REMS assessment report was the first submitted following the approval of the single, shared system REMS for mifepristone.

indication that any program deviation or noncompliance with the Mifepristone REMS Program contributed to these reported adverse events.

ii. FAERS/Postmarketing Safety Data

FDA routinely monitors postmarketing safety data for approved drugs through adverse events reported to our FAERS database,[78] through our review of published medical literature, and when appropriate, by requesting applicants submit summarized postmarketing data. For our recent review of the REMS, we searched our FAERS database, reviewed the published medical literature for postmarketing adverse event reports for mifepristone for medical termination of pregnancy, and requested that the Applicants submit a summary and analysis of certain adverse events. Our review of this postmarketing data indicates there have not been any new safety concerns with the use of mifepristone for medical termination of pregnancy through 70 days gestation, including during the time when in-person dispensing was not enforced.

In order to evaluate the periods when in-person dispensing was and was not enforced, we conducted a search of the FAERS database and the published medical literature to identify U.S. postmarketing adverse events that reportedly occurred from January 27, 2020 through September 30, 2021 with mifepristone use for medical termination of pregnancy. The data for this time period were then further divided into the date ranges when in-person dispensing was enforced per the REMS (January 27, 2020 - July 12, 2020 and January 13, 2021 - April 12, 2021) versus when in-person dispensing was not enforced: July 13, 2020 - January 12, 2021 (in-person dispensing enforcement was temporarily enjoined) and April 13, 2021 - September 30, 2021 (enforcement discretion for in-person dispensing because of the COVID-19 PHE).

Based on the above search, a total of eight cases were identified in FAERS and no additional case reports were identified in the medical literature. Two of the eight cases reported adverse events that occurred when in-person dispensing was being enforced (i.e., January 27, 2020-July 12, 2020 and January 13, 2021-April 12, 2021). These two cases reported the occurrence of uterine/vaginal bleeding (case 1) and uterine/vaginal bleeding and sepsis (case 2). Of note, uterine/vaginal bleeding and sepsis are labeled adverse events. Five of the eight cases reported adverse events that occurred when in-person dispensing was not enforced (i.e., July 13, 2020-January 12, 2021 and April 13, 2021-September 30, 2021); however, the narratives provided in the FAERS reports for three of the five cases explicitly stated that mifepristone was dispensed in-person. These five cases reported the occurrence of ongoing pregnancy (case 3), drug intoxication and death approximately 5 months after ingestion of mifepristone (case 4), death [cause of death is currently unknown] (case 5), sepsis and death (case 6), and pulmonary embolism (case 7). Of note, ongoing pregnancy and sepsis, including the possibility of fatal septic shock, are labeled adverse events. The remaining case reported the occurrence of oral pain/soreness (case 8) in July

[78] FAERS is a database that contains adverse event reports, medication error reports and product quality complaints resulting in adverse events that were submitted to FDA. The database is designed to support FDA's post-marketing safety surveillance program for drug and therapeutic biologic products.

2021, but did not provide sufficient information to determine the exact date of the adverse event.

As discussed in section II.A.2.d., the Applicants report adverse events, including serious adverse events, to FDA in accordance with applicable regulations.[79] To enable additional review of adverse events, Applicants were requested to provide a summary and analysis for adverse events reported with incomplete medical abortion requiring surgical intervention to complete abortion, blood transfusion following heavy bleeding or hemorrhage, ectopic pregnancies, sepsis, infection without sepsis, hospitalization related to medical abortion, and emergency department/urgent care encounter related to medical abortion. The Applicant for Mifeprex provided the requested summary of postmarketing safety information from March 29, 2016, when S-020 was approved, through September 30, 2021. The Applicant for the generic provided the requested summary of postmarketing safety information from April 11, 2019 (date of initial approval) through September 30, 2021. The information provided by the Applicants included the same cases identified in FAERS, as discussed above.

We analyzed the FAERS data referenced above to determine if there was a difference in adverse events when in-person dispensing was and was not enforced. Based on FDA's review of this data, we concluded that there does not appear to be a difference in adverse events when in-person dispensing was and was not enforced and that mifepristone may be safely used without in-person dispensing. FDA's review of the summary and analysis data submitted by the Applicants (which, as noted above, included the same cases identified from FAERS) did not change this conclusion.

iii. Published Literature

As noted above, we also conducted an extensive review of the published literature since March 29, 2016 (the date the S-020 efficacy supplement for Mifeprex was approved) through September 30, 2021.[80] Published studies have described alternatives in location and method for dispensing mifepristone by a certified prescriber (or equivalent healthcare provider in countries other than the United States). Some studies have examined replacing in-person dispensing in certain healthcare settings with dispensing at retail pharmacies[81]

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[79] See 21 CFR 314.98, 21 CFR 314.80, and 21 CFR 314.81.

[80] In support of your request that we retain the REMS and continue limiting the dispensing of Mifeprex to patients in clinics, medical offices, and hospitals by or under the supervision of a certified prescriber, you reference two studies that you assert do not comply with the REMS (Petition at 19-22). Outcomes from both of the studies you reference have been reported in the published literature and are addressed in the discussion that follows. We note that as a general matter, a clinical investigation of an approved drug that is subject to a REMS can take place in healthcare settings outside those provided for in the REMS. When an approved drug that is subject to a REMS is studied in a clinical trial, the REMS does not apply to the use of the drug in that clinical trial. However, FDA reviews the protocol to ensure that it will be conducted in a manner that adequately addresses the risks that the REMS is intended to mitigate, such that the trial participants will not be exposed to an unreasonable and significant risk of illness or injury. See 21 CFR 312.42(b)(1)(i) and (b)(2)(i).

[81] Grossman D, Baba CF, Kaller S, et al. Medication Abortion With Pharmacist Dispensing of Mifepristone. Obstet Gynecol 2021;137:613–22; Rocca CH, Puri M, et al. Effectiveness and safety of early medication

and dispensing mifepristone from pharmacies by mail.[82] Other studies have evaluated two modes of dispensing by prescribers: (1) prescribers mailing the medications to patients,[83] and (2) prescribers using couriered delivery of medications.[84] Different studies have evaluated dispensing mifepristone by mail by an entity described as "a partner organization."[85]

We note that the ability to generalize the results of these studies to the United States population is hampered by differences between the studies with regard to pre-abortion care (e.g., telemedicine versus in-person). In addition, the usefulness of the studies is limited in some instances by small sample sizes and lack of follow-up information on outcomes with regard to both safety and efficacy. There are also factors which complicate the analysis of the dispensing element alone. Some of these factors are: (1) only a few studies have evaluated alternatives for in-person dispensing of mifepristone in isolation (for example, most studies on mail dispensing of mifepristone also include telemedicine consultation); and (2) because most serious adverse events with medical abortion are infrequent, further evaluation of changes in dispensing would require studies with larger numbers of participants. We did not find any large clinical studies that were designed to collect safety outcomes in healthcare systems similar to the United States. Despite the limitations of the studies we reviewed, we have concluded that overall the outcomes of these studies are not inconsistent with our conclusion that, based on the 1st year REMS assessment report and postmarketing safety data, mifepristone will remain safe and efficacy will be maintained if the in-person dispensing requirement is removed from the Mifepristone REMS Program.

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abortion provided in pharmacies by auxiliary nurse-midwives: A non-inferiority study in Nepal. PLoS ONE 13(1): e0191174. https://doi.org/10.1371/journal.pone.019117; Wiebe ER, Campbell M, et al. Comparing telemedicine to in-clinic medication abortions induced with mifepristone and misoprostol. Contracept X. 2020; 2: 100023.

[82] Grossman D, Raifman S, Morris N, et.al. Mail-order pharmacy dispensing of mifepristone for medication abortion after in-person clinical assessment. Contraception 2021, ISSN 0010-7824, https://doi.org/10.1016/j.contraception.2021.09.008, Available online 20 September 2021; Upadhyay UD, Koenig LR, Meckstroth KR. Safety and Efficacy of Telehealth Medication Abortion in the US During the COVID-19 Pandemic. JAMA Network Open. 2021;4(8):e2122320, doi:10.1001/jamanetworkopen.2021.22320; Hyland P, Raymond EG, Chong E. A direct-to-patient telemedicine abortion service in Australia: Retrospective analysis of the first 18 months. Aust N Z J Obstet Gynaecol 2018;58: 335-340.

[83] See Anger HA, Raymond EG, et al. Clinical and service delivery implications of omitting ultrasound before medication abortion provided via direct-to-patient telemedicine and mail. Contraception 2021 Jul 28;S0010-7824(21)00342-5. doi: 10.1016/j.contraception.2021.07.108. Published online. Raymond E, Chong E, et al. TelAbortion: evaluation of a direct to patient telemedicine abortion service in the United States. Contraception 2019; 100:173-177. See also Chong et al., infra n. 103 Kerestes et al., infra n. 105, and Aiken et al., infra n. 106.

[84] Reynolds-Wright JJ, et al. BMJ Sex Reprod Health 2021;0:1–6. doi:10.1136/bmjsrh-2020-200976.

[85] Endler M, Beets L, Gemzell Danielsson K, Gomperts R. Safety and acceptability of medical abortion through telemedicine after 9 weeks of gestation: a population-based cohort study. BJOG 2019;126;609-618. Norten H, Ilozumba O, Wilkinson J, Gemzell Danielsson K, Gomperts R. 10-year evaluation of the use of medical abortion through telemedicine: a retrospective cohort study. BJOG 2021; https://doi.org/10.1111/1471-0528.16765; Aiken ARA, Digol I, Trussell J, Gomperts R. Self-reported outcomes and adverse events after medical abortion through online telemedicine: population based study in the Republic of Ireland and Northern Ireland. BMJ 2017;357:j2011 http://dx.doi.org/10.1136/bmj.j2011.

Below is a summary of our review of the literature, organized by the methods of dispensing mifepristone that were studied.

(a) Retail pharmacy dispensing

Three studies reported medical abortion outcomes for retail pharmacy dispensing of mifepristone after clinical evaluation (Grossman,[86] Rocca,[87] Wiebe[88]). Grossman conducted a US-based study in which mifepristone and misoprostol were dispensed from a pharmacy partnered with the clinic. Complete abortion without additional procedures occurred in 93.5 percent of participants with known outcomes. The reported proportion of complete abortion is within the range described in the approved mifepristone labeling. No participants experienced a serious adverse event, were hospitalized or required transfusion. Three participants had emergency department (ED) visits with treatment (intravenous hydration, pain medication, pelvic infection after uterine aspiration for incomplete abortion). The study safety and efficacy outcomes are consistent with labeled outcome frequencies. The study has limited generalizability because it was conducted in two US states and involved partnered pharmacies, some of which were in the same building as the clinic. Additionally, all participating pharmacies in this study were required to have a pharmacist on duty during clinic hours who had been trained in the study protocol and was willing to dispense mifepristone. The study conditions may not be generalizable to United States retail pharmacies; there is insufficient information to assess this.

Rocca[89] conducted an observational study evaluating participants who obtained medical abortions in Nepal by comparing the provision of medical abortion service by newly trained nurse midwives in pharmacies to medical abortion provided in government-certified clinics. The authors reported that, with respect to complete abortion (greater than 97 percent) and complications (no hospitalizations or transfusions), evaluation and dispensing in pharmacy was non-inferior to in-clinic evaluation and dispensing.

Wiebe,[90] in a retrospective, chart review study conducted in Canada, compared abortion outcomes of women who underwent medical abortion with telemedicine consult, and either received medications by courier or picked them up at a local pharmacy, with outcomes of a matched control cohort of women who received the medications at a pharmacy after an in-clinic visit. The groups had similar documented complete medical abortion outcomes (equal to or greater than 95 percent participants with known outcomes). The telemedicine group had one case of hemorrhage (0.5 percent) and one case of infection requiring antibiotics (0.5 percent) compared with no cases of hemorrhage or infection requiring antibiotics in the in-clinic cohort. The telemedicine group had more ED visits (3.3 percent compared to 1.5 percent in-clinic cohort). Both models of dispensing mifepristone resulted in efficacy and safety outcomes within labeled frequency.

[86] Grossman et al., supra n. 81.
[87] Rocca et al., supra n. 81.
[88] Wiebe et al., supra n. 81.
[89] Rocca et al., supra n. 81.
[90] Wiebe et al., supra n. 81.

None of the three studies allow a determination regarding differences in safety between in-person dispensing by a certified prescriber in a health care setting and dispensing through a retail pharmacy, due to limitations on the generalizability of the results of the studies to the current retail pharmacy environment in the United States. The outcome findings from the one United States study (Grossman)[91], in which the pharmacies were partnered with prescribers, are unlikely to be broadly generalizable to the current retail pharmacy environment and do not reflect typical prescription medication availability with use of retail pharmacy dispensing. For the retail pharmacy dispensing study in Canada (Wiebe),[92] timely provision of medication from the retail pharmacy was accomplished by either courier to the woman or faxed prescription to the woman's pharmacy. It is unknown whether conditions that would allow timely access to medications for medical abortion would occur in retail pharmacies throughout the United States, suggesting the findings from that study may not be broadly generalizable. The third study (Rocca)[93] evaluated medical abortion provided in Nepali pharmacies and essentially moved the abortion provider and clinical examination into the pharmacy, a scenario that is not, at this time, applicable to the United States retail setting.

(b) Mail order pharmacy

Three studies evaluated mail order pharmacy dispensing (Grossman,[94] Upadhyay,[95] Hyland[96]). Grossman published an interim analysis of an ongoing prospective cohort study evaluating medical abortion with mifepristone and misoprostol dispensed by mail-order pharmacy after in-person clinical assessment. Complete abortion without additional procedures occurred in 96.9 percent of participants with known outcomes. Two (0.9 percent) participants experienced serious adverse events; one received a blood transfusion and one was hospitalized overnight. Nine (4 percent) participants attended 10 ED visits. In this interim analysis, the outcomes are consistent with labeled frequencies.

Upadhyay[97] reports findings from a retrospective cohort study of women undergoing medical abortion in the United States without a consultation or visit. Eligibility was assessed based on a participant-completed online form collecting pregnancy and medical history. Participants who were considered eligible received medication delivered by a mail-order pharmacy. Abortion outcome was determined by either an assessment on day 3 or a 4-week pregnancy test. The investigators reported a complete abortion rate without additional procedures of 95 percent for participants with known outcomes and stated that no participants had any major adverse events. The proportion of abortion outcomes assessed at 3 days versus 4 weeks is not reported. Regardless, determining outcomes at 3 days is insufficient to determine outcome rates or safety findings because a 3-day follow-up period is too short. As recommended in Section 2.3 of the approved labeling, follow-up at

[91] Grossman et al., supra n. 81.
[92] Wiebe et al., supra n. 81.
[93] Rocca et al., supra n. 81.
[94] Grossman et al, supra n. 82.
[95] Upadhyay et al., supra n. 82.
[96] Hyland et al., supra n. 82.
[97] Upadhyay et al., supra n. 82.

7-14 days after administration of mifepristone is more appropriate to evaluate safety and efficacy. This study used a model with numerous deviations from standard provision of medical abortion in the United States, such as no synchronous interaction with the prescriber during informed consent or prior to prescribing medication and no confirmation of self-reported medical, surgical, and menstrual history. These deviations, limited follow-up information, and small sample size limit the usefulness of this study.

Hyland[98] describes findings from a cohort study in Australia evaluating medical abortion outcomes utilizing telemedicine and a central mail order pharmacy. Complete abortions without additional procedures occurred in 96 percent of participants with documented outcomes and is consistent with labeled efficacy. Of the participants included in the analysis, 95 percent had no face-to-face clinical encounters after medications were mailed while 3 percent were admitted to the hospital and 2 percent had an outpatient encounter. One participant who was hospitalized and underwent a surgical uterine evacuation received a transfusion. Not included in the findings are 7 hospitalizations occurring in 7 participants who did not have "full follow up." The authors do not report any other adverse events and conclude use of the telemedicine medical abortion service is safe. However, the reasons for hospitalization are not discussed by the authors; therefore, it is unknown why the patients were hospitalized. Although the reported frequency of hospitalizations (3 percent) is higher than the less than 1 percent in the FDA-approved mifepristone labeling, conclusions on the safety findings cannot be made in the absence of information about the reasons for hospitalization. Other limitations of this study include incomplete information about outcomes with face-to-face encounters.

Overall, the three studies evaluating mail order pharmacy dispensing suggest that efficacy of medical abortion is maintained with mail order pharmacy dispensing. With respect to safety, in the Grossman study[99] the interim analysis, although small, does not raise serious safety concerns. Safety findings from the Hyland[100] study are difficult to interpret. Although only one transfusion is reported and the authors state the findings demonstrate safety, a higher hospitalization rate and lack of information on the reasons for hospitalization preclude reaching any conclusions about the safety findings. Lastly, the Upadhyay[101] study had no reported adverse events, but the findings are less useful because of the limited follow-up, and because medical abortions were provided using a model with numerous deviations from standard provision of medical abortion in the United States.

(c) Clinic dispensing by mail

A total of five studies evaluated clinic dispensing by mail. Gynuity Health Projects conducted a prospective cohort study (the "TelAbortion" study) evaluating use of telemedicine for remote visits and mifepristone being dispensed from clinics via overnight or regular tracked mail. Three publications reviewed have reported outcomes for the Gynuity population exclusively: Raymond (outcomes from May 2016 to December

[98] Hyland et al., supra n. 82.
[99] Grossman et al., supra n. 82.
[100] Upadhyay et al., supra n. 82.
[101] Hyland et al., supra n. 82.

2018),[102] Chong (outcomes from May 2016 to September 2020)[103] and Anger (outcomes from March 2020 to September 2020).[104] A fourth study, Kerestes,[105] reports outcomes of medical abortion at the University of Hawai'i from April 2020 to November 2020 and a fifth study, Aiken (2021)[106] reports outcomes of medical abortion up to 70 days gestational age in the United Kingdom before and during the COVID-19 PHE in a retrospective cohort study.

In Raymond,[107] complete abortion without additional procedures occurred in 93 percent of participants with known outcomes. There were two hospitalizations (one participant received a transfusion for severe anemia despite having had a complete abortion) and 7 percent of participants had clinical encounters in ED/urgent care centers. The reported outcomes are similar to outcomes described in approved labeling except the combined ED/urgent care center encounters (7 percent) exceeded the ED visits in approved labeling (2.9-4.6 percent).[108] Of note, the authors state that half of the ED/urgent care visits did not entail any medical treatment. In Chong,[109] approximately 50 percent of the medical abortions occurred during the period of the COVID-19 PHE. Complete abortion without an additional procedure occurred in 95 percent of those with known outcomes. Transfusions were 0.4 percent and hospitalizations were 0.7 percent; 6 percent of participants had unplanned clinical encounters in ED/urgent care. Surgical interventions were required in 4.1 percent to complete abortion. The reported outcomes in Chong (which updated the findings described in Raymond) are similar to outcomes described in approved labeling except that (as with the Raymond study it updated) the combined ED/urgent care center encounters (6 percent) exceeded the ED visits in approved labeling (2.9-4.6 percent).

Anger,[110] which compared outcomes among participants enrolled in the Gynuity study who did ("test medical abortion cohort") versus did not ("no-test medical abortion cohort")[111]

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[102] Raymond et al., supra n. 83.
[103] Chong E, Shochet T, et al. Expansion of a direct-to-patient telemedicine abortion service in the United States and experience during the COVID-19 pandemic. Contraception 2021;104:43-48.
[104] Anger et al., supra n. 83.
[105] Kerestes C, Murayama S, et al. Provision of medication abortion in Hawai'i during COVID-19: Practical experience with multiple care delivery models. Contraception 2021 Jul;104(1):49-53. doi:10.1016/j.contraception.2021.03.025. Epub 2021 Mar 28.
[106] Aiken ARA, Lohr PA, et al. Effectiveness, safety and acceptability of no-test medical abortion (termination of pregnancy) provided via telemedicine: a national cohort study. BJOG 2021;128:1464–1474.
[107] Raymond, supra n. 83.
[108] The authors reported the combined frequency of emergency department/urgent care visits, whereas the approved labeling includes the frequency for emergency department (emergency room) visits. Therefore it is unknown whether the frequency of emergency department visits in the trial, as distinct from the combined frequency of emergency department/urgent care visits, is comparable to the frequency of emergency department visits reflected in approved labeling.
[109] Chong et al., supra n. 103.
[110] Anger et al., supra n. 83.
[111] "No-test medication abortion" refers to medical abortion provided without a pretreatment ultrasound, pelvic examination or laboratory tests when, in the judgment of the provider, doing so is medically appropriate (appropriateness based on history and symptoms); "no-test medication abortion" does include post-abortion follow up. A sample protocol is described by Raymond et al." (Raymond EG, Grossman D, Mark A, et.al. Commentary: No-test medication abortion: A sample protocol for increasing access during a pandemic and beyond. Contraception 2020;101:361-366)

have confirmation of gestational age/intrauterine location with an examination or ultrasound, found that those without an examination or ultrasound prior to medical abortion were more likely to require procedural interventions and had more unplanned clinical encounters.[112] There were no reported ectopic pregnancies in either group. The number of ED/urgent care visits and the proportion of unplanned clinical encounters that led to medical treatment were not reported. In the "test" group, complete medical abortion was confirmed in 98 percent of participants with known outcomes; one participant was "hospitalized and/or blood transfusion" and 8 percent had an unplanned clinic encounter (participant sought in-person medical care related to abortion and the visit was not planned prior to abortion). In the "no-test" group, complete medical abortion was confirmed in 94 percent of participants with known outcomes; two participants were "hospitalized and/or blood transfusion" and 12.5 percent had an unplanned clinical encounter.

Kerestes[113] included three different delivery models: traditional in-person visits, telemedicine consultation with in-person pick-up of medications, and telemedicine consultation with delivery of medications by mail (most of the latter were enrolled through Gynuity's TelAbortion study). Among participants with follow-up data, the rates of successful medical abortion without surgery were consistent with outcomes in approved labeling. Blood transfusion was given to two participants (both in the telemedicine plus in-person pickup group). Although ED visits occurred the most frequently in the telemedicine plus mail group (four participants or 5.8 percent) and the least in the in-person group (two participants or 2.1 percent), the study reported no increases in other serious adverse events. Aiken (2021)[114] reported outcomes before and during the pandemic in a retrospective cohort study in the United Kingdom. The study compared the two cohorts: one before the pandemic with in-person visits and dispensing (traditional model) and one during the pandemic with either an in-person visit and in-person dispensing or a telemedicine visit and dispensing by mail or picked up from the clinic (hybrid model). Complete abortion occurred in greater than 98 percent in both cohorts; the rate was slightly higher in the telemedicine group than in the in-person group. There were no significant differences in the rates of reported serious adverse events. The investigators' analysis determined that the efficacy and safety were comparable between both cohorts and concluded the hybrid model for medical abortion is effective and safe.

Taken together, data from the three Gynuity study reports (Raymond, Chong, and Anger), Kerestes, and Aiken (2021) support that efficacy of medical abortion was maintained when mifepristone was dispensed by mail from the clinic. Study reports of Raymond, Chong, and Kerestes all suggest there may be an increase in ED/urgent care visits with telemedicine visits and dispensing by mail from the clinic, but without increases in other serious adverse events. Anger's comparative analysis suggests a pre-abortion examination may decrease the occurrence of procedural intervention and decrease the number of unplanned visits for postabortion care. The Aiken (2021) study appears to be of sufficient

[112] We note that the two cohorts were not randomized in the Anger study; they had different baseline characteristics. Consequently, findings based on the comparisons between the two cohorts should be interpreted carefully.
[113] Kerestes et al., supra n. 105.
[114] Aiken et al., supra n. 106.

sample size to determine whether safety outcomes with mail dispensing differ from in-person dispensing; however, significant limitations include that the analysis was based on deidentified information and the investigators were unable to verify the outcomes extracted. Further, the study's design did not capture all serious safety outcomes, thus limiting the certainty of the findings.

Notwithstanding the limitations discussed above, these studies overall support that dispensing by mail from the clinic is safe and effective. Although the literature suggests there may be more frequent ED/urgent care visits related to the use of mifepristone when dispensed by mail from the clinic, there are no apparent increases in other serious adverse events related to mifepristone use.

(d) Clinic dispensing by courier

Reynolds-Wright[115] reported findings from a prospective cohort study of participants at less than 12 weeks gestational age in Scotland undergoing medical abortion at home that provided mifepristone for pick up at the service or by couriered delivery to woman's home. The outcomes from this study in Scotland are consistent with the outcomes in the approved mifepristone labeling. However, the number of couriered deliveries was not reported. Thus this study does not provide abortion outcomes separately for couriered delivery of mifepristone and misoprostol. The study shares the same limitations as the Aiken (2021) study; the study's design did not capture all serious safety outcomes, thus limiting the certainty of the findings.

(e) Partner organization dispensing by mail

Women on Web (WoW), an internet group, connects patients and providers outside of the US and provides medical abortion globally, dispensing mifepristone through "a partner organization" by mail. WoW uses a model with numerous deviations from the standard provision of medical abortion in the United States. For example, this model has no synchronous interaction with the prescriber during informed consent or prior to prescribing medication and no confirmation of self-reported medical, surgical, and menstrual history or confirmed pregnancy testing. Three studies (Endler, Norten, and Aiken (2017))[116] reported outcomes based on dispensing through this model. Endler and Norten reported outcomes from WoW cohorts but do not provide relevant information on mifepristone dispensing by mail because neither provide meaningful outcomes data for consideration. Although Aiken (2017) is a large cohort study, the outcomes are self-reported and an unusually high rate of outcomes are unaccounted for; these limitations result in the data being insufficient to determine the safety of dispensing mifepristone by mail though a partner organization.

In sum, there are insufficient data from the literature we have reviewed to determine the safety and efficacy of dispensing from a retail pharmacy, by courier, or by a partner organization. With respect to dispensing mifepristone by mail, our review of the literature indicates that dispensing mifepristone by mail from the clinic or from a mail order

[115] Reynolds-Wright JJ, et al. BMJ Sex Reprod Health 2021;0:1–6. doi:10.1136/bmjsrh-2020-200976.
[116] Endler et al., Norten et al., and Aiken et al., supra n. 85.

pharmacy does not appear to jeopardize the efficacy of mifepristone for medical abortion. While the studies we reviewed are not adequate on their own to establish the safety of the model of dispensing mifepristone by mail, the safety and efficacy outcomes reported in these studies remain within the ranges labeled for the approved mifepristone products. Although the literature suggests there may be more frequent ED/urgent care visits related to the use of mifepristone when dispensed by mail from the clinic, there are no apparent increases in other significant adverse events related to mifepristone use.

Based on the REMS assessment data, FAERS data from the time period when the in-person dispensing requirement was not being enforced, and our review of the literature, we conclude that mifepristone will remain safe and effective if the in-person dispensing requirement is removed, provided all the other requirements of the REMS are met and pharmacy certification is added. Removing the in-person dispensing requirement will render the REMS less burdensome to healthcare providers and patients, and provided all other requirements of the REMS are met, including the additional requirement for pharmacy certification, the REMS will continue to ensure that the benefits of mifepristone for medical abortion outweigh the risks. Therefore, to reduce the burden imposed by the Mifepristone REMS Program, the REMS must be modified to remove the in-person dispensing requirement, which would allow, for example, dispensing of mifepristone by mail via certified prescribers or pharmacies, in addition to in-person dispensing in clinics, medical offices and hospitals as currently outlined in ETASU C.

In your Petition, you state that "[e]liminating or relaxing the REMS to facilitate Internet or telephone prescriptions would be dangerous to women and adolescent girls" and that "health care providers prescribing abortion-inducing drugs over the Internet or phone or before a patient is even pregnant cannot adequately evaluate patients for contraindications to the drugs" (Petition at 18-19).

We do not agree that eliminating the REMS requirement for the dispensing of Mifeprex in certain healthcare settings will be dangerous to patients, nor do we agree that doing so will affect the ability of healthcare providers to evaluate women for contraindications to mifepristone in a regimen with misoprostol for medical termination of intrauterine pregnancy through 70 days gestation. There are many factors that contribute to patient safety, including evaluation of a patient, informed consent, development of a follow-up plan, and provision of a contact for emergency care. All of these can occur in many types of healthcare settings. The evaluation of patients for contraindications to medical abortion does not necessarily require direct physical contact with the certified prescriber.

You also assert that telemedicine abortion absolves abortion providers of responsibility for the well-being of their patients (Petition at 19). We do not agree. Healthcare providers who prescribe mifepristone are responsible for the well-being of their patients regardless of mode of evaluation or dispensing of medication. The Agency agrees with the American Medical Association that a healthcare provider-patient relationship is entered when the "physician serves a patient's medical needs;"[117] in the context of medical abortion, this

[117] See www.ama-assn.org/delivering-care/ethics/patient-physician-relationships.

healthcare provider-patient relationship continues until resolution of the pregnancy or transfer of care to another healthcare provider.[118]

We also note that patients who are not pregnant at the time of evaluation would not be appropriate candidates for being prescribed mifepristone for medical termination of pregnancy because they do not fulfill the approved indication of having an intrauterine pregnancy of up to 70 days gestation.

2. Other Safety Issues and Additional Studies

In support of your request that we retain the Mifeprex REMS, you cite the Council for International Organizations of Medical Sciences' (CIOMS) definition of "rare" to assert that because "about 1 out of 100 women" using Mifeprex and misoprostol require surgery, serious complications are common, not rare (Petition at 15-16).[119] Although we agree that certain elements of the Mifepristone REMS Program are necessary to assure the safe use of mifepristone, we do not agree with your assertion.

In the Petition, you state that the Medication Guide improperly downplays the risks of the use of Mifeprex in a regimen with misoprostol and you cite the Medication Guide as stating "'*rarely*, serious and potentially life-threatening bleeding, infections, and other problems can occur following . . . medical abortion.' Specifically, 'in about 1 out of 100 women [administered Mifeprex and misoprostol] bleeding can be so heavy that it requires a surgical procedure." (Petition at 15). Using these two separate statements in the Medication Guide, you argue that the CIOMS's definition of rare ("1 out of 1000") means that if 1 out of 100 women using Mifeprex in a regimen with misoprostol require surgery, serious complications are common, not rare. (Petition at 16). However, your reference to the two sentences in the Medication Guide conflates two different clinical scenarios: (1) the adverse event of serious and potentially life-threatening bleeding, and (2) treatment failure.

The first sentence you reference states: "Although cramping and bleeding are an expected part of ending a pregnancy, rarely, serious and potentially life-threatening bleeding, infections, or other problems can occur following a miscarriage, surgical abortion, medical abortion, or childbirth." This statement refers to life-threatening adverse events that can occur during termination regardless of gestational age or during miscarriage or childbirth regardless of the mode of delivery (e.g., vaginal delivery or cesarean section). At the time of our review of the clinical studies submitted to support the S-020 efficacy supplement, the reported rate of death in the studies reviewed, based on one death, was 0.007 percent (very rare under the CIOMS definition).[120] The rate of infections requiring hospitalization or

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[118] See https://www.ama-assn.org/delivering-care/ethics/ethical-practice-telemedicine.

[119] Council for International Organizations of Medical Sciences. Guidelines for Preparing Core Clinical Safety Information on Drugs Second Edition. 1999. https://cioms.ch/wp-content/uploads/2018/03/Guidelines-for-Preparing-Core-Clinical-Safety-Info-Drugs-Report-of-CIOMS-Working-Group-III-and-V.pdf. Accessed December 13, 2021 (CIOMS).

[120] Id. at 36 (defining the "very rare" standard category of frequency as less than 0.01 percent).

intravenous antibiotics was less than 0.1 percent (rare under the CIOMS definition),[121] and rates of transfusion were 0.03-0.7 percent (rare to uncommon under the CIOMS definition).[122] Therefore, "rarely" accurately refers to the frequency of the adverse events referenced in this statement.

The second sentence you reference from the Medication Guide states: "In about 1 out of 100 women, bleeding can be so heavy that it requires a surgical procedure (surgical aspiration or D&C)." This statement refers to the rate of surgical procedures for bleeding following treatment with mifepristone. Heavy bleeding or hemorrhage after medical abortion is a small subset of bleeding and can require a surgical procedure due to ongoing pregnancy or incomplete expulsion; these are considered failed treatment rather than adverse events and are not characterized using the CIOMS definitions. Even if heavy, bleeding after medical abortion may not be considered a serious adverse event unless clinically diagnosed as hemorrhage or requiring a transfusion. Furthermore, in the vast majority of medical abortions, surgical intervention is not necessary.

You also cite a 2009 study and a 2018 study to assert that medical abortions carry greater risks than surgical abortions (Petition at 16). The 2009 Niinimaki, et al.[123] study reported overall incidences of immediate adverse events (up to 42 days) in medical and surgical abortions performed in women undergoing induced abortion from 2000-2006 based on data from the Finnish national registries. We agree that the overall incidence of adverse events for medical abortion was fourfold higher when compared with surgical abortion (20.0 percent versus 5.6 percent). Specifically, the incidence of hemorrhage, incomplete abortion, and surgical (re)evacuation were higher for medical abortion. However, the authors specifically noted that because medical abortion is associated with longer uterine bleeding, the high rate of events, which were pulled from a national registry reflecting both inpatient and outpatient visits, is not surprising. They opined that uterine bleeding requiring surgical evacuation probably better reflects the severity of bleeding after termination of pregnancy; the incidence of such bleeding was relatively low, although it was more common with medical abortion. In addition, the authors acknowledged there are inherent weaknesses in registry-based studies; there is variable reliability both of diagnoses and of severity of diagnoses. Nevertheless, the authors concluded that both methods are generally safe and recommended discussing the adverse event profiles of different methods when counseling women seeking pregnancy termination.

We note that Ireland, et al.[124] reported findings from a more recent retrospective cohort study of 30,146 United States women undergoing pregnancy termination before 64 days of gestation from November 2010 to August 2013. Efficacy of pregnancy termination was 99.6 percent and 99.8 percent for medical and surgical abortion, respectively.

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[121] Id. at 36 (defining the "rare" standard category of frequency as greater than or equal to 0.01 percent and less than 0.1 percent).
[122] Id. at 36 (defining the "uncommon" standard category of frequency as greater than or equal to 0.1 percent and less than 1 percent); see also 2016 Clinical Review, supra n. 13, at 47 and 51.
[123] Niinimaki M, Pouta A, Bloigu A, et al. Immediate complications after medical compared with surgical termination of pregnancy. Obstet Gynecol. 2009;114(4):795-804.
[124] Ireland LD, Gatter, M, Chen, A. 2015. Medical Compared with Surgical Abortion for Effective Pregnancy Termination in the Frist Trimester. Obstetrics & Gynecology 126;22-28.

Unanticipated aspiration for persistent pain, bleeding or both were 1.8 percent and 0.4 percent for medical and surgical abortion respectively. These findings are compatible with the Niinimaki study findings. There was no difference in major adverse events as defined by the authors (emergency department visit, hospitalization, uterine perforation, infection, hemorrhage requiring transfusion) between the groups. The authors conclude medical and surgical abortion before 64 days of gestation are both highly effective with low complication rates.

The 2018 Carlsson study is addressed above in section II.A.2.b.ii. of this response; as discussed above, that study showed no statistically significant difference between the overall complication rates between an "at home" and "at the hospital" abortion.[125]

We acknowledge that medical abortion is known to have more days of bleeding and increased rates of incomplete abortion compared to surgical abortion. However, as noted above, in the vast majority of medical abortions, surgical intervention is not necessary. Thus, medical abortion and surgical abortion are two options; both have benefits, side effects, and potential complications. Patients and their healthcare providers should discuss which method is preferable and safer according to each woman's unique situation.

You state that the Mifeprex REMS should require a formal study for at-risk populations, including: patients under the age of 18; patients with repeat Mifeprex abortions; patients with limited access to emergency room services; and patients who self-administer misoprostol (Petition at 13-14). As we explain below, additional studies are not needed at this time.

In justifying your assertion that a formal study is required in patients under the age of 18, you state that Mifeprex was approved for use in the pediatric population in 2000 after the requirement for studies in the pediatric population was waived (Petition at 13-14). The approved indication for mifepristone does not limit its use by age. Although patients age 17 and under were not included in the clinical trials supporting the initial approval of Mifeprex in 2000, we stated at the time that the safety and efficacy were expected to be the same for postpubertal (i.e., post-menarchal) adolescents. Our conclusion in 2000 that pediatric studies of Mifeprex were not needed for approval was consistent with FDA's implementation of the regulations in effect at that time. Because we determined that there were sufficient data from studies of mifepristone, the original Mifeprex approval should have reflected the Agency's conclusion that the pediatric study requirements were waived for pre-menarchal females and that the pediatric study requirements were met for post-menarchal adolescents, rather than stating that the Agency was waiving the requirements for all pediatric age groups.

As currently required by the Pediatric Research Equity Act (PREA),[126] certain applications or supplemental applications must include pediatric assessments of the safety and effectiveness of the drug for the claimed indication(s) in all relevant pediatric

[125] Carlsson et al., supra n. 49.
[126] Section 505B of the FD&C Act (21 U.S.C. 355c).

subpopulations, unless that requirement is waived or deferred.[127] In accordance with PREA, when FDA reviewed the S-020 efficacy supplement, a partial waiver was granted for pediatric studies in pre-menarchal females because pregnancy does not occur in premenarchal females. We also determined that the applicant had fulfilled the pediatric study requirement in post-menarchal adolescents. This determination was based on data extrapolated from adults and information in literature. Review of these findings found the safety and efficacy in this population to be similar to the safety and efficacy in the adult population.[128] Therefore, we do not agree that a formal study is required in patients under 18.

With regard to your concerns about repeat abortions and your assertion that a study is necessary in this population, we acknowledge that published data concerning adverse reproductive health outcomes in U.S. women who undergo repeat medical abortions are limited. We concluded in our 2016 review of the S-020 efficacy supplement that there is no evidence that repeated medical or surgical abortion is unsafe or that there is a tolerance effect. We also noted that return to fertility after the use of mifepristone is well documented. [129] This is reflected both in Section 17 of the approved labeling, Patient Counseling Information, which states that the provider should "inform the patient that another pregnancy can occur following medical abortion and before resumption of normal menses," and in the Medication Guide, which states "You can become pregnant again right after your pregnancy ends." Although you state that more than one out of every three abortions in the United Sates is a repeat abortion (Petition at 14),[130] we are not aware of reports suggesting greater safety concerns in repeat abortions than a first-time abortion. Therefore, we do not agree that a study is necessary in this population. You also cite a published study, using a mouse model, of repeated medical termination of pregnancy that showed repeat medical abortion impaired the reproductive function of female mice (Petition at 14).[131] Per our 2016 review, there is no evidence in available clinical data that repeated medical or surgical abortion is unsafe, or that fertility is impaired by the use of mifepristone; therefore, data from a single non-clinical study in mice are not persuasive.[132]

With respect to your request for a formal study of mifepristone for medical abortion in women without access to emergency care, we disagree that such a study is necessary. In order to become a certified prescriber, a healthcare provider must agree that they have the ability to provide surgical intervention in cases of incomplete abortion or severe bleeding or have made plans to provide such care through others, and that they have the ability to assure patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary. These prescriber qualifications ensure that mifepristone is prescribed to women for whom emergency care is available.

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[127] Section 505B(a)(2) of the FD&C Act (21 U.S.C. 355c(a)(2)).
[128] 2016 Clinical Review, supra n. 13, at 74-76.
[129] Id. at 47.
[130] In support of this assertion, you cite Jones R, Jerman J, Ingerick M. Which abortion patients have had a prior abortion? Findings from the 2014 U.S. Abortion Patient Survey. J Womens Health.
[131] Lv F, Xu X, Zhang S, et al. Repeated abortion affects subsequent pregnancy outcomes in BALB/c mice. PLoS One. 2012;7(10):e48384. doi:10.1371/journal.pone.0048384.
[132] 2016 Clinical Review, supra n. 13, at 47.

Finally, you assert that FDA should require a formal study in patients who self-administer misoprostol. As explained in section II.A.2.b.ii of this response, FDA conducted a literature review of self-administration of misoprostol at home as part of its review of the S-020 efficacy supplement and found no safety or efficacy concerns with home self-administration of misoprostol. Therefore, we disagree that a formal study is required in this population.

With regard to safety generally, in addition to the FAERS data provided above (see section II.B.1.c.ii. in this response), FDA routinely monitors adverse events reported to FAERS and published in the medical literature for mifepristone for medical termination of pregnancy through 70 days gestation. We have not identified any new safety concerns with the use of mifepristone for this indication.

3. Other Articles

In your Petition, you reference several documents that discuss alternative models of providing abortion medications and advocate for the lifting of the REMS on mifepristone (Petition at 23-24). You assert that these recent publications demonstrate how abortion advocates will continue to pressure FDA to eliminate the REMS and move towards over-the-counter access for Mifeprex.[133]
We agree that the overarching message in the publications you reference appears to be advocating self-management of medical abortion. Nonetheless, as discussed in this response, we have determined that the Mifepristone REMS Program continues to be necessary for the safe use of this drug product, with some modifications.

III. CONCLUSION

For the reasons set forth above, we deny your request that FDA restore and strengthen elements of the Mifeprex regimen and prescriber requirements approved in 2000; and we grant in part and deny in part your request to retain the Mifepristone REMS Program. As with all approved drug products, we will continue to monitor the safety of mifepristone for the approved indication and take any appropriate actions.

Sincerely,

Patrizia A. Cavazzoni -S

Digitally signed by Patrizia A. Cavazzoni -S
Date: 2021.12.16 15:05:41 -05'00'

Patrizia Cavazzoni, M.D.
Director
Center for Drug Evaluation and Research

[133] You also reference clinical trials relating to the use of mifepristone for spontaneous miscarriage management and question the results of studies related to this use (Petition at 16-18). The use of mifepristone for the management of early miscarriage is not an approved indication for this drug product and is outside the scope of the Mifepristone REMS Program. Therefore, we do not address it in this response.

EXHIBIT

Center for Drug aluation and Re earc ,
Application umber 020 rig 020
Summary Re ie
(Mar. 2 , 20)
(FDA 20 Summary Re ie)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

020687Orig1s020

SUMMARY REVIEW

Summary Review for Regulatory Action

Date	March 29, 2016
Subject	Summary Review
NDA #/Supplement #	20687/S-020
Applicant name	Danco Laboratories, LLC
Date of submission	May 28, 2015
Date of submission receipt	May 29, 2015
PDUFA goal date	March 29, 2016
Proprietary name/established name	Mifeprex/mifepristone
Dosage form/strength	Oral tablet/200 mg
Dosage regimen	Mifeprex 200 mg tablet orally followed in 24-48 hours by 800 mcg buccal misoprostol
Proposed indication	Mifeprex is a progestin antagonist indicated, in a regimen with misoprostol, for the medical termination of intrauterine pregnancy through 70 days gestation
Action	Approval

1. **Introduction**
2. **Background**
3. **CMC**
4. **Nonclinical Pharmacology/Toxicology**
5. **Clinical Pharmacology**
6. **Clinical Microbiology**
7. **Efficacy/Statistics**
8. **Safety**
9. **Advisory Committee Meeting**
10. **Pediatrics**
11. **Other Relevant Regulatory Issues**
12. **Labeling**
13. **Decision/Action/Risk Benefit Assessment**

1. Introduction

Danco Laboratories, LLC, referred to hereafter as the Applicant, submitted an efficacy supplement (S-020) to NDA 20687 for Mifeprex (mifepristone). The Applicant sought the following changes to its approved application:

1. (b) (4) Decrease mifepristone dose from 600 to 200 mg, followed by misoprostol at a dose increased from 400 mcg to 800 mcg, administered buccally instead of orally; see below:
   - Day One: Mifeprex Administration (oral)
     One 200 mg tablet of Mifeprex is taken in a single oral dose
   - After a 24-48 hour interval: Misoprostol Administration (buccal)(minimum 24-hour interval between Mifeprex and misoprostol)
     Four 200 mcg tablets (total dose: 800 mcg) of misoprostol are taken by the buccal route
2. Removal of the instruction that administration of misoprostol must be done in-clinic, to allow for administration at home or other location convenient for the woman
3. Administration of misoprostol at 24-48 hours instead of 48 hours after Mifeprex
4. Follow-up, although still needed, not restricted to in clinic at 14 days after Mifeprex
5. Increase in the maximum gestational age from 49 days to 70 days
6. Change of the labeled time for expected expulsion of pregnancy from 4-24 hours to 2-24 hours post misoprostol administration
7. Addition that a repeat 800 mcg buccal dose of misoprostol may be used if needed
8. Change of "physician" to "healthcare provider" in the label and Risk Evaluation and Mitigation Strategies (REMS) document
9. Change in the indication statement to add reference to use of misoprostol: "Mifeprex is indicated, in a regimen with misoprostol, for the medical termination of pregnancy through 70 days gestation."
10. Removal of references to "under Federal law" from the Prescriber's Agreement under the REMS

11. Labeling changes addressing the pediatric requirements under the Pediatric Research Equity Act

This efficacy supplement submission includes information from published studies, review articles and additional information from the authors of some of the publications. These published studies evaluated reproductive age women in the U.S. and outside the U.S. who had early medical termination with mifepristone, in a regimen with misoprostol, including women up through 70 days of gestation.

This memorandum serves as the Division's decisional memorandum for the efficacy supplement.

2. Background

The active ingredient of Mifeprex, mifepristone, is a progestin antagonist. Mifeprex, in a regimen with misoprostol, is approved for the medical termination of pregnancy up through 49 days' gestation. The approved dosing regimen is currently labeled as follows:

- Day 1: The patient takes three 200 mg tablets of Mifeprex in a single oral dose in the clinic, medical office, or hospital.
- Day 3: The patient returns to the clinic, medical office, or hospital and takes two 200 mcg tablets of misoprostol orally.
- Day 14: The patient returns for a follow-up visit to confirm that a complete termination has occurred.

At the time of the September, 2000 approval, FDA restricted distribution of Mifeprex under 21 CFR 314.520, requiring that Mifeprex be dispensed only by or under the supervision of a physician who meets certain qualifications. With the passage of FDAAA in 2007, Mifeprex was deemed to have in effect an approved REMS. The Applicant submitted a formal REMS, which was approved on June 8, 2011 and consisted of the following: a Medication Guide, elements to assure safe use (ETASU A [special certification of healthcare providers who prescribe Mifeprex], ETASU C [dispensing only in certain healthcare settings], and ETASU D [safe use condition of a signed Patient Agreement]), an implementation system and a timetable for assessments. The goals of the REMS were 1) To provide information to patients about the benefits and risks of Mifeprex before they make a decision whether to take the drug and 2) To minimize the risk of serious complications by requiring prescribers to certify that they are qualified to prescribe Mifeprex and are able to assure patient access to appropriate medical facilities to manage any complications. The REMS for Mifeprex incorporated the restrictions under which the drug was originally approved.

Since 2011, the Applicant has submitted two REMS assessment reports. The Agency review of these reports determined that the REMS goals were being met and that no modifications were required to the REMS at that time.

FDA held a pre-NDA meeting with the Applicant on January 29, 2015, to discuss proposed labeling and REMS changes to be submitted in this efficacy supplement. These changes were submitted with the efficacy supplement.

The Applicant submitted published literature and supportive information to support changes to the dose, dosing regimen, gestational age, revisions to labeling, modifications to the REMS document, and to address PREA requirements. The Agency accepts the use of peer reviewed literature as primary data for an application under the framework of a 505(b)(2) application.

3. CMC

No new CMC information was submitted with this efficacy supplement. The CMC team determined no additional review or inspections were required. The CMC team completed a review of the labeling and found the CMC sections of labeling (sections 3, 11 and 16) acceptable (See review dated March 29, 2016). The CMC review team recommends approval of the efficacy supplement; refer also to the CMC review of the separate supplement proposing a single tablet blister pack for Mifeprex, dated January 11, 2016. There are no outstanding CMC issues or postmarketing commitments or requirements.

Comment*: On March 10, 2016, a separate CMC supplement was approved that allowed the packaging of individual 200 mg tablets of mifepristone; previously packaging consisted of three 200 mg tablets per blister pack (a total of 600 mg Mifeprex as administered under the originally approved dosing regimen).*

4. Nonclinical Pharmacology/Toxicology

No new nonclinical information was submitted in this supplement. The Pharmacology/Toxicology team revised labeling to conform to the Pregnancy and Lactation Labeling Rule. There are no outstanding nonclinical issues. The Pharmacology/Toxicology review team recommends approval of the efficacy supplement; refer to the Pharmacology/Toxicology review dated March 4, 2016.

5. Clinical Pharmacology

The Applicant did not conduct any new clinical pharmacology studies pertaining to the proposed (b) (4) regimen, but provided information on pharmacokinetics (PK) of misoprostol following various routes of administration. The PK of the 200 mg Mifeprex tablet has not been characterized in women, but data are available in men and were submitted in the original NDA. The Clinical Pharmacology review team determined that the PK data were appropriate for inclusion in labeling. Review of the labeling pertinent to the Clinical Pharmacology sections is complete and labeling relevant to pharmacokinetics and pharmacodynamics is acceptable. There are no outstanding Clinical Pharmacology issues or postmarketing commitments or requirements. The clinical pharmacology review team recommends approval of the efficacy supplement; refer to the Clinical Pharmacology review dated March 29, 2016.

6. Clinical Microbiology

Not applicable.

7. Efficacy/Statistics

The Applicant submitted published literature as the primary evidence to support the efficacy (and safety) of the proposed dosing regimen (refer to the Clinical Review dated March 29, 2016, Section 9.5 for a list of submitted references). Most published articles submitted by the Applicant and reviewed by the clinical review team reported the primary efficacy endpoint as complete termination of pregnancy without further medical or surgical intervention; the Division considers this to be a clinically relevant endpoint.

The majority of the publications included a statement that the study was conducted under institutional review board (IRB) or Ethical Review Committee approval and the women gave informed consent. The clinical review team concluded that the published literature was adequate as the primary information source to support the changes proposed in the efficacy supplement. During the course of the review, the team also requested and received more detailed information from select publications from their authors via communication with the Applicant.

Although there were slight demographic differences among the published studies from the database, these differences were not expected to alter the efficacy or safety of Mifeprex. Therefore, for the majority of the proposed efficacy changes, the clinical team assessed efficacy information from a subset of publications that evaluated a given proposed change. An independent statistical review was not needed for this review of published literature.

The clinical review team identified several major proposed clinical changes in the efficacy supplement. As these major changes are interrelated, in some cases data from a given study were relied on to provide evidence to support multiple changes. These major changes as considered by the clinical team included:

1. A proposed dosing regimen consisting of mifepristone 200 mg orally followed by the buccal administration of 800 mcg misoprostol including:
    a. Use of a revised interval between mifepristone and misoprostol from 48 hours to 24-48 hours
    b. Allowing home administration of misoprostol
    c. Use of an additional dose of misoprostol
2. Support for extending the gestation age through 70 days
3. Flexibility in follow-up visit: follow-up is needed in the range of 7-14 days after Mifeprex administration; the specific nature and exact timing of the follow-up to be agreed upon by the healthcare provider and patient.
4. Change in who can provide Mifeprex from physician to healthcare provider who prescribes

The following section summarizes the clinical review team's evaluations that supported the above proposed changes:

1. *Support for the proposed dose and dosing regimen of 200 mg of Mifeprex orally and 800 mcg of misoprostol buccally 24-48 hours after Mifeprex administration:* The clinical review team reviewed the submission and identified studies and review articles that evaluated over 35,000 women who were treated with efficacy in the 91-98% range. For additional details on the efficacy from these studies, please refer to Section 6 of the Clinical Review.

2. *Support for extending the gestational age to 70 days:*
The Applicant submitted a number of published articles and systematic reviews that supported the proposed dose and dosing regimen. Four studies and one systematic review evaluated the exact proposed dosing regimen through 70 days gestation. These include three prospective observational studies (Winikoff et al 2012[1], Boersma et al[2] , Sanhueza Smith et al[3]) and one randomized controlled trial (RCT) (Olavarrieta et al[4]) that had a primary objective of evaluating medical abortion provision by non-physicians. The systematic review by Chen and Creinin[5] covered 20 studies including over 30,000 women; all but one of the studies used the proposed regimen in gestations through 70 days (the remaining study used 400 mcg of buccal misoprostol). For those publications that provided overall success rates, these were in the range of 97-98%. Other relevant publications include the systematic review by Raymond[6] of 87 studies, which covered a variety of misoprostol doses and routes of administration used with 200 mg of mifepristone. Assessing the efficacy by misoprostol dose, the paper noted that doses ≥ 800 mcg had a success rate of 96.8%, with an ongoing pregnancy rate of 0.7%.

[1] Winikoff B, Dzuba IG, Chong E, et al. Extending outpatient medical abortion services through 70 days of gestational age. Obstet Gynecol 2012; 120: 1070-6
[2] Boersma AA, Meyboom-de Jong B, Kleiverda G. Mifepristone followed by home administration of buccal misoprostol for medical abortion up to 70 days of amenorrhoea in a general practice in Curacao. Eur J Contracept Reprod Health Care 2011; 16: 61-6
[3] Sanhueza Smith P, Pena M, Dzuba IG, et al. Safety, efficacy and acceptability of outpatient mifepristone-misoprostol medical abortion through 70 days since last menstrual period in public sector facilities in Mexico City. Reprod Health Matters 2015; 22: 75-82
[4] Olavarrieta CD, Ganatra B, Sorhaindo A, Karver TS, Seuc A, Villalobos A, Garcia SG, Pérez M, Bousieguez M, Sanhueza P. Nurse versus physician-provision of early medical abortion in Mexico: a randomized controlled non-inferiority trial. Bull World Health Organ 2015; 93: 249-258
[5] Chen MJ, Creinin MD. Mifepristone with Buccal Misoprostol for Medical Abortion Obstet Gynecol: a Systematic Review. Obstet Gynecol 2015; 126(1): 12-21
[6] Raymond EG & Grimes DA. The comparative safety of legal induced abortion and childbirth in the United States. Obstet Gynecol 2012; 119: 215-9

The original dosing regimen specifies taking misoprostol 2 days after Mifeprex. This efficacy supplement proposes a more flexible time frame of 24 to 48 hours between Mifeprex and misoprostol administration. Data from a review article by Wedisinghe et al[7] evaluated different time intervals using administration of misoprostol after Mifeprex. A meta-analysis of all five studies found a non-significant odds ratio for failure for shorter vs. longer dosing intervals, but a trend for lower success if a dosing interval < 8 hours is used. Chen & Creinin's systematic review[8] of 20 studies including over 33,000 women, all but one using the proposed regimen, compared the success of dosing intervals of 24 hours with intervals ranging from 24-48 hours. The success rate in six studies that used a 24-hour interval through 63 days gestation was 94.2%, compared to the rate of 96.8% in 14 studies that used a 24-48 hour interval, and this difference was statistically significant. The clinical team concluded that the efficacy of the revised dosing regimen was not compromised by revising the dosing interval to 24-48 hours. In addition, they noted that the overall rate of ongoing pregnancies did not differ significantly by dosing interval.

3. *Administration of misoprostol after Mifeprex administration at home:* Currently, the dosing regimen specifies that misoprostol is taken in the clinic setting following Mifeprex administration. No specific publication evaluated treatment outcomes with use of misoprostol at home compared to in-clinic dosing. However, one large literature review (Raymond et al[9]) evaluated a variety of mifepristone treatment regimens with different misoprostol doses, routes of administration and dosing intervals used in gestations through 63 days. Roughly half of the studies included in this review did not require women to take misoprostol in-clinic. Rates of treatment failure and of ongoing pregnancy were very similar regardless of whether misoprostol was taken in-clinic or at another location. The clinical review team concluded that the review provided sufficient data to support labeling that misoprostol does not need to be restricted to in-clinic administration.

4. *Use of a repeat misoprostol dose, if necessary:* The Applicant submitted several published studies that supported use of a repeat misoprostol dose, when complete uterine expulsion did not occur after the initial misoprostol dose following Mifeprex. In clinical practice, the usual treatment for incomplete expulsion (retained products of conception) may include either a repeat dose of misoprostol, expectant management or a surgical procedure (suction aspiration or a dilation and curettage). Studies that specifically report the success rate of a repeat dose of misoprostol are:

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[7] Wedisinghe L and Elsandabesee D. Flexible mifepristone and misoprostol administration interval for first-trimester medical termination. Contraception 2010; 81(4): 269-74. doi: 10.1016/ j.contraception.2009.09.007. Epub Oct 29, 2009

[8] Creinin MD, Fox MC, Teal S, Chen A, Schaff EA, Meyn LA. MOD Study Trial Group: A randomized comparison of misoprostol 6-8 hours versus 24 hours after mifepristone for abortion. Obstet Gynecol 2004; 103: 851-859

[9] Raymond EG & Grimes DA. The comparative safety of legal induced abortion and childbirth in the United States. Obstet Gynecol 2012; 119: 215-9

- Winikoff et al[10] – studied the proposed regimen through 70 days gestation; of the few women who received a second dose for an incomplete abortion at follow-up, the success rate was 91% at 57-63 days and 67% at 64-70 days.
- Chen and Creinin [11] – a systematic review of 20 studies, all but one of which used the proposed regimen up through 70 days; success of a second dose ranged from 91-100%
- Boersma et al[12] – included pregnancies through 70 days treated with the proposed regimen; five of 330 women took a second dose due to absence of bleeding 48 hours after first dose; the success rate was 80%
- Louie et al[13] – studied the proposed regimen to 63 days; in 16 women (of 863) who took a second dose of misoprostol, the success rate was 100%
- Chong et al[14] – compared the proposed regimen to a lower dose of misoprostol; the success of a second dose of misoprostol was 92% overall, but the number of women in each dose arm getting a second dose was not specified.
- Winikoff et al[15] – 14 women in the proposed regimen took a second dose of misoprostol with a success rate of 92.9%.

Using the information from the above studies and other supportive data, the clinical team concluded that the available data support the efficacy of a repeat dose of misoprostol if complete expulsion has not occurred. The relatively high complete pregnancy termination rates indicate that this option is likely to reduce the need for a surgical intervention.

5. *Requirements regarding follow-up care:* Current labeling states that women will return to the clinic 14 days after Mifeprex administration for follow-up. This provision was based on the follow up regimen in the U.S. phase 3 trial that supported the initial approval in 2000. Although the Applicant submitted several studies that evaluated flexibility in the time of follow-up, the key publication identified by the review team that addressed this issue was a 2013 article by

[10] Winikoff B, Dzuba IG, Chong E, et al. Extending outpatient medical abortion services through 70 days of gestational age. Obstet Gynecol 2012; 120: 1070-6
[11] Creinin MD, Fox MC, Teal S, Chen A, Schaff EA, Meyn LA. MOD Study Trial Group: A randomized comparison of misoprostol 6-8 hours versus 24 hours after mifepristone for abortion. Obstet Gynecol 2004; 103: 851-859
[12]Boersma AA, Meyboom-de Jong B, Kleiverda G. Mifepristone followed by home administration of buccal misoprostol for medical abortion up to 70 days of amenorrhoea in a general practice in Curacao. Eur J Contracept Reprod Health Care 2011; 16: 61-6
[13] Louie KS, Tsereteli T, Chong E, Ailyeva F, Rzayeva G, Winikoff B. Acceptability and feasibility of mifepristone medical abortion in the early first trimester in Azerbaijan. Eur J Contracept Reprod Health Care 2014; 19(6): 457-464
[14] Chong E, Tsereteli T, Nguyen NN, Winikoff B. A randomized controlled trial of different buccal misoprostol doses in mifepristone medical abortion. Contraception 2012; 86: 251-256
[15] Winikoff B, Dzuba IG, Creinin MD, Crowden WA, Goldberg AB, Gonzales J, Howe M, Moskowitz J, Prine L, Shannon CS. Two distinct oral routes of misoprostol in mifepristone medical abortion: a randomized controlled trial. Obstet Gynecol 2008; 112(6): 1303-1310

Raymond[16]. The impact of the timing of follow-up was assessed in Raymond's systematic review of studies using various treatment regimens. While some have posited that earlier follow-up may result in a higher rate of surgical intervention (for women who would have had complete expulsion had they been given a bit more time), Raymond's analyses found no difference in failure rates for women followed less than one week after mifepristone as compared to a week or more after mifepristone. As follow-up was anticipated to not alter the efficacy of the proposing dosing regimen, this change is also discussed below in Section 7.

6. *Allowing qualified healthcare providers to use Mifeprex.*

The Applicant provided data on the efficacy of medical abortion provided by non-physician healthcare providers, including four studies with 3,200 women in randomized controlled clinical trials and 596 women in prospective cohorts. These studies included a study by Warriner et al[17] that showed efficacy of 97.4% with nurses versus 96.3% by physicians.

Conclusions: I concur with the clinical review team's assessments and conclusions and these conclusions will be reflected in labeling. The data and information reviewed constitute substantial evidence of efficacy to support the proposed dosing regimen for Mifeprex for pregnancy termination through 70 days gestation. Other proposed changes to the Mifeprex labeling, including the time interval between Mifeprex and misoprostol dosing, and use of a repeat dose, were also adequately supported by evidence. Finally, I concur with the clinical review team that the information from the published literature also supported efficacious use of Mifeprex by non-physician providers.

Comment: Discussion was held as to whether the original dosing regimen approved in 2000 (i.e., Mifeprex 600 mg and misoprostol 400 mcg up to 49 days gestation) should remain in labeling. (b) (4) the clinical review team and I concur with their (b) (4) request to remove the current regimen from the labeling. Removal of the original dosing regimen simplifies labeling, and avoids any confusion regarding instructions. Therefore, the revised labeling, and REMS materials accompanying the approval of this efficacy supplement, will include only the proposed dosing regimen and instructions. It should be noted that there are no safety or efficacy concerns about the originally approved dosing regimen that led to removing it from the labeling.

[16]Raymond EG, et al. First-trimester medical abortion with mifepristone 200 mg and misoprostol: a systematic review. Contraception 2013;87(1):26-37.
[17] Warriner IK, Wang D, Huong NTM, Thapa K, Tamang A, Shah I et al. Can midlevel health-care providers administer early medical abortion as safely and effectively as doctors? A randomized controlled equivalence trial in Nepal. Lancet 2011; 377: 1155-61.

8. Safety

The safety of the proposed dosing regimen for Mifeprex was supported by the evidence from submitted published literature and postmarketing experience. The focus of the safety analysis was on published studies that evaluated the proposed dosing regimen (Mifeprex 200 mg followed by 800 mcg misoprostol buccally 24-48 hours later), with comparison to the known safety profile of the currently approved dosing regimen.

Exposure: Per the Applicant's submission, the clinical review concluded that there have been approximately 2.5 million uses of Mifeprex by U.S. women since the drug's approval in 2000. The clinical review team estimated that exposure to the proposed dosing regimen for their safety analysis was based on approximately 30,000 patients (refer to Table 11 for a list of references used to evaluate safety). Such exposure volume is sufficient to characterize the safety profile of the proposed dosing regimen and other proposed changes in this efficacy supplement.

Deaths: Deaths with medical abortion rarely occur and causality can be difficult to determine. Most of the publications did not specifically report any deaths with medical abortion with Mifeprex. Among the seven U.S. studies submitted to support the safety profile of Mifeprex and misoprostol, only one (Grossman, et al[18]) explicitly addressed deaths and noted that there were no deaths among 578 subjects evaluated in the study. Only one observational study (Goldstone, et al[19]) from Australia contained a report of a death after a mifepristone and misoprostol dosing regimen. In this retrospective review of 13,345 pregnancy terminations, the authors identified one death from sepsis. The article stated that the death was in an individual who failed to follow-up with her healthcare provider despite showing signs of illness. Based on this information, deaths in association with abortion are extremely rare.

Deaths reported from the postmarketing experience of Mifeprex are summarized below in the Postmarketing Experience section.

Nonfatal serious adverse events: The clinical review team identified key nonfatal serious adverse events (SAEs) associated with the proposed dosing regimen for Mifeprex. These SAEs include: hospitalization, serious infection, bleeding requiring transfusion and ectopic pregnancy. Section 7 of the clinical review dated March 29, 2016, provides a detailed discussion of reported rates of hospitalization, serious infection, bleeding requiring transfusion and ectopic pregnancy. The latter is not an adverse reaction because an ectopic pregnancy would exist prior to the Mifeprex regimen; it represents instead a failure to diagnose an ectopic pregnancy. Overall rates identified by the clinical review team from the published literature are as follows:

- Hospitalization: 0.04-0.6% in U.S. studies of over 14,000 women; 0-0.7% in international studies of over 1,200 women

[18]Grossman D, Grindlay K, Buchacker T, Lane K, Blanchard K. Effectivenesss and acceptability of medical abortion provided thorugh telemedicine. Obstet Gynecol 2011;118:296-303.
[19]Goldstone P, Michelson J, Williamson E. Early medical abortion using low-dose mifepristone followed by buccal misoprostol: A large Australian observational study. Med J Austral 2012; 197: 282-6.

- Serious infection/sepsis: 0-0.2% in U.S. and international studies of over 12,000 women
- Transfusion: 0.03-0.5% in U.S. studies of over 17,000 women; 0-0.1% in international studies of over 12,000 women

A study by Upadhyay et al[20] reported a 0.31% rate of major complications (including incomplete or failed abortion, hemorrhage, infection or uterine perforation that required hospitalization, surgery or transfusion) for medical abortions (dosing regimen unspecified) through 63 days; this was about double the rate reported for first trimester aspiration abortions and statistically significantly higher. However, these rates were driven by higher rates of incomplete/failed abortion; rates of hemorrhage (0.14%) and infection (0.23%) did not differ from those associated with aspirations.

Only one submitted study reported an ectopic pregnancy. This study (Winikoff et al[21]) reported one ectopic among 847 women (0.12%).

Comment: The proposed dosing regimen has been studied extensively in the literature using U.S. and global sites. Serious adverse events including deaths, hospitalization, serious infections, bleeding requiring transfusion and ectopic pregnancy are rarely reported. The rates of these serious adverse events are well below 1% and do not suggest a safety profile different from the original approved Mifeprex dosing regimen. Although there is less serious adverse event data on women who received Mifeprex and misoprostol between 64-70 days of gestation, the data from a U.S. study of 379 women (Winikoff et al)[22] in that gestational age is reassuring that the rates of these serious adverse events are not clinically different from that of other gestational age ranges.

In summary, based on the published literature, nonfatal serious adverse events occur with Mifeprex and misoprostol use with rates generally less than 1%. Increased gestational age (64-70 weeks) was not associated with an increased incidence of nonfatal SAEs. Other submission- specific safety issues that were evaluated including uterine rupture and angioedema/anaphylaxis are discussed in the Postmarketing Experience section below.

Loss to follow-up: The studies included in this safety review revealed a wide range of loss to follow-up, from 0.6% loss to follow-up in the study with telephone follow-up (Ngoc et al[23]) to 22% in the Grossman et al[24] study using telemedicine to deliver medical

[20]Upadhyay UD, Desai S, Lidar V, Waits TA, Grossman D, Anderson P, Taylor D. Incidence of emergency department visits and complications after abortion. Obstet Gynecol 2015;125(1):175-183.
[21]Winikoff B, Dzuba IG, Creinin MD, Crowden WA, Goldberg AB, Gonzales J, Howe M, Moskowitz J, Prine L, Shannon CS. Two distinct oral routes of misoprostol in mifepristone medical abortion: a randomized controlled trial. Obstet Gynecol 2008;112(6):1303-1310.
[22]Winikoff B, Dzuba IG, Chong E, et al. Extending outpatient medical abortion services through 70 days of gestational age. Obstet Gynecol 2012;120:1070-6.
[23] Ngoc NTN, et al. Acceptability and feasibility of phone follow-up after early medical abortion in Vietnam: A randomized controlled trial. Obstet Gynecol 2014;123:88-95.
[24] Grossman D, Grindlay K, Buchacker T, Lane K, Blanchard K. Effectivenesss and acceptability of medical abortion provided thorugh telemedicine. Obstet Gynecol 2011;118:296-303.

abortion services.

Comment: Based on these data reviewed by the clinical review team, there is no literature that suggests that follow-up modality alters safety. Therefore, labeling will not be directive regarding follow-up; that will be a decision left to the patient and provider.

Common adverse events: The clinical review team evaluated common adverse reaction data and compared U.S. and global study locations. The comparison revealed that there were differences in the frequency of common adverse reactions, with the reporting rates considerably higher among the U.S. studies. There is no reason to anticipate regional differences in the safety profile for the same treatment regimen, so these differences likely reflect lower ascertainment or subject reporting of adverse reactions in non-U.S. studies. Regardless, inclusion of this non-U.S. data in labeling would not be appropriate, as it is unlikely to be informative to the U.S. population of users. The data to be reported in labeling is outlined in Table 1 below:

Table 1: Common Adverse Events (≥ 15%) in U.S. Studies of the Proposed Dosing Regimen

Adverse Reaction	# U.S. studies	Number of Evaluable Women	Range of frequency (%)	Upper Gestational Age of Studies Reporting Outcome
Nausea	3	1,248	51-75%	70 days
Weakness	2	630	55-58%	63 days
Fever/chills	1	414	48%	63 days
Vomiting	3	1,248	37-48%	70 days
Headache	2	630	41-44%	63 days
Diarrhea	3	1,248	18-43%	70 days
Dizziness	2	630	39-41%	63 days

Source: Data from Middleton[25], Winikoff[26] and Winikoff[27] as outlined in Table 2 of the CDTL review dated March 29, 2016.

One concerning adverse event is severe vaginal bleeding. Severe vaginal bleeding can result in interventions such as hospitalization and transfusion and may be associated with infection. The overall rate of bleeding across publications varied between 0.5% and 4.2%. Two publications (Sanhueza Smith et al[28] and Gatter et al[29]) evaluated clinically significant bleeding by gestational age. Although the publications reported slightly different rates, there was no trend of increased bleeding requiring intervention with Mifeprex and misoprostol use with increasing gestational age.

[25] Middleton T, et al. Randomized trial of mifepristone and buccal or vaginal misoprostol for abortion through 56 days of last menstrual period. Contraception 2005; 72: 328-32

[26] Winikoff B, Dzuba IG, Chong E, et al. Extending outpatient medical abortion services through 70 days of gestational age. Obstet Gynecol 2012; 120: 1070-6

[27] Winikoff B, Dzuba IG, Creinin MD, Crowden WA, Goldberg AB, Gonzales J, Howe M, Moskowitz J, Prine L, Shannon CS. Two distinct oral routes of misoprostol in mifepristone medical abortion: a randomized controlled trial. Obstet Gynecol 2008; 112(6): 1303-1310

[28] Sanhueza Smith P, Pena M, Dzuba IG, et al. Safety, efficacy and acceptability of outpatient mifepristone-misoprostol medical abortion through 70 days since last menstrual period in public sector facilities in Mexico City. Reprod Health Matters 2015;22:75-82.

[29] Gatter M, Cleland K, Nucatola DL. Efficacy and safety of medical abortion using mifepristone and buccal misoprostol through 63 days. Contraception 2015; 91:269-273.

Comment: While not all of the studies reported common adverse events, those that reported did not have unexpected rates of common adverse events. These common adverse events are included in labeling in section 6.1 (Clinical Trial Experience) in the ADVERSE REACTIONS section.

Postmarketing experience – Spontaneous reports:

The safety profile for Mifeprex includes over 15 years of postmarketing safety data available on Mifeprex due to the reporting requirements under the REMS. The Year 3 REMS Assessment report was submitted by the Applicant in June, 2015. The (b) (6) (b) (6) provided a comprehensive review of adverse event reports submitted from 2000 through November 17, 2015. Findings include:

- No Clostridial septic deaths reported in the U.S. since 2009, and none worldwide since 2010.
- The postmarketing rates of hospitalization, severe infection, blood loss requiring transfusion and ectopic pregnancy reported from publications and remain stable and relatively low.

Submission-specific safety issues:

- Anaphylaxis/angioedema: The (b) (6) ((b) (6) identified a safety signal of anaphylaxis and angioedema with mifepristone administration. This signal was based on a comprehensive review of adverse event reports submitted from 2000 through November 17, 2015. A FAERS search retrieved one case of anaphylaxis and six cases of angioedema with mifepristone administration. Six of the seven cases were seen in women using mifepristone for termination of pregnancy. Six of the seven cases noted some type of medical intervention, such as treatment with an antihistamine, a histamine H2 antagonist, a corticosteroid, or a combination of various medications. Hospitalization was noted in three of the seven total cases; all three hospitalization cases occurred in patients who experienced angioedema. There were no additional cases of anaphylaxis or angioedema identified in the literature.

  Comment: (b) (6) and the clinical review team recommended that anaphylaxis and angioedema be described in the Contraindications and Adverse Reactions sections of labeling. These labeling sections were discussed with the Applicant and labeling was revised for those sections to describe these serious adverse events.

- Uterine rupture: As discussed in the clinical review, the potential risk of uterine rupture was considered because the current labeling for misoprostol includes a Boxed Warning against the use of misoprostol for gestations more than 8 weeks due to the risk of uterine rupture. Although misoprostol is used alone for various obstetric indications, including induction of labor at term, it was important to consider whether labeling about this potential risk is warranted for Mifeprex. Both the clinical reviewer and the (b) (6) ((b) (6) reviewed the literature and (b) (6) searched FAERS for adverse event reports.

Published literature reported three case reports[30,31,32] of uterine rupture with mifepristone/misoprostol treatment in the first trimester. Of these three reports, two patients had a risk factor for uterine rupture (prior uterine surgery). The third case was in a patient who received more than two doses of misoprostol. After consideration, the clinical review team decided that labeling should include information about this event. The FAERS search did not identify any reports of uterine rupture with use of mifepristone alone. Of 80 reports, 77 cited use of misoprostol alone, and three of mifepristone and misoprostol. Only two reports of uterine rupture in the first trimester were identified, both using misoprostol alone; one entailed an unspecified dose and route of misoprostol at 5 weeks gestation, and one involved vaginal administration of 800 mcg misoprostol at 8 weeks gestation for cervical preparation prior to a surgical abortion in a woman with a prior uterine scar.

Based on the available safety reports of uterine rupture, the review team from (b) (6) and clinical review team concluded that these data demonstrated that uterine rupture with Mifeprex and misoprostol in the first ten weeks (70 days) of gestation is exceedingly uncommon, and occurs most often in the face of a risk factor (previous uterine surgery).

Comment: I agree with the clinical review team and the (b) (6) team that the risk of uterine rupture with first trimester use of mifepristone and misoprostol appears to be extremely rare, and most often associated with a prior uterine scar, a known risk factor for uterine rupture. Labeling of these reports is included in section 2.3 of the DOSAGE AND ADMINISTRATION and section 6.2 of the ADVERSE REACTIONS of labeling to provide additional information to healthcare providers, but no restriction of use is needed based upon this extremely rare adverse reaction.

The clinical review team also evaluated the safety for each of the following major changes proposed in this efficacy supplement:

1. Changing the dosing interval between Mifeprex and misoprostol from 48 hours to 24-48 hours
2. Home administration of misoprostol
3. Use of a repeat dose of misoprostol
4. Change in the follow-up timeframe and method of follow-up
5. Allowing providers other than physicians to provide Mifeprex

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[30] Khan S et al. Uterine rupture at 8 weeks' gestation following 600 µg of oral misoprostol for management of delayed miscarriage. Journal of Obstet Gynaecol 2007; 27: 869-870

[31] Bika O, Huned D, Jha S, Selby K Uterine rupture following termination of pregnancy in a scarred uterus J Obstet Gynaecol 2014; 34(2): 198-9. doi: 10.3109/01443615.2013.841132

[32] Willmott F, et al. Rupture of uterus in the first trimester during medical termination of pregnancy for exomphalos using mifepristone/misoprostol. BJOG 2008;15:575-77

To evaluate each of these changes, the reviewers evaluated the adverse event information regarding:

- *Changing the timing interval between Mifeprex and misoprostol and change in the gestational age to 70 days:* Support for the 24-48 hour interval and use up through 70 days was primarily based on a large systematic review by Shaw et al[33]. This review evaluated studies looking at different follow-up modalities and demonstrated that there are a variety of acceptable alternatives to in-clinic follow-up that can identify cases in which there is need for additional intervention. In addition, the systematic review did not identify any significant difference in adverse events with different time intervals. Based on these findings, labeling will not be directive regarding specific details of how follow-up should be performed; this will be a decision between the patient and her healthcare provider.

- *Home administration of misoprostol:* The Applicant supplied several published studies that supported this change including Gatter et al[34] and Ireland et al[35]. These studies reported on large numbers of women in the U.S. who took misoprostol at home. The authors showed that home administration of misoprostol, as part of the proposed regimen, is associated with exceedingly low rates of serious adverse events, and with rates of common adverse events comparable to those in the studies of clinic administration of misoprostol that supported the initial approval in 2000. Given that information is available on approximately 45,000 women from the published literature, half of which incorporated home use of misoprostol, there is no clinical reason to restrict the location in which misoprostol may be taken. Given the fact that the onset of cramping and bleeding occurs rapidly (i.e., generally within 2 hours) after misoprostol dosing, allowing dosing at home increases the chance that the woman will be in an appropriate and safe location when the process begins.

- *Use of a repeat dose of misoprostol:* Safety reporting from studies that evaluated a repeat dose of misoprostol did not specifically assess the subset of women who received a second dose, but no unexpected findings were identified. One randomized controlled trial (Coyaji et al[36]) conducted in 300 women seeking medical abortion in India looked at a single misoprostol dose as compared to two misoprostol doses. Although there was no difference in the complete pregnancy termination rate in women who received a second misoprostol dose compared to those who did not, the repeat misoprostol dose reduced the need for surgical intervention. This study was reassuring in that there was no significant difference in the adverse events observed—similar percentages of women experienced

[33] Shaw KA, Topp NJ, Shaw JG, Blumenthal PB. Mifepristone-misoprostol dosing interval and effect on induction abortion times. Obstet Gynecol 2013;121(6):1335-1347.
[34] Gatter M, Cleland K, Nucatola DL. Efficacy and safety of medical abortion using mifepristone and buccal misoprostol through 63 days. Contraception 2015; 91:269-273.
[35] Ireland LD, Gatter M, Chen AY. Medical compared with surgical abortion for effective pregnancy termination in the first trimester. Obstet Gynecol 2015;126:22-8.
[36] Coyaji K, Krishna U, Ambardekar S, Bracken H, Raote V, Mandlekar A, Winikoff B. Are two doses of misoprostol after mifepristone for early abortion better than one? BJOG 2007;114:271-278.

cramping (87% in the single dose group, 89% in the repeat dose group), nausea (both groups 1%), vomiting (both groups 0%), and diarrhea (0% in the single dose group versus 2% in the repeat dose group). A supportive systematic review by Gallo et al[37] also provided safety information on subjects who received repeat misoprostol. In this review, the only side effects discussed in the trials were diarrhea, which was more common on those groups receiving misoprostol orally than in those receiving it exclusively vaginally (26-27% versus 9%). Rash was reported <1%. Based on these findings, labeling will be changed because the misoprostol dose does not need to be restricted to in clinic administration to assure safe pregnancy termination using the proposed dosing regimen. Given the onset of bleeding and cramping after misoprostol, allowing home administration increases the likelihood that a woman will be in an appropriate and safe location when the pregnancy termination process begins.

- *Change in the follow-up timeframe and method of follow-up:* The Applicant submitted several articles that described different methodologies in follow-up including phone calls and standardized instructions. The clinical reviewers evaluated a study in Scotland by Cameron et al[38] that evaluated self-assessment as compared to standard follow-up methodologies (clinic visit or phone call). Most of the women chose self-assessment over an in-clinic visit or phone call, and there were no significant differences in adverse outcomes between women who underwent self-assessment of health compared to those who had a clinic visit or phone call. Among women with an ongoing pregnancy after Mifeprex and misoprostol, the majority self-identified and presented within two-weeks for care. Based on this information and the other data from the Raymond systematic article[39] that did not identify a difference in failure rate for earlier (less than one week) as compared to one week or greater of follow-up, sufficient support was provided to use a broadened window of 7 to 14 days for follow-up. This revised follow-up time frame will be included in labeling.

- *Allowing providers other than physicians to provide Mifeprex*: The current Prescriber's Agreement in the REMS specifies that "…Mifeprex must be provided by or under the supervision of a physician who meets the following qualifications…" In addition, current labeling states that Mifeprex will be supplied only to licensed physicians who sign and return a Prescriber's Agreement. However, labeling states that other healthcare providers, acting under the supervision of a qualified physician, may also provide Mifeprex to patients. Several published studies submitted by the Applicant indicate that health care providers such as nurse practitioners, nurse midwives, and physician assistants are

[37] Gallo MF, Cahill S, Castelman L, Mitchell EMH. A systematic review of more than one dose of misoprostol after mifepristone for abortion up to 10 weeks gestation. Contraception 2006;74:36-41.
[38] Cameron ST, Glasier A, Johnstone A, Dewart H, Campbell A. Can women determine the success of early medical termination of pregnancy themselves? Contraception 2015;91:6-11.
[39] Raymond EG & Grimes DA. The comparative safety of legal induced abortion and childbirth in the United States. Obstet Gynecol 2012; 119: 215-9

currently providing abortion services. One of these studies (Kopp Kallner et al[40]) was a randomized controlled trial of 1,068 women in Sweden who were randomized to receive medical abortion care from two nurse midwives experienced in medical terminations and trained in early pregnancy ultrasound versus a group of 34 physicians with varying training and experience. Success rates were ≥ 96% regardless of gestational age. The nurse midwife group had few complications, though this was not statistically significant (4.1% for nurse midwives, versus 6.1% for doctors, p=0.14). No serious complications were reported and no blood transfusions were administered in the study. Based on this and other supportive studies, the information supports the efficacy and safety of allowing healthcare providers other than physicians can effectively and safely provide abortion services, provided that they meet the requirements for certification described in the REMS. The clinical team also felt that the term "healthcare provider who prescribes" would be the appropriate terminology as prescribing ability is a critical factor in dispensing Mifeprex.

The clinical review team concluded that the evidence demonstrated acceptable safety for each of the above proposed changes, and I concur with their conclusion. The proposed dosing regimen has a similar safety profile as the original regimen approved in 2000. Adverse outcomes of interest, such as deaths, serious infection, transfusions, ectopic pregnancies and uterine rupture, remain rare, and are not necessarily attributable to Mifeprex use. Overall, the rate of deaths and nonfatal serious adverse events are acceptably low, and data for the proposed regimen do not suggest a safety profile that deviates from that of the originally approved regimen No association between adverse outcomes and increasing gestational age was identified. Finally, the available information supports the safety of the other proposed changes, including increasing the flexibility of the time interval between Mifeprex and misoprostol, at home use of misoprostol, use of a repeat dose of misoprostol, change in the follow-up timeframe and allowing health care providers other than physicians to prescribe and dispense Mifeprex were acceptable.

9. Advisory Committee Meeting

Mifeprex is not a new molecular entity requiring discussion before an advisory committee. In addition, an advisory committee was not necessary as the application did not raise complex scientific or other issues that would warrant holding an AC before approval.

10. Pediatrics

This efficacy supplement triggered requirements under the Pediatric Research Equity Act (PREA). The Agency granted a partial PREA waiver for pre-menarcheal females ages birth to 12 years because it would be impossible to conduct studies in this pediatric population, as pregnancy does not exist in premenarcheal females.

[40] Kopp Kallner H, Fiala C, Stephansson O, Gemzell-Danielsson K. Home self-administration of vaginal misoprostol for medical abortion at 50-63 days compared with gestation of below 50 days. Human Reprod 2010;25(5):1153-1157.

The Applicant fulfilled the remaining PREA requirement in postmenarcheal females by submitting published studies of Mifeprex for pregnancy termination in postmenarcheal females less than 17 years old. Efficacy and safety information in these adolescents was based on a U.S. study in 322 postmenarcheal adolescents (Gatter et al[41]). Of the 322 adolescents, 106 of these adolescents were under 16; see Table 2 below:

Table 2: Age and Number of Adolescents Undergoing Medical Abortion (Gatter et al[42])

Age of Subject	Number of Subjects evaluated
11	1
12	1
13	2
14	20
15	82
16	216

Source: Refer to Table 17 of the Medical Officer's review dated March 29, 2016

The Gatter et al[43] study reported that postmenarchal females less than 18 years old had a 98.7% pregnancy termination rate as compared to females aged 18-24, who had a rate of 98.1%. This article reported that loss to follow-up was slightly higher in those less than 18 years old, however, age did not adversely impact efficacy outcomes.

One issue was whether adolescents would comply with at home use of misoprostol. The Gatter[44] et al study incorporated at home use of misoprostol into the Mifeprex dose regimen given to all females, including postmenarchal females less than 18 years old. The overall efficacy in adolescents was similar to that of all older women. This information supports at home administration of misoprostol in postmenarchal females under 17.

Two other published studies provided additional efficacy on Mifeprex use by adolescents for pregnancy termination:

- Phelps et al[45] evaluated data from 28 adolescents aged 14 to 17, at ≤ 56 days gestation, using Mifeprex 200 mg followed 48 hours later by misoprostol 800 mcg vaginally. In this study, 100% of subjects had a complete pregnancy termination, with five not requiring misoprostol.

[41]Gatter M, Cleland K, Nucatola DL. Efficacy and safety of medical abortion using mifepristone and buccal misoprostol through 63 days. Contraception 2015; 91:269-273.
[42] Ibid.
[43]Gatter M, Cleland K, Nucatola DL. Efficacy and safety of medical abortion using mifepristone and buccal misoprostol through 63 days. Contraception 2015; 91:269-273.
[44]Gatter M, Cleland K, Nucatola DL. Efficacy and safety of medical abortion using mifepristone and buccal misoprostol through 63 days. Contraception 2015; 91:269-273.
[45]Phelps RH, et al. Mifepristone abortion in minors. Contraception 2001;64:339-343.

- Niinimaki et al[46] used data from a Finnish Registry from 2000-2006. An analysis of efficacy between adolescents under age 18 compared to the women ≥ age 18 indicated that the adolescent group had a lower rate of incomplete abortions as compared to adults. And efficacy outcomes in adolescents were similar to those of adult women.

The safety of Mifeprex in postmenarcheal adolescents was primarily supported by adverse event information from the Gatter et al[47] study. (b) (6), (b) (4) Supportive data from a Finnish registry (Niinimaki et al) from 3024 adolescent females under 18 years of age reported that, compared to adult women, the risks of hemorrhage (adjusted odds ratio 0.87 [95% confidence interval: 0.77 to 0.99]), incomplete abortion (0.69, [95% confidence interval: 0.59 to 0.82]), and surgical evacuation (0.78, [95% confidence interval: 0.67 to 0.90]) were lower in the adolescent cohort. In the Finnish registry study, a majority of adolescents and adults received both Mifeprex and misoprostol. Safety findings from the Gatter et al and Niinimaki et al studies are reassuring and indicate that the safety profile of Mifeprex is similar between postmenarcheal adolescents and adult women.

Additional details from this article and other published data on Mifeprex use in adolescents (females under 17) are described in the clinical review (Refer to the Medical Officer's review dated March 29, 2016).

(b) (6) concurred that the efficacy and safety data in postmenarcheal adolescents less than 17 years old was sufficient to support the use of Mifeprex in this pediatric population and to fulfill the PREA pediatric study requirement. The revised Mifeprex labeling will state that that efficacy and safety are similar to adult women in the Pediatric Use section (8.4).

11. Other Relevant Regulatory Issues

(b) (6)

reviewed the Medication Guide in conjunction with the (b) (6) ((b) (6) Both (b) (6) and (b) (6) found the Medication Guide to be acceptable with recommended changes (See review dated March 29, 2016). The Division considered all of the recommendations from (b) (6) in revising and updating the text in

[46]Niinimaki M, et al. Comparison of rates of adverse events in adolescent and adult women undergoing medical abortion: population register based study. BJM 2011;342: d2111.
[47]Gatter M, Cleland K, Nucatola DL. Efficacy and safety of medical abortion using mifepristone and buccal misoprostol through 63 days. Contraception 2015; 91:269-273.
[48]Niinimaki M, et al. Comparison of rates of adverse events in adolescent and adult women undergoing medical abortion: population register based study. BJM 2011;342: d2111.

the Medication Guide and incorporated appropriate changes into the final agreed upon Medication Guide.

(b) (6) (b) (6)

reviewed the Prescribing Information (PI) in addition to the joint review with (b) (6) of the Medication Guide in conjunction with (b) (6) After review, (b) (6) provided recommended changes (See (b) (6) review dated March 29, 2016). The Division considered all of the recommendations from (b) (6) in revising and updating the text in the PI and incorporated appropriate changes into the final label.

(b) (6) (b) (6)

(b) (6) (b) (6) in the (b) (6)) reviewed the proposed modifications to the REMS. The (b) (6) review reflected agreement with the Applicant's proposed REMS changes which include:

- Removal of the term "under Federal law" from the Prescriber's Agreement.
- Replacement of the word "physician" with a broader term to describe appropriate healthcare professionals who may order, prescribe and administer Mifeprex. (b) (6) believes that the Applicant's proposed terminology of " (b) (4) is too broad and that a more appropriate description is "healthcare provider who prescribes," which limits acceptable healthcare providers to those who are licensed in their state to prescribe medications.
- Removal of the Medication Guide from the REMS. The Medication Guide remains an important education tool for patients. It will still be dispensed to each patient in accordance with 21 CFR part 208. As described in the Medication Guide Guidance, a Medication Guide is not necessary to ensure that the benefits outweigh the risks of Mifeprex
- Modification of Element to Assure Safe Use (ETASU) A, the Prescriber's Agreement. (b) (6) recommends changing the name of the document to the Prescriber's Agreement Form to be consistent with other REMS programs. References to "physician" should be changed to "healthcare provider who prescribes."
- (b) (6) recommends removing the Patient Agreement from the REMS for a number of reasons:
  1. The established safety profile over 15 years of experience with Mifeprex is well-characterized, stable, and known serious risks occur rarely
  2. The Medication Guide contains the same risk information addressed in the Patient Agreement, and will still be provided to patients under 21 CFR part 208
  3. The Prescriber's Agreement Form will continue to require providers to explain the treatment, its effects and risks associated with Mifeprex and to answer any questions that a patient may have
  4. Established clinical practice provides for counseling, informing the patient about follow-up, when to contact the provider/clinic, answering questions and obtaining signed informed consent before treatment. FDA has removed REMS

requirements in other programs based on the integration of the REMS safe use condition into clinical practice.

Other revisions to the REMS document will be made for consistency with changes described above and to reflect current FDA thinking and practice regarding format, language and flow in REMS documents. These changes include modification of the Mifeprex REMS goal, changes in requirements to certify prescribers (removal of the requirement to obtain a Patient Agreement) and other minor edits.

In summary, the overall (b) (6) recommendation for the REMS modification for this efficacy supplement was approval (Refer to (b) (6) review dated March 29, 2016).

12. Labeling

Carton and container labeling was reviewed by the (b) (6) ((b) (6) the (b) (6) ((b) (6) and the (b) (6) ((b) (6) (b) (6) Their comments were conveyed to the Applicant as appropriate.

The label was submitted in the format prescribed by the PLR. Although the supplement was submitted prior to when it would otherwise have been required to comply with the PLLR requirements, the review team believed it would be of value to harmonize with this labeling standard to the extent possible.

Specific issues discussed during labeling negotiations included the selection of studies for inclusion in Section 6.1 (Clinical Trial Experience in the ADVERSE REACTIONS section) and 14 (CLINICAL STUDIES section). Only studies that evaluated the specific proposed regimen were included in these sections. For the Adverse Reactions section, examination of the common adverse reaction data by U.S. compared to non-U.S. study location revealed that there were large differences in the frequency of common adverse reactions, with the reporting rate considerably higher among the U.S. studies. This may reflect differences in ascertainment or subject reporting of adverse reactions in non-U.S. studies. Regardless, inclusion of this non-U.S. data would not be appropriate, as it is unlikely to be informative to the U.S. population of users. In the case of serious adverse reactions, the reported frequency was quite similar regardless of study location; for this reason, serious adverse reaction information from global studies is reported. Agreement on labeling was reached on March 29, 2016.

Post-Marketing Requirement/Commitment and Risk Evaluation and Mitigation Strategies (REMS):

Postmarketing Requirements/Postmarketing Commitments: None.

Risk Evaluation and Mitigation Strategies (REMS): The Applicant proposed a REMS modification for the Mifeprex REMS program with the submission of this efficacy supplement. The review teams from the (b) (6) evaluated the current Mifeprex REMS program and the proposed REMS modifications to determine whether each Mifeprex REMS element remains necessary to ensure that the benefits of Mifeprex outweigh the risks. Factors that impacted the decision included findings from two REMS assessments (the more recent REMS assessment review was completed in October 2015), an unchanged safety profile, and published literature that documented adequate safeguards in clinical practice with the use of Mifeprex in a regimen with misoprostol.

The teams determined that the following REMS modifications were warranted:

1. Revisions to the Prescriber Agreement Form to reflect the new dosing regimen and to reflect current REMS formatting and language standards
2. Removal of the Medication Guide as a REMS element, as distribution of the Medication Guide is required under 21 CFR 208
3. Removal of the Patient Agreement as a Documentation of Safe Use Condition (ETASU D)
4. Updating of the REMS goals to reflect the above 3 changes.
5. Removal of the phrase "Under Federal law" from the Prescriber's Agreement
6. Replacing the term "licensed physician" with "healthcare provider who prescribes"

The above modifications to the Mifeprex REMS program were discussed with the (b) (6) (b) (6) on January 15, 2016, as per (b) (6) .

The (b) (6) concurred with conforming changes to the Prescriber's Agreement to reflect the new dosing regimen, and with removal of the Medication Guide from the REMS. The Medication Guide would remain a part of labeling to inform patients about the risks associated with Mifeprex use. The (b) (6) also concurred with revisions to the REMS goals to reflect these changes.

The (b) (6) concurred with the removal of the term "under Federal law". A rationale for the original inclusion of the phrase "Under Federal law" cannot be discerned from available historical documents, nor is it consistent with REMS materials for other products. All the conditions of approval, including the REMS materials, are under Federal law; therefore, the phrase is unnecessary and it was decided that the phrase be removed from the Prescriber's Agreement.

The (b) (6) concurred with use of the term "healthcare providers who prescribe." To support a change in the REMS that would allow qualified healthcare providers other than physicians to prescribe Mifeprex through the Mifeprex REMS program, the Applicant provided information from over 3,200 women in randomized controlled trials and 596 women in prospective cohort studies comparing medical abortion care by physicians versus other providers (nurses or nurse midwives). These studies were conducted in a variety of settings (international, urban, rural, and low-resource). No differences in serious adverse events, ongoing pregnancy or incomplete abortion were identified between the groups. Given that providers other than physicians are providing family planning and abortion care under supervision and that the approved labeling and REMS program stipulate that prescribers must be able to refer patients for additional care, including surgical management, allowing these prescribers to participate in the Mifeprex REMS program is acceptable.

The (b) (6) also concurred with the teams' recommendation to remove the Patient Agreement (ETASU D) from the REMS although some (b) (6) members commented that additional support for the review team's rationale for this modification was needed. The review team's rationale for this change was:

APPEARS THIS WAY ON ORIGINAL

- The safety profile of Mifeprex is well-characterized over 15 years of experience, with known risks occurring rarely; the safety profile has not changed over the period of surveillance.
- Established clinical practice includes patient counseling and Informed Consent, and, more specifically with Mifeprex, includes counseling on all options for termination of pregnancy, access to pain management and emergency services if needed.
- Medical abortion with Mifeprex is provided by a well-established group of organizations and their associated providers who are knowledgeable in this area of women's health. Their documents and guidelines cover all the safety information that also appears in the Patient Agreement.
- ETASUs A and C remain in place: The Prescriber's Agreement under ETASU A requires that providers "explain the procedure, follow-up, and risks to each patient and give her an opportunity to discuss them." The REMS will continue to require that Mifeprex be dispensed to patients only in certain healthcare settings, specifically, clinics, medical offices, and hospitals. This ensures that Mifeprex can only be dispensed under the direct supervision of a certified prescriber.
- Labeling mitigates risk: The Medication Guide, which will remain a part of labeling, contains the same risk information covered under the Patient Agreement.

The Mifeprex REMS program will have a modified ETASU REMS that will continue to ensure that Mifeprex can only be prescribed by certified prescribers and be dispensed to patients in certain healthcare settings, specifically, clinics, medical offices and hospitals. The Medication Guide will continue to be distributed to patients required under 21 CFR part 208. As required for all ETASU REMS, ongoing assessments of the Mifeprex REMS program will continue to ensure that the modified Mifeprex REMS program is meeting its goals.

13. Decision/Action/Risk Benefit Assessment

Decision:

All regulatory and scientific requirements have been adequately addressed in this efficacy supplement. Review teams involved in this supplement have recommended approval of the supplement from their disciplines' perspective. The submitted efficacy and safety information supported approval of the proposed dosing regimen through 70 days gestation, and other changes discussed in this summary memo. This supplement will receive an Approval action.

Benefit Risk Assessment:

This efficacy supplement provided substantial evidence of efficacy for the proposed dosing regimen through 70 days gestation. The efficacy findings were similar to those that led to the approval of the original dosing regimen in 2000. In addition, the submitted published literature supported other changes sought in this efficacy supplement that will

be reflected in labeling: 1) a more flexible time interval of 24 to 48 hours between Mifeprex and misoprostol administration, 2) the option of at home administration of misoprostol, 3) the option of repeat misoprostol dosing, if clinically indicated, 4) flexibility in the follow–up time frame of 7 to 14 days, and 5) permitting qualified healthcare providers other than physicians to prescribe Mifeprex.

The safety findings of the proposed dosing regimen were acceptable and were similar to those seen with the original dosing regimen approved in 2000.

After review of the REMS modifications proposed by the Sponsor, I concur with the clinical team and (b) (6) recommendations that:

1. The Medication Guide can be removed from the Mifeprex REMS program. The Medication Guide requirements under 21 CFR part 208 require the Medication Guide to be distributed to patients. Mifeprex will only be dispensed by a healthcare professional who will be knowledgeable and able to provide the patient instructions on appropriate use of the drug, including what potential side effects may occur or follow-up that may be required as appropriate, and who will answer any questions the patient may have. In that setting, the Medication Guide will already be a required available tool for counseling. Therefore, given the existing requirements under 21 CFR part 208, I concur that there is no reason for the Medication Guide to specifically be a part of the REMS.

2. The Prescriber Agreement Form (ETASU A) as revised reflects current FDA format and content to conform to current REMS programs and reflect the labeling changes that will be approved in this supplement. I concur that the changes are acceptable.

3. Revision of the Mifeprex REMS goals (ETASU C) will adequately mitigate the risk of serious complications by requiring certification of healthcare providers who prescribe and ensuring the Mifeprex is dispensed only in certain healthcare settings by or under the supervision of a certified prescriber.

4. Removal of the Patient Agreement Form (ETASU D): I concur with the clinical review team that the Patient Agreement Form, which requires a patient's signature, does not add to safe use conditions for the patient for this REMS and is a burden for patients. It is standard of care for patients undergoing pregnancy termination to undergo extensive counseling and informed consent. The Patient Agreement Form contains duplicative information already provided by each healthcare provider or clinic. I believe that it is much more critical for the healthcare provider who orders or prescribes Mifeprex to provide and discuss informed consent derived from their own practice so that care can be individualized for the patient.

I support that the Mifeprex REMS with ETASUs A and C remain in place to support conditions critical to the use of the drug. Therefore, the implementation system and timetable for assessments should continue.

I also agree with the clinical review team that the reporting requirements should only be required for deaths. It is important that the Agency be informed of any deaths with Mifeprex to monitor new safety signals or trends. However, after 15 years of reporting serious adverse events, the safety profile for Mifeprex is essentially unchanged. Therefore, I agree that reporting of labeled serious adverse events other than deaths can be collected in the periodic safety update reports and annual reports to the Agency.

In summary, I believe that the benefit-risk profile for Mifeprex continues to be favorable and with the agreed-to labeling changes and REMS modifications, the Mifeprex REMS program will continue to assure safe use. Therefore, I support approval of this efficacy supplement and REMS modifications.

Addendum:

On March 28, 2016, Dr. Janet Woodcock, the Director, Center for Drug Evaluation and Research, asked [redacted] (b) (6) and the [redacted] (b) (6) to continue to include a Patient Agreement Form in the REMS for Mifeprex (see March 28, 2016 Memorandum from Janet Woodcock, MD, Director, Center for Drug Evaluation and Research, through the [redacted] (b) (6) (6) Therefore, the Patient Agreement Form will be retained and other changes will be made in the REMS to reflect that it is being retained.

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/s/

(b) (6)

03/29/2016

EXHIBIT

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The Abortion Pill Harms Women: Insurance Data Reveals One in Ten Patients Experiences a Serious Adverse Event,
t ic Pub. Pol y Ctr. (Apr. 2 , 2025)

LIFE AND FAMILY INITIATIVE

ETHICS AND PUBLIC POLICY CENTER
Shaping Policy, Renewing Culture.

The Abortion Pill Harms Women: Insurance Data Reveals One in Ten Patients Experiences a Serious Adverse Event

Jamie Bryan Hall, Director of Data Analysis, Ethics and Public Policy Center
Ryan T. Anderson, President, Ethics and Public Policy Center

APRIL 28, 2025

Summary

- This largest-known study of the abortion pill is based on analysis of data from an all-payer insurance claims database that includes 865,727 prescribed mifepristone abortions from 2017 to 2023.
- 10.93 percent of women experience sepsis, infection, hemorrhaging, or another serious adverse event within 45 days following a mifepristone abortion.
- The real-world rate of serious adverse events following mifepristone abortions is at least 22 times as high as the summary figure of "less than 0.5 percent" in clinical trials reported on the drug label.
- The FDA should immediately reinstate its earlier, stronger patient safety protocols to ensure physician responsibility for women who take mifepristone under their care, as well as mandate full reporting of its side effects.
- The FDA should further investigate the harm mifepristone causes to women and, based on objective safety criteria, reconsider its approval altogether.

Danco Laboratories markets Mifeprex as "the safe and effective abortion pill," but our research shows that mifepristone abortion, as currently practiced in the U.S., is not safe and effective.[1] The manufacturer and the FDA rely on the results of 10 clinical trials with a total of 30,966 participants, less than 0.5 percent of whom reportedly experienced serious adverse reactions. In contrast, we analyzed real-world insurance claims data for 865,727 prescribed mifepristone abortions, broadly representative of women who obtain mifepristone abortions in the U.S. today, and we find a serious adverse event rate of 10.93 percent—at least 22 times as high as the summary figure reported on the drug label. In light of this research, we urge the FDA to reinstate earlier, stronger patient safety protocols and reconsider its approval of mifepristone altogether. Women deserve better than the abortion pill.

Our Key Findings

10.93 percent of women experience sepsis, infection, hemorrhaging, or another serious or life-threatening adverse event within 45 days following a mifepristone abortion, far greater than the summary figure of "less than 0.5 percent" in clinical trials reported on the drug label. *Figure 1, next page.*

[1] Danco Laboratories, "The Safe and Effective Abortion Pill | Mifeprix (mifepristone)," https://www.earlyoptionpill.com (accessed April 14, 2025)

Figure 1

Serious Adverse Events by Category

	Number with adverse events	Serious adverse event rate
Sepsis	824	0.10%
Infection	11,707	1.34%
Transfusion	1,257	0.15%
Hemorrhage	28,658	3.31%
Hospitalization (related to the abortion)	5,699	0.66%
ER visit (related to the abortion)	40,960	4.73%
Ectopic pregnancy	3,062	0.35%
Other life-threatening adverse events (cardiac, pulmonary, thrombosis, anaphylaxis, surgery)	1,956	0.22%
Repeated (surgical) abortion	24,563	2.84%
Other abortion-specific complications	49,169	5.68%
Overall	94,605	10.93%

Note: The overall serious adverse event rate of 10.93% is adjusted for the fact that some women suffer from adverse events in multiple categories.

Simply stated, mifepristone, as used in real-world conditions, is not "safe and effective."

Our real-world post-market observational study of mifepristone is, to our knowledge, the most comprehensive study of chemical abortion safety ever conducted in the U.S.:

- We identify and include 865,727 prescribed mifepristone abortions, 28 times as many as were included in all FDA-cited clinical trials combined.
- Our dataset is more recent, no earlier than 2017, while the FDA approval of mifepristone relies entirely on data from more than a decade ago.
- The women in our dataset are broadly representative of the women who obtain mifepristone abortions in the U.S.; they are not a prescreened group of generally healthy women recruited into various clinical trials conducted at different times around the world.
- The women in our dataset receive (or fail to receive) pre- and post-abortion healthcare of the real-world quality that prevails in the U.S. today, not the carefully controlled regimen of care that ordinarily prevails in a clinical trial.

Policy Implications

The FDA should reinstate the original patient safety protocols that were required when mifepristone was first approved. Doing so will likely reduce the harms to women and permit better monitoring to determine whether this drug should remain on the market:

- Prescribing mifepristone and misoprostol for the termination of pregnancy should require at least three in-person office visits by the patient—as originally required by the FDA.
- Mifepristone should be prescribed only by physicians—as originally required by the FDA—who have read and understood the prescribing information.
- Mifepristone should be administered only in a clinic, medical office, or hospital, by or under the supervision of a physician, able to assess the gestational age of an embryo and to diagnose ectopic pregnancies—all of which was originally required by the FDA.
- Physicians must be able to provide surgical intervention in cases of incomplete abortion or severe bleeding, or have made plans to provide such care through others, and be able to assure patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary.
- Healthcare providers should be required once again to report to the FDA (and manufacturers of mifepristone) all serious adverse events resulting from the use of mifepristone.
- Mifepristone should only be prescribed to a woman who is confirmed by a physician to be in the first seven weeks of pregnancy—as originally required by the FDA.

Background on FDA Approval and Regulation of Mifepristone

Mifepristone was developed by the French pharmaceutical company Roussel Uclaf S.A. and brought to the United States at the urging of President Clinton and after Congressional pressure. The FDA approved it under a little-used approval process for "certain new drug products that have been studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit to patients over existing treatments."[2] Thus, to grant approval in this manner, the FDA had to consider an unwanted pregnancy a "serious or life-threatening illness" and find that mifepristone was more effective than surgical abortion in treating it. The FDA's decision cites minimal data: clinical trials with only 859 participants in the U.S. and 1,800 in France.[3]

The original FDA-approved drug label for Mifeprex (the brand name of mifepristone) from September 2000 indicated use of the drug for "the medical termination of intrauterine pregnancy through 49 days' pregnancy."[4] It required several modest safeguards for women's health:

> Treatment with Mifeprex and misoprostol for the termination of pregnancy requires three office visits by the patient. Mifeprex should be prescribed only by physicians who have read and understood the prescribing information. Mifeprex may be administered only in a clinic, medical office, or hospital, by or under the supervision of a physician, able to assess the gestational age of an embryo and to diagnose ectopic pregnancies. Physicians must also be able to provide surgical intervention in cases of incomplete abortion or severe bleeding, or have made plans to provide such care through others, and be able to assure patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary.[5]

During the Obama and Biden administrations, the FDA chipped away at these initial safeguards, risking women's health in order to increase access to abortion. Under the current Risk Evaluation and Mitigation Strategy (REMS) in effect since 2023:

1. a mifepristone abortion now requires as a little as one telehealth visit with any approved healthcare provider (not necessarily a physician),
2. a woman may self-administer drugs obtained from a mail-order pharmacy, and
3. the prescriber need not report any adverse events unless he or she knows that a patient has died. *Figure 2.*

Figure 2

Weakening FDA Safeguards for Mifepristone

	2000 Clinton Initial Approval	2016 Obama REMS Changes	2023 Biden REMS Changes
Required number of in-person visits	3	1	0
Maximum gestational age (LMP)	7 weeks	10 weeks	10 weeks
Drugs prescribed only by physician	✓	✗	✗
Drugs dispensed only in office	✓	✓	✗
Drugs taken only in office	✓	✗	✗
Required in-office follow-up	✓	✗	✗
Required reporting of adverse events	✓	✗	✗

2 Alliance for Hippocratic Medicine v. FDA, Complaint, https://adflegal.org/wp-content/uploads/2022/11/Alliance-for-Hippocratic-Medicine-v-FDA-2022-11-18-Complaint.pdf
3 Mifeprex (mifepristone) drug label, September 2000, page 3, https://www.accessdata.fda.gov/drugsatfda_docs/label/2000/20687lbl.pdf
4 Mifeprex (mifepristone) drug label, September 2000, page 6, https://www.accessdata.fda.gov/drugsatfda_docs/label/2000/20687lbl.pdf
5 Mifeprex (mifepristone) drug label, September 2000, page 14, https://www.accessdata.fda.gov/drugsatfda_docs/label/2000/20687lbl.pdf

The current FDA-approved drug label refers to the results of 10 clinical trials with a total of 30,966 participants, less than 0.5 percent of whom reportedly experienced serious adverse reactions.[6] But these figures are based entirely on data from trials taking place more than a decade ago.

The Increasing Market Share of Chemical Abortion

Increased access to chemical abortion has coincided with a rapid increase in its prevalence. Chemical abortions—the vast majority of which are performed using a combination of mifepristone and misoprostol—now account for roughly two-thirds of all abortions in the United States. *Figure 3.*

In fact, Danco Laboratories boasts that more than 5 million U.S. women have used its abortion pill since it was approved in 2000.[7] Thus, it has become increasingly important to understand the risks and harms to women from chemical abortion in general and from mifepristone in particular.

How We Identified Mifepristone Abortions

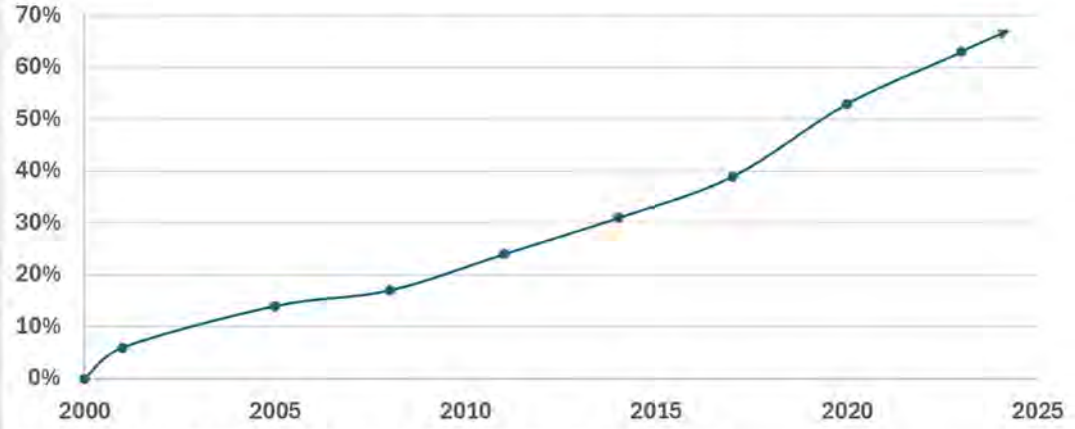
In our data, a mifepristone abortion was identified in one of three ways:

1. procedure code S0199: medically induced abortion by oral ingestion of medication including all associated services and supplies,
2. a prescription for mifepristone (with or without misoprostol within the next 3 days), or
3. a diagnosis code for elective termination or unwanted pregnancy, along with other billing coding consistent with manufacturer instructions for reimbursement for a mifepristone abortion for a given state and insurer combination.[8]

Following this method, we identified a total of 865,727 mifepristone abortions prescribed for a total of 692,873 women from 2017 to 2023. This includes 566,446 women, each of whom had one such abortion, and 126,427 women with multiple such abortions.

Figure 3

Chemical abortion has increased rapidly since approval in 2000 and now accounts for approximately two-thirds of all abortions.



Source: Guttmacher Abortion Provider Census and Monthly Abortion Provision Study, via https://www.guttmacher.org/2024/03/medication-abortion-accounted-63-all-us-abortions-2023-increase-53-2020

6 Page 7 of the drug label states, "Serious adverse reactions were reported in <0.5% of women. Information from the U.S. and non-U.S. studies is presented in Table 2." Table 2 on page 8 indicates that some categories of serious adverse reactions were observed at higher rates in some trials, but this is never discussed in the text, leaving only the previous statement with which to interpret the table. See Mifeprex (mifepristone) drug label, January 2023, https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/020687Orig1s026lbl.pdf

7 Danco Laboratories, "The Safe and Effective Abortion Pill | Mifeprex (mifepristone)," https://www.earlyoptionpill.com (accessed April 14, 2025)

8 Danco Laboratories, "Mifeprex State Payer Policies," https://www.earlyoptionpill.com/how-do-i-get-mifeprex/state-payer-policies (accessed April 14, 2025)

How We Identified Serious Adverse Events

We followed the official FDA definition of "serious adverse event."[9] To do so, we identified relevant ICD-10 diagnosis codes and CPT/HCPCS procedure codes for adverse events from multiple sources:

- CDC Severe Maternal Morbidity (SMM) indicators,[10]
- CMS Diagnosis-Related Group (DRG) 770 and 769 codes,[11]
- FDA Adverse Events Reporting System (FAERS) reports (interpreted and translated into diagnosis and procedure codes by the doctors on our team),[12] and
- a small number of (mostly gynecological) codes suggested by our doctors.

These codes were then graded by a team of physicians using the the NIH Common Terminology Criteria for Adverse Events (CTCAE version 5), which categorizes adverse events by severity on a 5-point scale.[13] We included CTCAE Grade 3 (severe) and Grade 4 (life-threatening). We did not include Grade 1 (mild) or Grade 2 (moderate). (Grade 5 is death, which would count as a serious adverse event under the FDA definition but could not necessarily be observed in the insurance claims data. We hope to show the rate of death in a subsequent report.)

For reporting, we have grouped the relevant diagnosis and procedure codes as follows:

1. The mifepristone label divides serious adverse events into six categories identified in the clinical trials: sepsis, infection, transfusion, hemorrhage, hospitalization, and emergency room visit. Only those hospitalizations and emergency room visits with abortion-related diagnosis and procedure codes are included in our analysis.
2. FAERS received reports of various events that our doctors judge to be life-threatening and have grouped into broad categories: ectopic pregnancy, surgery, cardiac, pulmonary, thrombosis, and anaphylaxis.
3. Repeated (surgical) abortion procedures are considered serious adverse events.
4. Other abortion complications include codes specifically related to an abortion or miscarriage, as well as life-threatening mental health diagnoses, etc.

We consider only serious adverse events that occurred within 45 days following the abortion. This is conservative, as some adverse events may present later (and studies relied on by the FDA used a timeframe as long as 72 days). Additionally, the likelihood of a subsequent pregnancy within this timeframe is negligible, which ensures that adverse events are related to the abortion rather than to a subsequent pregnancy.

Our Data

Our team has purchased access to a commercially available all-payer health insurance claims database including de-identified data for all U.S. patients during the years 2017 to 2023. It includes information on hospital and office visits, diagnoses, procedures, and prescriptions processed through private health insurance, Medicaid, Medicare, TRICARE, and the Department of Veterans Affairs (VA). The data excludes transactions for which the insurer is also the provider (as is the case with some HMOs and much VA care), as well as cash pay transactions (which are disproportionately common for abortion). This dataset provides longitudinal tracking of medical diagnoses, procedures, and prescriptions for each patient and is widely used in academic and regulatory research.

9 FDA, "What is a Serious Adverse Event?," https://www.fda.gov/safety/reporting-serious-problems-fda/what-serious-adverse-event
10 CDC, "Identifying Severe Maternal Morbidity (SMM)," https://www.cdc.gov/maternal-infant-health/php/severe-maternal-morbidity/icd.html
11 CMS, "ICD-10-CM/PCS MS-DRG v37.0 Definitions Manual," https://www.cms.gov/icd10m/version37-fullcode-cms/fullcode_cms/P0287.html
12 FDA, "FDA Adverse Events Reporting System (FAERS) Public Dashboard," https://fis.fda.gov/sense/app/95239e26-e0be-42d9-a960-9a5f-7f1c25ee/sheet/33a0f68e-845c-48e2-bc81-8141c6aaf772/state/analysis
13 NIH, "Common Terminology Criteria for Adverse Events (CTCAE)," https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm

Our Research Project Team

Our research project was conducted and validated by a team of data scientists, analysts, and engineers, with assistance from our clinical team of board-certified obstetricians and gynecologists. Members have a history of academic research and peer-reviewed publication.

Conclusion

Our research shows unequivocally that mifepristone abortion, as currently practiced in the U.S., is considerably more dangerous to women than is represented on the FDA-approved drug label. The FDA should immediately reinstate its earlier, stronger patient safety protocols to ensure physician responsibility for women who take mifepristone under their care, as well as mandate full reporting of its side effects. The FDA should further investigate the harm this drug causes to women and, based on objective safety criteria, reconsider its approval altogether. Women deserve better than the abortion pill.

This paper is the first in a series investigating women's health and abortion using real-world data.

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Research Article

Comparative Acuity of Emergency Department Visits Following Pregnancy Outcomes Among Medicaid Eligible Women, 2004-2015

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Abstract:

Objectives: We sought to compare the acuity of emergency department (ED) visits following various pregnancy outcomes.

Methods: Cohorts of ED visits by continuously eligible Medicaid women between 2004-2015 were determined by the type of pregnancy outcome and a control group as follows: within 30 days of a chemical (mifepristone) abortion, surgical abortion, or live birth; and at any time for women who were never pregnant. The primary outcome was the percent of ED visits coded as either severe or critical (CPT codes 99284-99285). The study population was extracted from the 17 states where Medicaid pays for abortion services.

Results: All cohorts exhibited a pattern of both increasing incidence and acuity of ED visits. For the entire observation period, an ED visit following a chemical abortion was significantly more likely to have a severe or critical acuity rating than a visit following surgical abortion, live birth, or an ED visit at any time by a woman who was never pregnant. With never-pregnant women as a reference cohort, odds ratios (ORs) are as follows: chemical abortion 2.01 [1.93-2.28]; surgical abortion 1.53 [1.43-1.63]; live birth 1.01 [1.00-1.01]. With chemical abortion as the reference cohort, odds ratios (ORs) are: never-pregnant 0.48 [0.44-0.54]; live birth 0.52 [0.49-0.55]; surgical abortion 0.73 [0.68-0.77].

Conclusion: Consistent with national trends for ED visits, both the number and acuity of ED visits following pregnancy outcomes are increasing. ED visit acuity following chemical abortion is persistently and significantly higher than for surgical abortion or live birth.

Keywords: pregnancy outcomes; induced abortion; emergency department visits; patient acuity

Introduction

Background: There is consensus that the overall incidence of adverse events and emergency department (ED) complication rates are higher following chemical abortion than surgical abortion (1,2). However, the acuity of ED visits following each type of abortion has been contested.

Importance: Some investigators have suggested that ED visits following abortion, especially chemical abortion, are frequently for observation care only rather than treatment purposes (3). This view, if demonstrated, would support the notion that the risks of chemical abortion are exaggerated by the high incidence of ED utilization. To date, no objective independently derived

acuity methodology has been applied to ED visits following pregnancy outcomes.

Goals of This Investigation: We sought to compare the acuity of ED visits within a defined population of women who had undergone abortion or birth.

Methods

Study Design: Analytic observational prospective cohort
Setting and Selection of Participants: Centers for Medicare and Medicaid Services (CMS) Medicaid Analytic eXtract files for the 17 states which funded abortion services were used to identify emergency department (ED) visits within 30 days following a chemical (mifepristone) abortion, surgical abortion, or live birth between 2004-2015. ED visits following a defined pregnancy outcome were determined for women who were 16 years of age in 1999 and who were enrolled in Medicaid in at least a single month in every calendar year 1999-2015. Observation years of 2004-2015 were selected based upon the availability of ED visits related to chemical abortion which was approved by the Food and Drug Administration (FDA) in 2000. The first chemical abortions (n=15) and related ED visits (n=1) appeared in the data in 2001 and were not of sufficient volume for analysis until 2004. In the first observation year, 2004, there were 1,319 chemical abortions and 198 related ED visits. A 5% sample from a control cohort of Medicaid enrollees with no history of pregnancy was also analyzed.

Exposures: The primary exposure of interest was the type of pregnancy outcome. Live births were identified using ICD-9 codes V27.0, V27.2, and V27.5x and ICD-10 codes Z37.0, Z37.2, and Z37.5x. Induced abortions were identified using ICD-9 codes 635.xx and ICD-10 codes O04.xx; CPT4 codes 59840, 59841, 59850, 59852, 59855, 59856, and 59857; and HCPCS codes S0199, S2260, S2265, S2267, X7724, X7726, S0190 and S0191.
Outcomes: The primary outcome of interest was the percent of ED visits coded as either severe or critical. The acuity determination uses five Current Procedure Terminology (CPT) codes to stratify ED visits: nonurgent (99281), urgent (99282), moderate (99283), severe (99284) and critical (99285). ED visits were identified using Place of Service code 23. This coding considers the severity of the presenting problem and the complexity of the medical decision making required for treatment. This method is part of the Ambulatory Payment System (APC) of coding by which the federal government prospectively pays hospitals for covered services by considering resource utilization, clinical intensity and cost (4,5).

Data Analysis: We calculated the percentage change in counts of ED visits between 2004-2015. For each cohort, we derived a linear equation to express the trend in the proportion of severe and critical (99284 and 99285) visits to total visits. Coefficients of determination (R^2, Microsoft Excel, version 16) and Cochran-Armitage Chi-squared (X^2, MedCalc) trend tests were calculated for each cohort. Logistic regression adjusted odds ratios and 95% confidence limits (SAS/STAT, version 10) were calculated with chemical abortion and never-pregnant as reference cohorts.

Ethics Approval: The study has been exempted from Institutional Review Board (IRB) review pursuant to the U.S. Department of Health and Human Services Policy for the Protection of Human Research Subjects at C.F.R. 46.101(b). See IRB ID: 7269, www.sterlingirb.com.

Results

Between 2004 and 2015, the total number of ED visits across all four cohorts increased from 51,307 to 68,798, or 17,491, which is more than a third (34.1%) larger than the 2004 number. Specific percentage increases in each of the cohorts in total visits were: no pregnancy (42.8%); surgical abortion (280.4%); chemical abortion (2649.7%); and live birth (9.2%). ED visits coded severe or critical (99284-5) increased as follows: no pregnancy (101.0%); surgical abortion (450.6%); chemical abortion (4041.1%); and live birth (20.9%) (Table 1).

CPT codes	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2004-15	Δ 2004-15
No Pregnancy														
99281-83(%)	162(61.3)	167(66.8)	162(62.3)	167(53.8)	203(57.0)	182(56.1)	184(51.8)	240(50.2)	242(50.5)	191(48.1)	205(44.8)	172(45.6)	2277(52.8)	6.2%
99284(%)	78(29.5)	59(23.6)	71(27.3)	95(30.6)	107(30.0)	92(28.3)	130(36.6)	172(35.9)	169(35.2)	131(33.0)	149(32.6)	126(33.4)	1379(32.7)	61.5%
99285(%)	24(09.1)	24(09.6)	27(10.3)	48(15.4)	46(12.9)	51(15.6)	41(11.5)	66(13.8)	68(14.1)	75(18.8)	103(22.5)	79(20.9)	652(14.5)	229.2%
Total	264	250	260	310	356	325	355	478	479	397	457	377	4,308	42.8%
99284+5(%)	102(38.6)	83(32.3)	98(34.7)	143(36.7)	153(39.8)	143(42.3)	171(46.3)	238(48.1)	237(50.2)	206(52.1)	252(54.5)	205(54.0)	2031(47.2)	101.0%
Surgical Abortion														
99281-83(%)	1502(54.3)	2144(51.7)	2565(51.3)	2876(47.9)	3281(47.6)	3362(42.8)	3538(40.4)	3828(38.3)	3926(34.9)	3611(31.1)	3228(32.5)	3562(33.9)	37423(39.5)	137.2%
99284(%)	1005(36.3)	1381(33.3)	1692(33.8)	2119(35.3)	2299(33.3)	3051(38.9)	3444(39.3)	3667(36.7)	4201(37.4)	4287(36.9)	3600(36.2)	3891(37.0)	34637(36.6)	287.2%
99285(%)	259(09.4)	621(15.0)	747(14.9)	1013(16.9)	1316(19.1)	1434(18.3)	1776(20.3)	2488(24.9)	3120(27.7)	3719(32.0)	3104(31.3)	3069(29.2)	22666(23.9)	1084.9%
Total	2766	4146	5004	6008	6896	7847	8758	9983	11247	11617	9932	10522	94,726	280.4%
99284+5(%)	1264(45.7)	2002(48.3)	2439(48.7)	3132(52.1)	3615(52.4)	4485(57.2)	5220(59.6)	6155(61.7)	7321(65.1)	8006(68.9)	6704(67.5)	6960(66.1)	57303(60.5)	450.6%
Chemical Abortion														
99281-83(%)	98(49.7)	164(51.7)	114(32.5)	174(38.6)	307(38.4)	440(39.3)	605(35.8)	899(34.1)	917(30.6)	618(27.5)	557(22.8)	1317(24.3)	6210(30.1)	1243.9%
99284(%)	70(35.5)	103(32.5)	184(52.4)	200(44.3)	299(37.4)	446(39.8)	722(42.8)	995(37.8)	1113(37.1)	912(40.5)	1100(45.1)	2269(41.9)	8413(40.7)	3141.4%
99285(%)	29(14.7)	50(15.8)	53(15.1)	77(17.1)	194(24.3)	235(21.0)	361(21.4)	740(28.1)	967(32.3)	720(32.0)	784(32.1)	1831(33.8)	6041(29.2)	6213.8%
Total	197	317	351	451	800	1121	1688	2634	2997	2250	2441	5417	20,664	2649.7%
99284+5(%)	99(50.3)	153(48.3)	237(67.5)	277(61.4)	493(61.6)	681(60.7)	1083(64.2)	1735(65.9)	2080(69.4)	1632(72.5)	1884(77.2)	4100(75.7)	14454(69.9)	4041.4%
Live Birth														
99281-83(%)	23505(48.9)	26127(47.6)	25880(45.6)	26903(44.2)	29780(43.6)	31411(42.1)	31991(41.9)	34398(42.6)	35383(41.3)	33661(41.0)	29240(44.1)	22774(43.4)	351053(43.5)	-3.1%
99284(%)	16244(33.8)	18763(34.2)	20132(35.4)	21524(35.4)	24606(36.0)	27024(36.2)	28262(37.0)	29052(36.0)	30789(35.9)	29553(36.0)	22447(33.9)	17972(34.2)	286368(35.5)	10.6%
99285(%)	8331(17.3)	9966(18.2)	10792(19.0)	12388(20.4)	13969(20.4)	16246(21.8)	16036(21.0)	17258(21.4)	19595(22.8)	18913(23.0)	14573(22.0)	11736(22.4)	169803(21.0)	40.9%
Total	48080	54856	56804	60815	68355	74681	76289	80708	85767	82127	66260	52482	807224	9.2%
99284+5(%)	24575(51.1)	28729(52.4)	30924(54.4)	33912(55.8)	38575(56.4)	43270(57.9)	44298(58.1)	46310(57.4)	50384(58.7)	48466(59.0)	37020(55.9)	29708(56.6)	456171(56.5)	20.9%
Grand Total	51307	59569	62419	67584	76407	83974	87090	93803	100490	96391	79090	68798	926922	34.1%
Grand Total 99284+5 (%)	26040(50.7)	30967(51.9)	33698(53.9)	37464(55.4)	42836(56.0)	48579(57.8)	50772(58.2)	54438(58.0)	60022(59.7)	58310(60.4)	45860(57.9)	40973(59.5)	529959(57.1)	57.3%

Table 1: ED visit acuity by pregnancy outcome

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The percentage of total visits coded severe or critical (99284-85) increased for all cohorts from 2004-2015: no pregnancy (38.6%-54.0%); surgical abortion (45.7%-66.1%); chemical abortion (50.3%-75.7%); and live birth (51.1%-56.6%). The trends in the proportion of severe and critical visits are all significant (X^2, $p<.0001$) for each cohort: never-pregnant (58.80); surgical abortion (1848.18); chemical abortion (347.88); and live birth (818.02) (Figure 1).

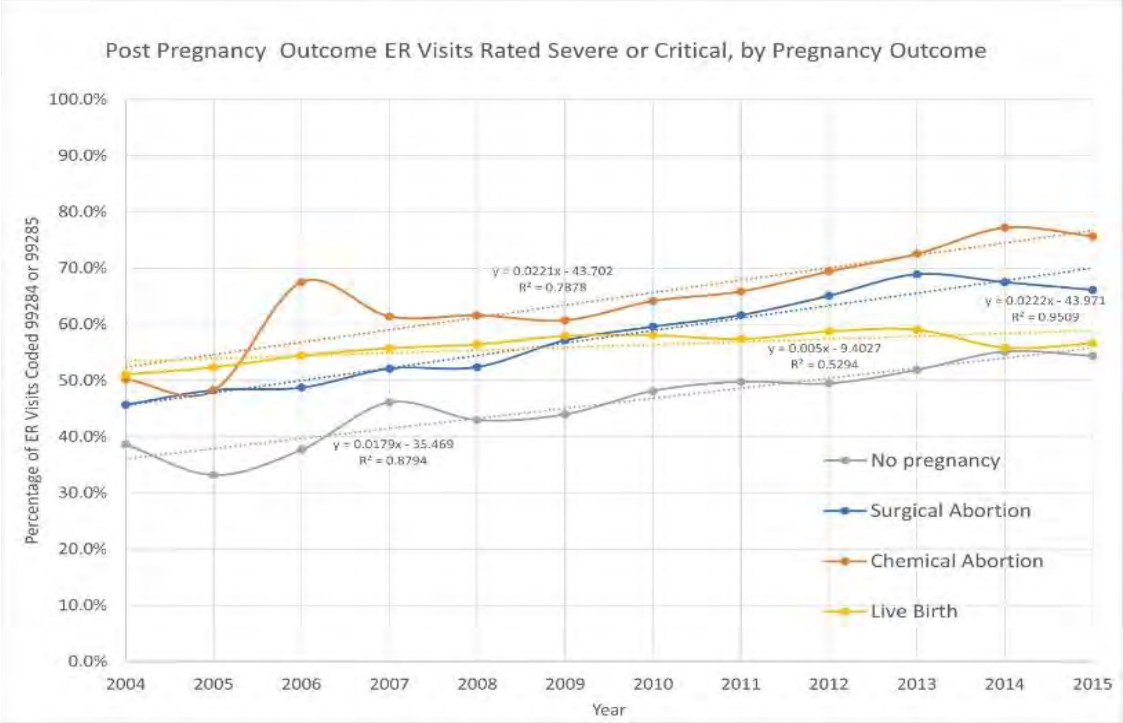

Figure 1: Post pregnancy outcome ED visits rated severe or critical, by pregnancy outcome

The logistic multiple regression adjusted odds ratios for the entire observation period (2004-2015) with never-pregnant as the reference cohort are: chemical abortion, OR 2.01 [1.93-2.28]; surgical abortion, OR 1.53 [1.43-1.63]; and live birth, OR 1.01 [1.00-1.01]. The adjusted odds ratios with chemical abortion as the reference cohort are: never-pregnant, OR 0.48 [0.44-0.54]; live birth, OR 0.52 [0.49-0.55]; surgical abortion, OR 0.73 [0.68-0.77].

Limitations

Findings from a Medicaid population may not be generalizable to populations of a different socioeconomic and demographic composition. The use of administrative claims data has recognized limitations including inconsistent and mistaken coding which may vary from state to state, the exclusion of codes considered unnecessary for billing purposes, and the possible upcoding to maximize revenue (6,7,8). Acuity increases may reflect a pattern of ED use by sicker patients (9). The use of a comprehensive measure of total acuity does not allow for comparison of specific complication rates between cohorts.

Discussion

This pattern of increasing ED utilization and acuity aligns with previous research (10). Both the volume and acuity of ED visits by Medicaid eligible women following a pregnancy outcome increased between 2004 and 2015. ED visits following chemical abortion had the greatest comparative increase in incidence, likely reflecting the rapidly growing percentage that they represented of all abortions during the observation period (11). Similarly, the growth in the percentage of high acuity ED visits was the largest for the chemical abortion cohort followed by the surgical abortion cohort. Increases in both incidence and acuity were smallest following live birth.

While multiple factors may influence these results, persistently and significantly higher ED visit acuity following chemical abortion is clearly evident. ED visit acuity for either method of abortion is significantly higher than for visits following a live birth. The increasing preference for this method of induced abortion, along with this evidence of the growing acuity of related ED visits, suggests that a greater level of surveillance will enhance patient safety for these patients.

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Conflicts of Interest: None declared

Author Contributions: conceptualization (J.S.); data collection (J.S., J.W.F., C.C.); data analysis (J.S., J.W.F., C.C.); critical review and evaluation of results (all authors); primary authorship of paper (J.S.); review and editing of paper (all authors); study supervision (J.S.); procurement of funding (J.S.).

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EXHIBIT 2

Robert arro Jr.,
Dru s S Mar eter Remains Elusive,
Wa . Po t (ct. , 2000)

Democracy Dies in Darkness

Drug's U.S. Marketer Remains Elusive

Fearing Abortion Foes, Danco Keeps Location, Phone Number Secret

October 11, 2000 More than **24 years ago**

By Robert O'Harrow Jr.

NEW YORK -- When many pharmaceutical companies win federal approval to market a new drug, they rush out predictions of potential riches for investors. Not so with Danco Laboratories LLC.

"A lot of what we're about is not driven by the profit motive," explained Richard Hausknecht, medical director of the firm, which just received permission to market the abortion pill known as RU-486.

"I'm not in this to get rich, because it's not going to make me any money," said Hausknecht, who said he is paid by the hour for his part-time work at Danco. "Here's a chance to offer to American women a real new option, something that has been denied to them for political reasons for 15 years."

Secretive and obscure, Danco is one of the most enigmatic companies in the pharmaceutical industry. It has worked for years and spent millions of dollars to bring to market a drug that investors knew would immediately face intense resistance--and they feared possibly violent intervention--from people opposed to abortion.

Danco has only a handful of employees. For security reasons, company officials say, Danco's telephone number is unlisted and the details of its whereabouts are carefully guarded. Company officials will say only that Danco is housed in an ordinary suite of offices somewhere in midtown Manhattan.

They say Danco intends to make a profit eventually. Its immediate plan is to make RU-486 available in the United States within a month as an early alternative to surgical abortion. The cost of the procedure, which includes two drugs and three office visits, is expected to be about $300, around the same as a surgical abortion.

The company also intends to research the possibility that the drug could also be a treatment for ovarian cancer and other life-threatening ailments.

Food and Drug Administration officials agree that Danco is not the usual pharmaceutical company. The agency "followed all normal" procedures in approving the drug, including inspecting the manufacturing facilities, officials said. But regulators determined that information about the manufacturer was confidential under statutes governing trade secrets and freedom of information.

FDA Commissioner Jane E. Henney said the agency broke with precedent by not publishing the names of the experts who reviewed RU-486 for the agency. In another first, it did not publish the name or location of the company that will manufacture the drug.

Some antiabortion activists fear that because of Danco's secretive approach, it will not be held accountable the way other drug companies have.

"This company seems rather clandestine and, I believe, suspicious," said Judie Brown, president of the American Life League, an antiabortion group based in Stafford, Va. "Women should be able to know immediately who the provider of a particular product is."

Danco has a close relationship with the Population Council, a nonprofit reproductive-rights group that sponsored the drug for approval. In 1994, the Population Council was given the rights to sell RU-486 by French drugmaker Roussel-Uclaf SA, which was put off by the controversy surrounding the drug in the United States.

The council, supported by the Buffett Foundation and others intent on making abortion more accessible, in turn gave Danco the rights to manufacture and distribute the drug.

According to records filed in Delaware on Feb. 7, Danco was formed in the Cayman Islands on July 25, 1995. On those papers, Hausknecht was listed as vice president--a formality, he said, that lasted only a week.

Apart from some basic facts, company officials are chary with details about Danco's structure, its investors and its plans.

The chief executive is Roy Karnovsky, a former marketing executive for the Merck Human Health Division of Merck & Co. Through a spokesman, he declined to discuss the company.

Medical director Hausknecht is an associate professor of obstetrics and gynecology at Mount Sinai School of Medicine in New York. He also serves on an advisory board for Planned Parenthood and was the medical director for Planned Parenthood of New York City.

Danco's director of public affairs is Heather M. O'Neill, who has helped prepare materials for FDA hearings about the drug. O'Neill, a graduate of Harvard University's John F. Kennedy School of Government, previously worked as a consultant at the Population Council.

O'Neill, who joined Danco in 1997, declined to provide the names of individual investors. But she acknowledged that supporters generally share the company's desire to make RU-486 available.

Instead of talking about company profits, she refers to its "project."

"Everyone here is committed to this project, to making Mifeprex [the trade name for RU-486] available to all women," she said. "We've been singleminded in our determination in making Mifeprex an option American woman can have."

"It's extremely unusual," Kevin Schulman, director of the Center for Clinical and Genetic Economics at the Duke Clinical Research Institute. "Only people who are truly dedicated to 'the cause' would have stuck with it. The unique thing here is how everybody [involved] has a shared vision."

O'Neill said the company may eventually try to market RU-486 abroad but has no plans to do so now. "We, I think, would be interested in looking at certain other countries around the world," she said.

She said the company will soon have a higher profile at medical conferences and will begin providing educational material on how to use the drug safely and effectively.

The fact the manufacturer is not named would not prevent someone from filing an RU-486-related lawsuit. The target would be Danco, O'Neill said. "Danco is responsible for all aspects of the drug's introduction into the United States, from FDA compliance to manufacturing, marketing and distribution," she said.

O'Neill acknowledged that crucial financial support over the past decade came from several foundations.

The Buffett Foundation, which was begun by investor Warren E. Buffett and places a strong emphasis on reproductive issues, made at least $2 million in interest-free loans to the Population Council, according to tax documents filed in 1995. That money was in turn used to conduct clinical trials of RU-486.

One of Danco's main backers has been the David and Lucile Packard Foundation, which lent Danco $10 million in 1998 to support approval and marketing of RU-486.

Sarah Clark, director of the Packard Foundation's Population Program, said her group and other Danco backers share an array of motivations for taking on responsibility for such a controversial drug.

"We're trying to make sure this choice is available and is not kept out for the wrong reasons," she said. If it were up to more profit-oriented drug companies alone, she added, RU-486 would probably not be on the market: "We wouldn't have to make loans to Danco if the commercial market were there."

EXHIBIT

ec. rder o. 40 , Protecting Acce to Reproducti e ealt care Ser ice , Fed. Reg. 42053 (July , 2022)

Presidential Documents

Executive Order 14076 of July 8, 2022

Protecting Access to Reproductive Healthcare Services

By the authority vested in me as President by the Constitution and the laws of the United States of America, it is hereby ordered as follows:

Section 1. *Policy.* Nearly 50 years ago, *Roe* v. *Wade,* 410 U.S. 113 (1973), articulated the United States Constitution's protection of women's fundamental right to make reproductive healthcare decisions. These deeply private decisions should not be subject to government interference. Yet today, fundamental rights—to privacy, autonomy, freedom, and equality—have been denied to millions of women across the country.

Eliminating the right recognized in *Roe* has already had and will continue to have devastating implications for women's health and public health more broadly. Access to reproductive healthcare services is now threatened for millions of Americans, and especially for those who live in States that are banning or severely restricting abortion care. Women's health clinics are being forced to close—including clinics that offer other preventive healthcare services such as contraception—leaving many communities without access to critical reproductive healthcare services. Women seeking abortion care—especially those in low-income, rural, and other underserved communities—now have to travel to jurisdictions where services remain legal notwithstanding the cost or risks.

In the face of this health crisis, the Federal Government is taking action to protect healthcare service delivery and promote access to critical reproductive healthcare services, including abortion. It remains the policy of my Administration to support women's right to choose and to protect and defend reproductive rights. Doing so is essential to justice, equality, and our health, safety, and progress as a Nation.

Sec. 2. *Definitions.* (a) The term ''agency'' means any authority of the United States that is an ''agency'' under 44 U.S.C. 3502(1), other than one considered to be an independent regulatory agency, as defined in 44 U.S.C. 3502(5).

(b) The term ''reproductive healthcare services'' means medical, surgical, counseling, or referral services relating to the human reproductive system, including services relating to pregnancy or the termination of a pregnancy.

Sec. 3. *Protecting Access to Reproductive Healthcare Services.* (a) Within 30 days of the date of this order, the Secretary of Health and Human Services shall submit a report to the President:

(i) identifying potential actions:

(A) to protect and expand access to abortion care, including medication abortion; and

(B) to otherwise protect and expand access to the full range of reproductive healthcare services, including actions to enhance family planning services such as access to emergency contraception;

(ii) identifying ways to increase outreach and education about access to reproductive healthcare services, including by launching a public awareness initiative to provide timely and accurate information about such access, which shall:

(A) share information about how to obtain free or reduced cost reproductive healthcare services through Health Resources and Services Administration-Funded Health Centers, Title X clinics, and other providers; and

(B) include promoting awareness of and access to the full range of contraceptive services, as well as know-your-rights information for those seeking or providing reproductive healthcare services; and

(iii) identifying steps to ensure that all patients—including pregnant women and those experiencing pregnancy loss, such as miscarriages and ectopic pregnancies—receive the full protections for emergency medical care afforded under the law, including by considering updates to current guidance on obligations specific to emergency conditions and stabilizing care under the Emergency Medical Treatment and Labor Act, 42 U.S.C. 1395dd, and providing data from the Department of Health and Human Services concerning implementation of these efforts.

(b) To promote access to reproductive healthcare services, the Attorney General and the Counsel to the President shall convene a meeting of private pro bono attorneys, bar associations, and public interest organizations in order to encourage lawyers to represent and assist patients, providers, and third parties lawfully seeking these services throughout the country.

Sec. 4. *Protecting Privacy, Safety, and Security.* (a) To address potential heightened safety and security risks related to the provision of reproductive healthcare services, the Attorney General and the Secretary of Homeland Security shall consider actions, as appropriate and consistent with applicable law, to ensure the safety of patients, providers, and third parties, and to protect the security of clinics (including mobile clinics), pharmacies, and other entities providing, dispensing, or delivering reproductive and related healthcare services.

(b) To address the potential threat to patient privacy caused by the transfer and sale of sensitive health-related data and by digital surveillance related to reproductive healthcare services, and to protect people seeking reproductive health services from fraudulent schemes or deceptive practices:

(i) The Chair of the Federal Trade Commission (FTC) is encouraged to consider actions, as appropriate and consistent with applicable law (including the Federal Trade Commission Act, 15 U.S.C. 41 *et seq.*), to protect consumers' privacy when seeking information about and provision of reproductive healthcare services.

(ii) The Secretary of Health and Human Services shall consider actions, including providing guidance under the Health Insurance Portability and Accountability Act, Public Law 104–191, 110 Stat. 1936 (1996) as amended by Public Law 111–5, 123 Stat. 115 (2009), and any other statutes as appropriate, to strengthen the protection of sensitive information related to reproductive healthcare services and bolster patient-provider confidentiality.

(iii) The Secretary of Health and Human Services shall, in consultation with the Attorney General, consider actions to educate consumers on how best to protect their health privacy and limit the collection and sharing of their sensitive health-related information.

(iv) The Secretary of Health and Human Services shall, in consultation with the Attorney General and the Chair of the FTC, consider options to address deceptive or fraudulent practices related to reproductive healthcare services, including online, and to protect access to accurate information.

Sec. 5. *Coordinating Implementation Efforts.* (a) The Secretary of Health and Human Services and the Director of the Gender Policy Council shall establish and co-chair an Interagency Task Force on Reproductive Healthcare Access (Task Force). Additional members shall include the Attorney General and the heads of other agencies as determined by the Secretary of Health and Human Services and the Director of the Gender Policy Council. The Task Force shall work to identify and coordinate activities to protect and strengthen access to essential reproductive healthcare services. In addition, the Task Force shall coordinate Federal interagency policymaking, program development, and outreach efforts to address barriers that individuals and entities may face in seeking and providing reproductive healthcare services.

The Department of Health and Human Services shall provide funding and administrative support as may be necessary for the performance and functions of the Task Force.

(b) The Attorney General shall provide technical assistance, as appropriate and consistent with applicable law, concerning Federal constitutional protections to States seeking to afford legal protection to out-of-State patients and providers who offer legal reproductive healthcare.

Sec. 6. *General Provisions.* (a) Nothing in this order shall be construed to impair or otherwise affect:

(i) the authority granted by law to an executive department or agency, or the head thereof; or

(ii) the functions of the Director of the Office of Management and Budget relating to budgetary, administrative, or legislative proposals.

(b) This order shall be implemented consistent with applicable law and subject to the availability of appropriations.

(c) This order is not intended to, and does not, create any right or benefit, substantive or procedural, enforceable at law or in equity by any party against the United States, its departments, agencies, or entities, its officers, employees, or agents, or any other person.

THE WHITE HOUSE,
July 8, 2022.

[FR Doc. 2022–15138
Filed 7–12–22; 11:15 am]
Billing code 3395–F2–P

EXHIBIT

ec. rder o. 40 , Securing Acce to Reproducti e and t er ealt care Ser ice , Fed. Reg. 4 505 (Aug. 3, 2022)

Federal Register
Vol. 87, No. 154
Thursday, August 11, 2022

Presidential Documents

Title 3—

The President

Executive Order 14079 of August 3, 2022

Securing Access to Reproductive and Other Healthcare Services

By the authority vested in me as President by the Constitution and the laws of the United States of America, it is hereby ordered as follows:

Section 1. *Policy*. On July 8, 2022, following a decision by the Supreme Court to overrule *Roe* v. *Wade*, 410 U.S. 113 (1973), I signed Executive Order 14076 (Protecting Access to Reproductive Healthcare Services). As that order recognized, eliminating the right recognized in Roe has had and will continue to have devastating implications for women's health and public health more broadly.

Following that order, the Department of Health and Human Services (HHS) has taken critical steps to address those effects. These steps include clarifying the obligation of hospitals and providers under the Emergency Medical Treatment and Labor Act, 42 U.S.C. 1395dd, to provide to patients presenting at an emergency department with an emergency medical condition stabilizing care, including an abortion, if that care is necessary to stabilize their emergency medical condition, and issuing guidance to the Nation's retail pharmacies on their obligations under Federal civil rights laws—including section 504 of the Rehabilitation Act, 29 U.S.C. 794, and section 1557 of the Affordable Care Act, 42 U.S.C. 18116—to ensure equal access to comprehensive reproductive and other healthcare services, including for women who are experiencing miscarriages.

However, the continued advancement of restrictive abortion laws in States across the country has created legal uncertainty and disparate access to reproductive healthcare services depending on where a person lives, putting patients, providers, and third parties at risk and fueling confusion for hospitals and healthcare providers, including pharmacies. There have been numerous reports of women denied health- and life-saving emergency care, as providers fearful of legal reprisal delay necessary treatment for patients until their conditions worsen to dangerous levels. There are also reports of women of reproductive age being denied prescription medication at pharmacies—including medication that is used to treat stomach ulcers, lupus, arthritis, and cancer—due to concerns that these medications, some of which can be used in medication abortions, could be used to terminate a pregnancy. Reportedly, a healthcare provider, citing a State law restricting abortion, even temporarily stopped providing emergency contraception.

As it remains the policy of my Administration to support women's access to reproductive healthcare services, including their ability to travel to seek abortion care in States where it is legal, I am directing my Administration to take further action to protect access to reproductive healthcare services and to address the crisis facing women's health and public health more broadly.

Sec. 2. *Definition*. The term ''reproductive healthcare services'' means medical, surgical, counseling, or referral services relating to the human reproductive system, including services relating to pregnancy or the termination of a pregnancy.

Sec. 3. *Advancing the Ability to Obtain Reproductive Healthcare Services*. In furtherance of the policy set forth in section 1 of this order, the Secretary of HHS shall consider actions to advance access to reproductive healthcare

services, including, to the extent permitted by Federal law, through Medicaid for patients traveling across State lines for medical care.

Sec. 4. *Promoting Compliance with Non-Discrimination Law in Obtaining Medical Care*. In furtherance of the policy set forth in section 1 of this order, and to ensure that individuals are not denied necessary healthcare on the basis of any ground protected by Federal law, including current pregnancy, past pregnancy, potential or intended pregnancy, or other medical conditions, the Secretary of HHS shall consider all appropriate actions to advance the prompt understanding of and compliance with Federal non-discrimination laws by healthcare providers that receive Federal financial assistance. Such actions may include:

(a) providing technical assistance for healthcare providers that have questions concerning their obligations under Federal non-discrimination laws;

(b) convening healthcare providers to provide information on their obligations under Federal non-discrimination laws and the potential consequences of non-compliance; and

(c) issuing additional guidance, or taking other action as appropriate, in response to any complaints or other reports of non-compliance with Federal non-discrimination laws.

Sec. 5. *Data Collection*. The Secretary of HHS shall evaluate the adequacy of research, data collection, and data analysis and interpretation efforts at the National Institutes of Health, the Centers for Disease Control and Prevention, and other relevant HHS components in accurately measuring the effect of access to reproductive healthcare on maternal health outcomes and other health outcomes. Following that evaluation, the Secretary shall take appropriate actions to improve those efforts.

Sec. 6. *General Provisions*. (a) Nothing in this order shall be construed to impair or otherwise affect:

(i) the authority granted by law to an executive department or agency, or the head thereof; or

(ii) the functions of the Director of the Office of Management and Budget relating to budgetary, administrative, or legislative proposals.

(b) This order shall be implemented consistent with applicable law and subject to the availability of appropriations.

(c) This order is not intended to, and does not, create any right or benefit, substantive or procedural, enforceable at law or in equity by any party against the United States, its departments, agencies, or entities, its officers, employees, or agents, or any other person.

THE WHITE HOUSE,
August 3, 2022.

[FR Doc. 2022–17420
Filed 8–10–22; 8:45 am]
Billing code 3395–F2–P

EXHIBIT

W ite ou e,

FAC S Pre ident iden Announce Action n

ig t of oday Supreme Court Deci ion on *Dobbs v ac son Women s Health Or ani ation*

(June 24, 2022)

JUNE 24, 2022

FACT SHEET: President Biden Announces Actions In Light of Today's Supreme Court Decision on Dobbs v. Jackson Women's Health Organization

Today, President Biden announced actions that his Administration is taking to protect women who will face the grave consequences of today's Supreme Court decision. This decision expressly took away a Constitutional right from the American people that it had recognized for nearly 50 years – a woman's right to choose, free from government interference.

This decision will have devastating consequences in the lives of women around the country.

The President made clear that the only way to secure a woman's right to choose is for Congress to restore the protections of Roe as federal law. Until then, he has announced two actions the Administration is taking to protect women.

Protecting the Right to Seek Medical Care

As the Attorney General made clear, women must remain free to travel safely to another state to seek the care they need.

A person has the right to travel between states for whatever reason they want – it is no one else's business – especially the government's. If a woman lives in a state that restricts abortion, the Supreme Court's

decision does not prevent her from traveling from her home to a state that allows it.

If any state or local official tries to interfere with women exercising this basic right, the Biden Administration will fight that deeply un-American attack.

Protecting Access to Medication

The President directed the Secretary of Health and Human Services to protect women's access to critical medications for reproductive health care that are approved by the Food and Drug Administration—including essential preventive health care like contraception and medication abortion.

More than 20 years ago, the FDA approved mifepristone to safely end an early pregnancy; this drug is also commonly used to treat miscarriages. The American Medical Association and the American College of Obstetricians and Gynecologists wrote to President Biden and Vice President Harris, asking the federal government to protect access to this care. In the face of threats from state officials saying they will try to ban or severely restrict access to medication for reproductive health care, the President directed the Secretary of Health and Human Services to identify all ways to ensure that mifepristone is as widely accessible as possible in light of the FDA's determination that the drug is safe and effective including when prescribed through telehealth and sent by mail.

***

EXHIBIT

Pre Relea e, S,
S Secretary ecerra Statement on Supreme Court
Ruling in *Dobbs v ac son Women s Health Or ani ation*
(June 24, 2022)

An official website of the United States government Here's how you know

U.S. Department of Health and Human Services
Enhancing the health and well-being of all Americans
</replay-web-page/w/id-aae9c8b5e5f5/mp_/https://www.hhs.gov/>

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FOR IMMEDIATE RELEASE
June 24, 2022

Contact: HHS Press Office
202-690-6343
media@hhs.gov

HHS Secretary Becerra's Statement on Supreme Court Ruling in Dobbs v. Jackson Women's Health Organization

Today, U.S. Department of Health and Human Services Secretary Xavier Becerra released the following after the Supreme Court's decision to overturn Roe v. Wade:

"Today's decision is unconscionable. Abortion is a basic and essential part of health care – and patients must have the right to make decisions about their health care and autonomy over their own bodies. For decades, both as a member of Congress and as California's Attorney General, I have stood with people around the country to fight for reproductive freedom for everyone, no matter who you are, where you live or how much you make. At the Department of Health and Human Services, we stand unwavering in our commitment to ensure every American has access to health care and the ability to make decisions about health care -- including the right to safe and legal abortion, such as medication abortion that has been approved by the FDA for over 20 years. I have directed every part of my Department to do any and everything we can here. As I have said before, we will double down and use every lever we have to protect access to abortion care. To everyone in this fight: we are with you."

###

Note: All HHS press releases, fact sheets and other news materials are available at https://www.hhs.gov/news </replay-web-page/w/id-aae9c8b5e5f5/mp_/https://www.hhs.gov/news>.
Like HHS on Facebook </replay-web-page/w/id-aae9c8b5e5f5/mp_/https://www.hhs.gov/disclaimer.html>, follow HHS on Twitter @HHSgov <https://rejouer.perma.cc/replay-web-page/w/id-aae9c8b5e5f5/mp_/https://twitter.com/#!/hhsgov> </replay-web-page/w/id-aae9c8b5e5f5/mp_/https://www.hhs.gov/disclaimer.html>, and sign up for HHS Email Updates <https://rejouer.perma.cc/replay-web-page/w/id-aae9c8b5e5f5/mp_/https://cloud.connect.hhs.gov/subscriptioncenter>.
Last revised: June 24, 2022

EXHIBIT

Pre Relea e, S,
Remar by Secretary a ier ecerra at t e Pre
Conference in Re pon e to Pre ident iden Directi e
follo ing erturning of *Roe v Wade*
(June 2 , 2022)

Remarks by Secretary Xavier Becerra at the Press Conference in Response to President Biden's Directive following Overturning of Roe v. Wade

Xavier Becerra
June 28, 2022
Hubert H. Humphrey Building
Washington, D.C.

As Prepared for Delivery

On Friday, June 24th, five Americans decided to use the vast power bestowed upon them by our democracy and our Constitution to unconscionably put at risk the life and health of millions of their fellow Americans. They chose to unconscionably limit Americans' established freedom and autonomy to control their own body — decisions usually made in consultation with their doctor, not a politician. And they chose to unconscionably strip away the fundamental health care protections that every American of child-bearing age has known all their lives.

Friday's Supreme Court decision was despicable, but it was also predictable. HHS has been preparing for this for some time. That's why, earlier this year, we launched our HHS Reproductive Access Task Force to plan for every action necessary to protect women's access to reproductive health care.

There is no magic bullet. But if there is something we can do, we will find it and we will do it at HHS. Indeed, that was the instruction I received from the President of the United States.

Last Friday, President Biden announced the actions he is taking to ensure medication abortion is available to the fullest extent possible and that women can travel safely from states where abortion is banned to states where abortion is legal. Here is how HHS will support these issues:

- First, HHS will take steps to increase access to medication abortion.

  - Federal law requires our programs to provide medication abortion in limited circumstances, including life of the woman, rape, or incest.

- Now more than ever it is imperative that all federally-supported programs and services are complying and providing this under the law.

- Second, I am directing the Office for Civil Rights within HHS to ensure patient privacy and nondiscrimination for patients seeking reproductive health care, as well as for providers who offer reproductive health care.

- Third, I am directing the Department to examine its authority under the Emergency Medical Treatment Act (EMTALA) to ensure that clinical judgment of doctors and hospitals is supported in treating pregnant patients, including those experiencing pregnancy loss or complications, and reaffirming that abortion care can be appropriate to stabilize patients.

- Fourth, I am directing all agencies in my Department to work to ensure that all providers – from doctors to pharmacists -- and clinics have appropriate training and resources to handle family planning needs, including administering patient referrals for care, and helping patients navigate this new reality.

- Fifth, I am directing the Centers for Medicare and Medicaid Services (CMS) to take every legally available step to protect family planning care, including emergency contraceptives and long acting reversable contraceptives, such as IUDs. Health care is a matter to be decided by patients and their providers, not politicians. As part of these efforts, we will make clear that family planning providers are able to participate in the Medicaid program. These clinics provide safe care and have a vast expertise in providing reproductive health care.

Let me now tell you a little more about why I think medication abortion is so critical.

- Medication abortion has been approved by the FDA for years and is safe for patients.

- It is the gold standard for care when someone who's pregnant experiences a miscarriage, which is all too real for many expectant mothers across the country.

- The Supreme Court's decision will result in worsened health outcomes and death for some patients. Working to increase access to this drug is a national imperative and in the public interest.

- We will continue to support the FDA and its rigorous scientific review for these safe and effective drugs.

- We will also work with the Attorney General and the Justice Department as they work to ensure that states may not ban medication abortion, based on a disagreement with the FDA's expert judgment about the drug's safety and efficacy.

- And we will issue guidance to providers to ensure they receive accurate and robust information on medication abortion.

The HHS Reproductive Access Task Force will report to me on additional impactful ways to ensure appropriate information about, access to, and coverage for sexual and reproductive health care – as well as coordinate with other federal agencies.

I was at a Planned Parenthood clinic in St. Louis, Missouri, on Friday morning when the Supreme Court overturned Roe v. Wade. I saw in real time the impact of this unconscionable decision. The Clinic Director had to almost immediately start turning away patients as the state's ban went into effect. This clinic has stopped providing safe and legal abortion care. People in the room were visibly shaken, there were tears and an unshakeable sense of sadness.

After my visit to the clinic in St. Louis, I traveled across the state line to another clinic in Fairview Heights, Illinois – a state that, unlike Missouri, still had lawful abortion care. There, I visited a site that helps patients get care by providing assistance – ranging from helping patients find appointments to paying for their travel expenses –and abortion care. It was shocking that, in the United States of America, a short drive can make such a dire and draconian difference in health care outcomes. I saw restrictions that leave women and families on unequal footing and widen maternal health disparities.

The impact was visible and real.

This is a critical moment in history. How we respond will speak to how we view the rights, dignity and wellbeing of women everywhere. This is a moment of crisis in health care. We will leave no stone unturned. All options are on the table. We will do everything within the legal limit of the law to reach patients and support providers.

I know we are all tired and our hearts are broken by this loss of rights and dignity. But now is the time for us to continue on for the many people across the country who live in banned abortion states, who lack voices that represent them.

I stand with you and I have your back.

HHS Headquarters

U.S. Department of Health & Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201
Toll Free Call Center: 1-877-696-6775

EXHIBIT

Center for Drug aluation and Re earc , Application umber 020 rig 025 Summary Re ie

(Jan. 3, 2023)

(FDA 2023 Summary Re ie)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

020687Orig1s025

SUMMARY REVIEW

[redacted] and [redacted]

Center for Drug Evaluation and Research (CDER)

Application Type	NDA and ANDA
Application Number	NDA 020687 and ANDA 091178
Supplement Number, Date Received	NDA Supplement-025 and ANDA Supplement-004 received June 22, 2022 (sequences 18 and 87 respectively) and amended October 19, 2022 (sequences 22 and 91 respectively), November 30, 2022 (sequences 24 and 92 respectively), December 9, 2022 (sequences 25 and 93 respectively) and December 16, 2022 (sequences 26 and 95 respectively). This supplement is on a 180-Day clock.
Targeted Action Date	December 19, 2022
[redacted] #	2022-1169
Reviewer Names	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
Review Completion Date	January 3, 2023
Subject	Review of proposed Major REMS Modification
Established Name	Mifepristone REMS
Name of Sponsor	Danco Laboratories, LLC and GenBioPro, Inc.
Therapeutic Class	Progestin antagonist
Formulation	Oral tablet

TABLE OF CONTENTS

EXECUTIVE SUMMARY 3
1. Introduction 4
2. Background 4
2.1. Product Information and REMS Information 4
2.2. Regulatory History 6
3. Review of Proposed REMS Modification 8
3.1. REMS Goal 8
3.2. REMS Document 8
3.3. REMS Requirements 9
3.3.1. Addition and Removal of ETASU 9
3.3.2. REMS Participant Requirements and Materials 9
3.3.2.1. Prescriber Requirements 9
3.3.2.2. Patient Requirements 11
3.3.2.3. Pharmacy Requirements 12
3.3.2.4. Distributor Requirements 15
3.3.3. REMS Sponsor Requirements 15
3.3.3.1. Sponsor Requirements to Support Prescriber Certification 15
3.3.3.2. Sponsor Requirements to Support Pharmacy Certification 16
3.3.3.3. Sponsor Implementation Requirements 16
3.4. REMS Assessment Timetable 16
4. Supporting Document 17
5. REMS Assessment Plan 17
6. Discussion 19
7. Conclusions and Recommendations 21
8. References 21
9. Appendices 22

EXECUTIVE SUMMARY

This is a review of the proposed modification to the single, shared system Risk Evaluation and Mitigation Strategy (REMS) for mifepristone 200 mg (hereafter referred to as the Mifepristone REMS Program) submitted by Danco Laboratories, LLC (Danco) for new drug application (NDA) 020687 and by GenBioPro, Inc. (GBP) for abbreviated new drug application (ANDA) 091178. The Sponsors submitted proposed modification to the Mifepristone REMS Program on June 22, 2022, and amended their submissions on October 19, 2022 (Danco), October 20, 2022 (GBP), November 30, 2022 (both), December 9, 2022 (both) and December 16, 2022 (both).

The Mifepristone REMS Program was originally approved on April 11, 2019, to mitigate the risk of serious complications associated with mifepristone 200 mg. The most recent REMS modification was approved on May 14, 2021.[a] The Mifepristone REMS Program consists of elements to assure safe use (ETASU) A, C and D, an implementation system, and a timetable for submission of assessments of the REMS.

The Sponsors submitted the proposed modification to the REMS in response to the Agency's REMS Modification Notification letters dated December 16, 2021, which required removal of the requirement that mifepristone be dispensed only in certain healthcare settings, specifically clinics, medical offices, and hospitals (i.e., the "in-person dispensing requirement") and the addition of certification of pharmacies that dispense the drug.

In addition, the following were addressed during the course of the review:

- revisions to the REMS goal to align with the updated REMS requirements.
- replacing serial number with recording of NDC and lot number of mifepristone dispensed.
- additional edits for clarification and consistency in the REMS Document and REMS materials (*Prescriber Agreement Forms*, *Patient Agreement Form*, and *Pharmacy Agreement Forms*).

The review team finds the proposed modification to the Mifepristone REMS Program last submitted on December 16, 2022, to be acceptable and recommends approval of the REMS modification. The proposed REMS modification includes changes to the REMS goal, additional REMS requirements for prescribers to incorporate dispensing from certified pharmacies and new REMS requirements for pharmacy certification.

The proposed goal of the modified REMS for mifepristone 200 mg is to mitigate the risk of serious complications associated with mifepristone by:

a) Requiring healthcare providers who prescribe mifepristone to be certified in the Mifepristone REMS Program.

b) Ensuring that mifepristone is only dispensed by or under the supervision of certified prescribers, or by certified pharmacies on prescriptions issued by certified prescribers.

c) Informing patients about the risk of serious complications associated with mifepristone.

[a] The May 14, 2021 REMS modification approved the inclusion of gender neutral language in the Patient Agreement Form as well as corresponding minor changes to the REMS document to be consistent with the changes made to the Patient Agreement Form.

The timetable for submission of assessments of the REMS was modified to one year from the date of the approval of the modified REMS and annually thereafter. The assessment plan was revised to align with the changes to the REMS and capture additional metrics for drug utilization and REMS operations.

The modified REMS includes ETASU A, B and D, an implementation system, and a timetable for submission of assessments of the REMS. Mifepristone will no longer be required to be dispensed only in certain healthcare settings, specifically clinics, medical offices, and hospitals (referred to as the "in-person dispensing requirement" for brevity) and will be able to be dispensed from certified pharmacies.

1. Introduction

This review evaluates the proposed modification to the single, shared system Risk Evaluation and Mitigation Strategy (REMS) for mifepristone 200 mg (hereafter referred to as the Mifepristone REMS Program) submitted by Danco Laboratories, LLC (Danco) for new drug application (NDA) 020687 and by GenBioPro, Inc. (GBP) for abbreviated new drug application (ANDA) 091178.

The Sponsors initially submitted proposed modification to the Mifepristone REMS Program on June 22, 2022, in response to the Agency's REMS Modification Notification letters issued on December 16, 2021, to Danco and GBP, requiring the following modification to minimize the burden on the healthcare delivery system of complying with the REMS and to ensure that the benefits of the drug outweigh the risks:

- removal of the requirement that mifepristone be dispensed only in certain healthcare settings, specifically clinics, medical offices, and hospitals (i.e., the "in-person dispensing requirement")
- addition of certification of pharmacies that dispense the drug

Per the Agency's December 16, 2021, REMS Modification Notification letters, the proposed REMS was required to include the following ETASU to mitigate the risk of serious complications associated with mifepristone, including at least the following:

- healthcare providers have particular experience or training, or are specially certified
- pharmacies, practitioners, or health care settings that dispense the drug are specially certified
- the drug is dispensed to patients with evidence or other documentation of safe use conditions

The REMS was also required to include an implementation system and timetable for submission of assessments.

2. Background

2.1. Product Information and REMS Information

Mifepristone is a progestin antagonist indicated, in a regimen with misoprostol, for the medical termination of intrauterine pregnancy (IUP) through 70 days gestation. Mifepristone is available as 200 mg tablets for oral use.

Mifeprex (mifepristone) was approved on September 28, 2000, with a restricted distribution program under 21 CFR 314.520 (subpart H)[b] to ensure that the benefits of the drug outweighed

[b] NDA approval letter Mifeprex (NDA 020687) dated September 28, 2000.

the risk of serious complications associated with mifepristone when used for medical abortion.[c] Mifeprex was deemed to have in effect an approved REMS under section 505-1 of the Federal Food, Drug, and Cosmetic Act with the passage of the Food and Drug Administration Amendments Act of 2007 (FDAAA), and the Mifeprex REMS was approved on June 8, 2011.

On March 29, 2016, FDA approved an efficacy supplement for Mifeprex, which included changes in the dose of Mifeprex and the dosing regimen for taking Mifeprex and misoprostol, as well as a modification of the gestational age up to which Mifeprex has been shown to be safe and effective and a modification to the process for follow-up after administration of the drug. FDA also approved modification to the Mifeprex REMS that reflected the changes approved in the efficacy supplement.[1-5] On April 11, 2019, FDA approved ANDA 091178 and the Mifepristone REMS Program.[6-7] The Mifepristone REMS Program is a single, shared system REMS that includes NDA 020687 and ANDA 091178. The goal of the approved Mifepristone REMS Program is to mitigate the risk of serious complications associated with mifepristone by:

a) Requiring healthcare providers who prescribe mifepristone to be certified in the Mifepristone REMS Program (under ETASU A).
b) Ensuring that mifepristone is only dispensed in certain healthcare settings by or under the supervision of a certified prescriber (under ETASU C).
c) Informing patients about the risk of serious complications associated with mifepristone (under ETASU D).

The Mifepristone REMS Program was last modified and approved in 2021 to revise the *Patient Agreement Form* to include gender-neutral language; however, the goal of the Mifepristone REMS Program has not changed since the initial approval in 2019.

Under ETASU A, to become specially certified to prescribe mifepristone, a healthcare provider must review the prescribing information, complete and sign the *Prescriber Agreement Form,* and agree to follow the guidelines for use of mifepristone. Under ETASU C, in the Mifepristone REMS Program as approved prior to today's action, mifepristone was required to be dispensed to patients only in certain healthcare settings, specifically clinics, medical offices, and hospitals, by or under the supervision of a certified prescriber. Under ETASU D, mifepristone must be dispensed to patients with evidence or other documentation of safe use conditions (i.e., the patient must sign a *Patient Agreement Form*). The approved Mifepristone REMS Program includes an implementation system, and a timetable for assessments (one year from the date of the initial approval of the REMS on April 11, 2019, and every three years thereafter).

In April 2021, FDA communicated its intent to exercise enforcement discretion during the COVID-19 public health emergency (PHE) regarding the in-person dispensing requirement in the Mifepristone REMS Program. Specifically, FDA communicated that provided all other requirements of the Mifepristone REMS Program are met, the Agency intended to exercise enforcement discretion with respect to the in-person dispensing requirement of the Mifepristone REMS Program, including any in-person requirements that may be related to the *Patient Agreement Form*, during the COVID-19 PHE. This determination, which FDA made on April 12, 2021, was effective immediately. We also note that from July 13, 2020, to January 12, 2021, per a court order, FDA was enjoined from enforcing the in-person dispensing requirement of the Mifepristone REMS Program.[8]

[c] Mifepristone is also approved in approximately 80 other countries. https://gynuity.org/assets/resources/biblio_ref_lst_mife_en.pdf

Further, and as we also communicated on April 12, 2021, to the extent all of the other requirements of the Mifepristone REMS Program are met, the Agency intended to exercise enforcement discretion during the COVID-19 PHE with respect to the dispensing of Mifeprex or the approved generic version of Mifeprex, Mifepristone Tablets, 200 mg, through the mail, either by or under the supervision of a certified prescriber, or through a mail-order pharmacy when such dispensing is done under the supervision of a certified prescriber.

2.2. Regulatory History

The following is a summary of the regulatory history relevant to this review:

- 04/11/2019: Approval of the Mifepristone REMS Program, a single, shared system REMS that includes NDA 020687 and ANDA 091178.
- 04/12/2021: The Agency issued a General Advice letter to both the NDA and ANDA Applicants, explaining that FDA intended to exercise enforcement discretion during the COVID-19 PHE with respect to the in-person dispensing requirement in the Mifepristone REMS Program, including any in-person requirements that may be related to the Patient Agreement Form.
- 05/07/2021: The Agency stated that it would be reviewing the elements of the Mifepristone REMS Program in accordance with section 505-1 of the FD&C Act.
- 12/16/2021: The Agency completed its review of the Mifepristone REMS Program and determined, among other things, that the REMS must be modified to remove the in-person dispensing requirement and add pharmacy certification.[9]
- 12/16/2021: REMS Modification Notification letters were sent to both Sponsors stating that the approved Mifepristone REMS Program must be modified to minimize the burden on the healthcare system of complying with the REMS and ensure that the benefits of the drug outweigh the risks.
- 04/08/2022: Final written responses to a Type A meeting request were provided to Danco, the point of contact for the Mifepristone REMS Program. The questions pertained to the 12/16/2021 REMS Modification Notification letter requirements.
- 04/13/2022: The Sponsors requested an extension to 6/30/2022, to submit a proposed REMS modification in response to the Agency's 12/16/2021 REMS Modification Notification letters.
- 04/15/2022: The Agency granted the Sponsors' request for an extension to submit a proposed REMS modification and conveyed that the modification must be submitted no later than 06/30/2022.[10]
- 06/22/2022: Danco and GBP submitted a proposed REMS modification to their respective applications in response to the 12/16/2021 REMS Modification Notification letters.
- 07/22/2022: An Information Request was sent to the Sponsors requesting clarification of the proposed prescriber and dispenser requirements and additional rationale to support their proposal.
- 08/26/2022: Sponsors submitted responses to 07/22/2022 Information Request.
- 09/19/2022: Teleconference was held between Agency and Sponsors where the Agency communicated the REMS requirements that are necessary to support the addition of pharmacy

certification. The Agency proposed focusing on the pharmacy settings where a closed system[d] REMS could be implemented using the existing email and facsimile based system, (b) (4) , as the best strategy for an approvable modification by the goal date.

- 09/22/2022: An Information Request was sent to Sponsors requesting confirmation that the Sponsors agree with the pharmacy distribution approach outlined in the 09/19/2022 teleconference so that the Agency's feedback could be appropriately tailored.
- 09/23/2022: The Sponsors confirmed via email that they were willing to pursue (b) (4) , as discussed in the 09/19/2022 teleconference. The Sponsors also requested a teleconference to discuss the current modification (b) (4) .
- 09/27/2022: Comments from the 09/19/2022 teleconference sent to Sponsors with additional comments and requests regarding what will be necessary for pharmacy certification.
- 09/29/2022: An Information request was sent to the Sponsors asking for agenda items, questions, and a request to walk through their proposed system for pharmacy certification, including dispensing through mail-order or specialty pharmacies, at the 10/06/2022 scheduled teleconference.
- 10/04/2022: Sponsors emailed that they will focus the 10/06/2022 teleconference on the 09/27/2022 Agency comments and their mail order and specialty pharmacy distribution model.
- 10/06/2022: Teleconference was held between Agency and Sponsors where Sponsors outlined their proposal for pharmacy certification, including dispensing through mail order and specialty pharmacies, as well as their concerns with certain requirements and general timelines.
- 10/19/2022: Danco submitted a REMS amendment to their pending sNDA, which included a REMS document and REMS materials. They did not submit a REMS Supporting Document.
- 10/20/2022: GBP submitted a REMS amendment to their pending sANDA, which included a REMS document and REMS materials. They did not submit a REMS Supporting Document.
- 10/25/2022: Teleconference was held between Agency and Sponsors to discuss the *Patient Agreement Form* and timing related to shipping a mifepristone prescription from a certified pharmacy to the patient.
- 11/23/2022: An Information Request was sent to Sponsors with comments on their proposed REMS Document, submitted on 10/19/2022 (Danco) and 10/20/2022 (GBP).
- 11/30/2022: Danco and GBP submitted REMS amendments, which included the REMS Document, to their respective pending supplemental applications.
- 12/01/2022: Teleconference was held between Agency and Sponsors to discuss the REMS Document.
- 12/05/2022: An Information Request was sent to Sponsors with comments on their proposed REMS Document submitted on 11/30/2022 and discussed at the teleconference on 12/01/2022, and REMS materials submitted to their applications on 10/19/2022 and 10/20/2022.

[d] "Closed system" in this case refers to a system where prescribers, pharmacies, and distributors are certified or authorized in the REMS and the certification of the stakeholder must be verified prior to distribution or dispensing, as per the REMS.

- 12/07/2022: Teleconference was held between Agency and Sponsors to discuss the REMS Document and REMS materials the Agency sent to the Sponsors on 12/05/22.
- 12/08/2022: Danco and GBP submitted REMS amendments, including the REMS Document, *Prescriber Agreement Form, Pharmacy Agreement Form, Patient Agreement Form* and REMS Supporting Document, to their respective pending applications.
- 12/09/2022: An Information Request was sent to Sponsors with the Agency's comments on the REMS assessment plan.
- 12/14/2022: An Information Request was sent to Sponsors with the Agency's comments on the REMS Document, *Prescriber Agreement Form, Pharmacy Agreement Form*, and REMS Supporting Document.
- 12/15/2022: Two teleconferences were held between Agency and Sponsors to discuss the proposed REMS Document and REMS materials the Agency sent to the Sponsors on 12/14/22.
- 12/16/2022: Sponsors submitted a REMS amendment to their respective applications.

3. Review of Proposed REMS Modification

(b) (6) has discussed the Sponsors' proposed modification with the review team, which includes members of the (b) (6) and the (b) (6) ; hereafter referred to as the review team. This review includes their input and concurrence with the analysis and proposed changes to the Mifepristone REMS Program.

3.1. REMS Goal

The Sponsors proposed modification to the goal for the Mifepristone REMS Program to add that mifepristone can also be dispensed from certified pharmacies on prescriptions issued by certified prescribers. The proposed REMS goal is:

The goal of the REMS for mifepristone is to mitigate the risk of serious complications associated with mifepristone by:

a) Requiring healthcare providers who prescribe mifepristone to be certified in the Mifepristone REMS Program.

b) Ensuring that mifepristone is only dispensed by or under the supervision of certified prescribers, or by certified pharmacies on prescriptions issued by certified prescribers.

c) Informing patients about the risk of serious complications associated with mifepristone.

Reviewer Comment: *We agree with the Sponsors' proposal.*

3.2. REMS Document

The proposed REMS Document is not in the format as outlined in the 2017 Draft Guidance for Industry, Format and Content of a REMS Document.[11]

Reviewer Comment: *To avoid the misperception that this REMS modification is making major changes to the REMS document that go beyond our December 16, 2021, determination that the REMS must be modified to remove the in-person dispensing requirement and add pharmacy certification, CDER staff and management discussed whether to change the format of the REMS document to that described in the 2017 draft guidance.*[11] *After internal discussion, CDER staff and management aligned not to transition the REMS document at this time to the format described in the 2017 draft guidance.*

3.3. REMS Requirements

3.3.1. Addition and Removal of ETASU

The December 16, 2021, REMS Modification Notification letters specified that the ETASU must be modified to minimize the burden on the healthcare delivery system of complying with the REMS and to ensure the benefits of the drug outweigh the risks by:

- Removing the requirement that mifepristone be dispensed only in certain healthcare settings, specifically clinics, medical offices and hospitals (i.e., the "in-person dispensing requirement"), and;
- Adding a requirement that pharmacies that dispense the drug be specially certified.

The Sponsors proposed changes to the REMS as reflected in the subsections below.

3.3.2. REMS Participant Requirements and Materials

3.3.2.1. Prescriber Requirements

Consistent with the approved Mifepristone REMS Program prescribers must be specially certified. To become specially certified to prescribe mifepristone, healthcare providers who prescribe must review the Prescribing Information for mifepristone and complete the *Prescriber Agreement Form*. In signing the *Prescriber Agreement Form*, prescribers agree they meet certain qualifications and will follow the guidelines for use of mifepristone. The guidelines for use include ensuring i) that the *Patient Agreement Form* is reviewed with the patient and the risks of the mifepristone treatment regimen are fully explained; ii) that the healthcare provider (HCP) and the patient sign the *Patient Agreement Form*, iii) the patient receives a copy of the *Patient Agreement Form* and Medication Guide, iv) the *Patient Agreement Form* is placed in the patient's medical record; v) that any patient deaths are reported to the Mifepristone Sponsor that provided the mifepristone, identifying the patient by a non-identifiable reference and including the NDC and lot number from the package of mifepristone that was dispensed to the patient. The language on the guidelines for use was revised from the Mifepristone REMS Program approved in 2021 to clarify that, if the certified prescriber supervises the dispensing of mifepristone, they must ensure the guidelines for use of mifepristone are followed by those under their supervision. This clarification reflects the ongoing implementation of the approved Mifepristone REMS Program. For example, consistent with the approved REMS, the *Patient Agreement Form* does not require the certified prescriber's signature, but rather the signature of the healthcare provider counseling the patient on the risks of mifepristone. Additional changes were made globally to provide consistency and clarity of the requirements for certified prescribers and healthcare providers who complete tasks under the supervision of certified prescribers.

A certified prescriber may submit the *Prescriber Agreement Form* to an authorized distributor if the certified prescriber wishes to dispense or supervise the dispensing of mifepristone; this is consistent with the current requirements of the Mifepristone REMS Program. Additional requirements were

added to incorporate mifepristone dispensing by a certified pharmacy. If a healthcare provider wishes to prescribe mifepristone by sending a prescription to a certified pharmacy for dispensing, the healthcare provider must become certified by providing the pharmacy a *Prescriber Agreement Form* signed by the provider. A certified prescriber must also assess the appropriateness of dispensing mifepristone when contacted by a certified pharmacy about patients who will receive mifepristone more than four calendar days after the prescription was received by the certified pharmacy.

The NDC and lot number of the dispensed drug will be recorded in the patient's record when mifepristone is dispensed by or under the supervision of a certified prescriber, replacing the requirement that serial numbers from each package of mifepristone be recorded in the patient's record. If prescribers become aware of the death of a patient for whom the mifepristone was dispensed from a certified pharmacy, the prescribers will be required to obtain the NDC and lot number of the package of mifepristone the patient received from the pharmacy.

The following materials support prescriber requirements:

- *Prescriber Agreement Form* for Danco Laboratories, LLC
- *Prescriber Agreement Form* for GenBioPro, Inc.
- *Patient Agreement Form*

Reviewer Comment: *We agree with the Sponsors' proposal.*

Although certain activities (review of the Patient Agreement Form with patients and answering any questions about treatment, signing, providing a copy to the patient and retaining the Patient Agreement Form, providing a copy of the Medication Guide, and ensuring any deaths are reported to the Mifepristone Sponsor, recording the NDC and lot number from drug dispensed from the certified prescriber or those under their supervision) may be conducted by healthcare providers under the supervision of a certified prescriber, the certified prescriber remains responsible for ensuring compliance with the requirements of the Mifepristone REMS Program. We agree with the additional language to further clarify that the certified prescriber must ensure the guidelines for use of mifepristone are followed.

As proposed, certified prescribers may either, 1) continue to submit the Prescriber Agreement Form to an authorized distributor if the certified prescriber is dispensing or supervising the dispensing of the drug (as already required in the REMS), or 2) if the drug will be dispensed from a certified pharmacy, submit the Prescriber Agreement Form to the certified pharmacy that will dispense the drug (as proposed in the modification). Regarding #2, the pharmacy can only fill prescriptions written by a certified prescriber.

Based on our review of the proposed changes, the review team finds it acceptable for prescribers to submit their Prescriber Agreement Form directly to the certified pharmacy. Although certified prescribers still have the option of in-person dispensing of the drug, not all prescribers may want to stock mifepristone. Typically due to the number of drugs that are available and the expense associated with stocking prescription medications intended for outpatient use, most prescribers do not stock many medications, if they stock medications at all.

The proposal to submit a Prescriber Agreement Form to a certified pharmacy provides another option for dispensing mifepristone. The burden of providing the Prescriber Agreement Form prior to or when the prescription is provided to a certified pharmacy does not create unreasonable burden for prescribers. The burden of prescriber certification has been minimized to the extent possible. The Prescriber Agreement Form is designed to require minimal time to complete and requires that the prescriber submit it to the authorized distributor once, and if the prescriber chooses to use a certified pharmacy to dispense mifepristone, they will need to submit the form to the certified pharmacy.

There is an additional requirement added for certified pharmacies and certified prescribers in the event that a patient will not receive their medication from the certified pharmacy within four calendar days of the pharmacy's receipt of the prescription (for example, if the medication is not in stock). In this circumstance, the pharmacy will be required to contact the certified prescriber to make them aware of the delay and will be required to obtain from the prescriber confirmation that it is appropriate to dispense mifepristone to the patient even though they will receive mifepristone more than four calendar days after the prescription was received by the certified pharmacy. This confirmation is intended to ensure timeliness of delivery in light of the labeled indication and gestational age. Additional details and rationale on the pharmacy requirements to dispense and ship drug in a timely manner are described in section 3.3.2.3.

If a certified prescriber becomes aware of a patient death that occurs subsequent to the use of mifepristone dispensed from a pharmacy, the certified prescriber must obtain the NDC and lot number of the package of mifepristone the patient received from the pharmacy. This information will be reported to the appropriate Mifepristone Sponsor in the same manner prescribers have done previously. This additional requirement to obtain the NDC and lot number from the pharmacy is needed to ensure consistent adverse event reporting when mifepristone is dispensed from a certified pharmacy.

Prescriber Agreement Form

The Sponsors' proposed changes to the *Prescriber Agreement Form* aligned with those described above. The proposed *Prescriber Agreement Form* explains the two methods of certification which are: 1) submitting the form to the authorized distributor and 2) submitting the form to the dispensing certified pharmacy. Further clarification was added that healthcare settings, such as medical offices, clinics, and hospitals, where mifepristone will be dispensed by or under the supervision of a certified prescriber in the Mifepristone REMS Program do not require pharmacy certification. The statement that certified prescribers are responsible for overseeing implementation and compliance with the REMS Program was also added. The following statement was added to the form: "I understand that the pharmacy may dispense mifepristone made by a different manufacturer than that stated on the Prescriber Agreement Form." The account set up information was removed and replaced with prescriber information response fields.

***Reviewer Comment**: We agree with the Sponsors' proposal. Changes in the above prescriber requirements were incorporated in the Prescriber Agreement Form.*

3.3.2.2. Patient Requirements

The *Patient Agreement Form* was updated to clarify that the signatures may be written or electronic, to reorganize the risk information about ectopic pregnancy, and to remove the statement that the Medication Guide will be taken to an emergency room or provided to a healthcare provider who did not prescribe mifepristone so that it is known that the patient had a medical abortion with mifepristone.

The following materials support patient requirements:

- *Patient Agreement Form*

***Reviewer Comment:** We agree with the Sponsors' proposal.*

The Patient Agreement Form continues to be an important part of standardizing the medication information on the use of mifepristone that prescribers communicate to their patients, and also provides the information in a brief and understandable format for patients. The requirement to counsel the

patient, to provide the patient with the Patient Agreement Form, and to have the healthcare provider and patient sign the Patient Agreement Form, ensures that each provider, including new providers, informs each patient of the appropriate use of mifepristone, risks associated with treatment, and what to do if the patient experiences symptoms that may require emergency care. The form is signed by the patient and the provider and placed in the patient's medical record, and a copy is provided to the patient, to document the patient's acknowledgment of receiving the information from the prescriber. The Agency agrees that the further clarification that signatures can be written or electronic is appropriate for the continued use of the form.

The reference to ectopic pregnancy has been reorganized in the document since it is not a risk of the drug. The signs and symptoms of an untreated ectopic pregnancy that may persist after mifepristone use have been clarified in the section of the form that explains the signs and symptoms of potential problems that may occur after mifepristone use.

The review team agrees with removing the patient's agreement to take the Medication Guide with them if they visit an emergency room or HCP who did not give them mifepristone so the emergency room or HCP will understand that the patient is having a medical abortion. Although this statement has been in the Medication Guide for a number of years, upon further consideration, the Agency has concluded that patients seeking emergency medical care are not likely to carry a Medication Guide with them, the Medication Guide is readily available online, and information about medical conditions and previous treatments can be obtained at the point of care.

3.3.2.3. Pharmacy Requirements

The Sponsors proposed that certified pharmacies, in addition to certified prescribers and HCPs under the supervision of certified prescribers, can dispense mifepristone. In order for a pharmacy to become certified, the pharmacy must designate an authorized representative to carry out the certification process and oversee implementation and compliance with the Mifepristone REMS Program on behalf of the pharmacy. The Authorized Representative must certify that they have read and understood the Prescribing Information for mifepristone. Each location of the pharmacy must be able to receive *Prescriber Agreement Forms* by email and fax and be able to ship mifepristone using a shipping service that provides tracking information.

Additionally, each dispensing pharmacy location must put processes and procedures in place to fulfill the REMS requirements. Certified pharmacies must verify prescriber certification by confirming they have obtained a copy of the prescriber's signed *Prescriber Agreement Form* before dispensing. Certified pharmacies must dispense mifepristone such that it is received by the patient within four days from the day of prescription receipt by the pharmacy. If the pharmacy will not be able to deliver mifepristone to the patient within four days of receipt of the prescription, the pharmacy must contact the prescriber to confirm the appropriateness of dispensing mifepristone and document the certified prescriber's decision. The pharmacy must also record the NDC and lot number from each package of mifepristone dispensed in the patient's record, track and verify receipt of each shipment of mifepristone, dispense mifepristone in its original package, and only distribute, transfer, loan, or sell mifepristone to certified prescribers or between locations of the certified pharmacy. The pharmacy must also report any patient deaths to the prescriber, including the NDC and lot number from the package dispensed to the patient, and remind the prescriber of their obligation under the REMS to report patient deaths to the Sponsor that supplied the mifepristone; the certified pharmacy also must notify the Sponsor that supplied the mifepristone that the pharmacy submitted a report of a patient death to the prescriber and include the name and contact information for the prescriber as well as the NDC and lot number of the dispensed

product. Record-keeping requirements of the pharmacy include records of *Prescriber Agreement Forms*, mifepristone dispensing and shipping, and all processes and procedures and compliance with those processes and procedures. Pharmacies must train all relevant staff and participate in compliance audits. Pharmacies must also maintain the identity of patients and providers as confidential, including limiting access to patient and provider identity only to those personnel necessary to dispense mifepristone in accordance with the Mifepristone REMS Program requirements, or as necessary for payment and/or insurance purposes. The requirement that mifepristone not be dispensed from retail pharmacies was removed.

The following materials support pharmacy requirements:

- *Pharmacy Agreement Form* for Danco Laboratories, LLC
- *Pharmacy Agreement Form* for GenBioPro, Inc.

Reviewer Comment: *We agree with the Sponsors' proposal. The Mifepristone REMS Program continues to require that mifepristone be prescribed only by certified prescribers. With the removal of the in-person dispensing requirement, however, mifepristone can be dispensed from a pharmacy, provided the product is prescribed by a certified prescriber and all other requirements of the REMS are met. Given this modification to the dispensing requirements in the REMS, it is necessary to add a requirement for certification of pharmacies. Adding the pharmacy certification requirement incorporates pharmacies into the REMS, ensures that pharmacies are aware of and agree to follow applicable REMS requirements, and ensures that mifepristone is only dispensed pursuant to prescriptions that are written by certified prescribers. Without pharmacy certification, a pharmacy might dispense product that was not prescribed by a certified prescriber. Adding pharmacy certification ensures that the prescriber is certified prior to dispensing the product to a patient; certified prescribers, in turn, have agreed to meet all the conditions of the REMS, including ensuring that the Patient Agreement Form is completed. In addition, wholesalers and distributors can only ship to certified pharmacies. Based on our review and our consideration of the distribution model implemented by the Sponsors during the periods when the in-person dispensing requirement was not being enforced, as well as REMS assessment data and published literature, we conclude that provided all other requirements of the REMS are met, the REMS program, with the removal of the in-person dispensing requirement and the addition of a requirement for pharmacy certification, will continue to ensure the benefits of mifepristone for medical abortion outweigh the risks while minimizing the burden imposed by the REMS on healthcare providers and patients.*

The requirement to maintain confidentiality, including limiting access to patient and provider identity only to those personnel necessary for dispensing under the Mifepristone REMS Program or as necessary for payment and/or insurance purposes, is included to avoid unduly burdening patient access.

The Sponsors proposed inclusion of this requirement because of concerns that patients may be reluctant or unwilling to seek to obtain mifepristone from pharmacies if they are concerned that confidentiality of their medical information could be compromised, potentially exposing them to intimidation, threats, or acts of violence by individuals opposed to the use of mifepristone for medical abortion.[e] *Further, unwillingness on the part of prescribers to participate in the Mifepristone REMS Program on the basis of*

[e] See e.g., *2020 Violence and Disruption Statistics,* National Abortion Federation (Dec. 16, 2021), https://prochoice.org/national-abortion-federation-releases-2020-violence-disruption-statistics/; Amanda Musa, CNN, *Wyoming Authorities Search for a Suspect Believed to Have Set an Abortion Clinic on Fire*, CNN WIRE (June 10, 2022), https://abc17news.com/news/2022/06/10/wyoming-authorities-search-for-a-suspect-believed-to-have-set-an-abortion-clinic-on-fire/.

Reference ID: 5103819

similar confidentiality concerns may unduly burden patient access by limiting the number of prescribers who are willing to send prescriptions to certified pharmacies. Addition of this requirement protects patient access by requiring the pharmacy to put processes and procedures in place to limit access to confidential information to only those individuals who are essential for dispensing mifepristone under the Mifepristone REMS Program or as necessary for payment or insurance purposes. Inclusion of this requirement for certified pharmacies is consistent with the requirement in the current Mifepristone REMS Program, that distributors maintain secure and confidential records.

Reference to mifepristone not being available in retail pharmacies was removed from the REMS. There is no single definition of the term "retail pharmacy" and therefore the scope of the exclusion in the REMS was not well defined. Including a restriction in the Mifepristone REMS Program that retail pharmacies cannot participate in the REMS may unintentionally prohibit the participation of mail order and specialty pharmacies that could, under one or more definitions, also be considered a "retail pharmacy."

After reconsideration of the term, "retail," the Agency concluded that a more appropriate approach was to articulate the specific requirements that would be necessary for pharmacy certification. As modified, the REMS will not preclude the participation of any pharmacy that meets the certification requirements. However, we acknowledge that the provision in the REMS related to pharmacies' verification of prescriber enrollment will likely limit the types of pharmacies that will choose to certify in the REMS. The REMS requires that pharmacies dispense mifepristone only after verifying that the prescriber is certified. The REMS further requires that pharmacies be able to receive the Prescriber Agreement Forms by email and fax. (b) (4)

The pharmacy certification requirements include that the drug reach patients within four days of the certified pharmacy receiving the prescription. During the course of the review, the review team concluded that requiring medication delivery to the patient within four days of the pharmacy's receipt of a prescription is acceptable based on the labeled indication and literature,[13] while taking into account practical shipping considerations (e.g., shipping over weekends and holidays). For patients who will not receive the drug within four calendar days of the date the pharmacy receives the prescription, the pharmacy must notify the certified prescriber and the certified prescriber must determine if it is still appropriate for the certified pharmacy to dispense the drug. The pharmacy must document the certified prescriber's decision. A prescriber's confirmation that it is appropriate to dispense mifepristone when it will not be delivered to the patient within the allotted four days is intended to ensure timeliness of delivery in light of the labeled indication and gestational age.

Pharmacy Agreement Form

The proposed *Pharmacy Agreement Form* is a new form and is the means by which a pharmacy becomes certified to dispense mifepristone. The form, which is submitted by an authorized representative on behalf of a pharmacy seeking certification, outlines all requirements proposed above. Clarification is included in the form that healthcare settings, such as medical offices, clinics, and hospitals, where mifepristone will be dispensed by or under the supervision of a certified prescriber in the Mifepristone REMS Program, do not require pharmacy certification. Any new authorized representative must complete and submit the *Pharmacy Agreement Form*. Spaces for specific authorized representative information and pharmacy name and address are included. The completed form can be submitted by email or fax to the authorized distributor.

Reviewer Comment: *We agree with the Sponsors' proposal. The Pharmacy Agreement Form aligns with the pharmacy requirements discussed above.*

3.3.2.4. Distributor Requirements

The Sponsors proposed that the distributors' processes and procedures in the approved Mifepristone REMS Program be updated to ensure that mifepristone is only shipped to clinics, medical offices and hospitals identified by certified prescribers and to certified pharmacies. Distributors will continue to complete the certification process for any *Prescriber Agreement Forms* they receive and also will complete the certification process for pharmacies upon receipt of a *Pharmacy Agreement Form*, including notifying pharmacies when they become certified. FDA was removed as a potential auditor for distributors.

Reviewer Comment: *We agree with the Sponsors' proposal. At this time, FDA does not audit distributors directly, it carries out inspections of Sponsors to monitor industry compliance with REMS requirements.*

3.3.3. REMS Sponsor Requirements

3.3.3.1. Sponsor Requirements to Support Prescriber Certification

The Sponsors proposed additions to this section of the REMS document, including that Sponsors will ensure prescribers can complete the certification process by email or fax to an authorized distributor and/or certified pharmacy, and that Sponsors will ensure annually with each certified prescriber that their locations for receiving mifepristone are up to date. Sponsors will also ensure prescribers previously certified in the Mifepristone REMS Program complete the new *Prescriber Agreement Form*: (1) within 120 days after approval of this modification, for those previously certified prescribers submitting prescriptions to certified pharmacies, or (2) within one year after approval of this modification, if previously certified and ordering from an authorized distributor.

Reviewer Comment: *We agree with the Sponsors' proposal. The requirement to confirm that the locations associated with the certified prescriber are current is parallel to the pharmacy requirement that the authorized representative's contact information is up to date. In determining the pharmacy requirement, which is necessary to ensure program compliance and is consistent with other approved REMS that include pharmacy certification, the Agency also concluded that a parallel requirement for certified prescribers should be added.*

With respect to recertification, it is important that active certified prescribers are informed of and agree to new REMS requirements to ensure the continued safe use of mifepristone. There is minimal burden to recertification and the timelines allow sufficient time to accomplish recertification.

3.3.3.2. Sponsor Requirements to Support Pharmacy Certification

The Sponsors proposed the addition of Sponsor requirements to support pharmacy certification and compliance, including ensuring that pharmacies are certified in accordance with the requirements in the Mifepristone REMS Program, de-certifying pharmacies that do not maintain compliance with the certification requirements, and ensuring that pharmacy certification can be completed by email and fax to an authorized distributor. Annually, the authorized representative's name and contact information will be verified to ensure it corresponds to that of the current designated authorized representative for the certified pharmacy, and if different, a new authorized representative must certify for the pharmacy. All reference to the requirement in the 2021 Mifepristone REMS Program that mifepristone to be dispensed to patients only in clinics, medical offices and hospitals by or under the supervision of a certified prescriber, and not from retail pharmacies, was removed.

Reviewer Comment: *We agree with the Sponsors' proposal. Changes are in line with the REMS Modification Notification letters sent December 16, 2021. Refer to section 3.3.2.3 Reviewer Comments on Pharmacy Certification for rationale for removing the statement that mifepristone is not distributed to or dispensed from retail pharmacies. Ensuring that the authorized representative's contact information is up to date is necessary to ensure that there is always a point person who is responsible for implementing the Mifepristone REMS Program in their pharmacy and can address any changes that are needed if pharmacy audits identify a need for improvement.*

3.3.3.3. Sponsor Implementation Requirements

The Sponsors proposed that they will ensure that adequate records are maintained to demonstrate that REMS requirements have been met (including but not limited to records of mifepristone distribution, certification of prescribers and pharmacies, and audits of pharmacies and distributors), and that the records must be readily available for FDA inspections. The distributor audit requirement was updated to audit new distributors within 90 calendar days of becoming authorized and annually thereafter (a one-time audit requirement was previously required). The Sponsors also proposed a pharmacy audit requirement whereby certified pharmacies that order mifepristone are audited within 180 calendar days after the pharmacy places its first order of mifepristone, and annually thereafter for pharmacies that ordered in the previous 12 months.

Reviewer's Comment: *We agree with the Sponsors' proposal.*

The number of pharmacies that will certify in the REMS is uncertain; therefore, to obtain a reliable sample size for the audits, the Sponsors will need to audit all certified pharmacies within 180 calendar days after the pharmacy places its first order and annually thereafter for pharmacies that have ordered mifepristone in the previous 12 months. Audits performed at 180 days should allow time for establishment and implementation of audit protocols and for the Sponsors to perform the audits. With the addition of more stakeholders (i.e., certified pharmacies), it is also necessary to audit distributors annually to ensure the REMS requirements are followed. The requirement to conduct audits annually may be revisited if assessment data shows that the REMS is meeting its goal.

3.4. REMS Assessment Timetable

The Sponsors proposed that assessments must be submitted one year from the approval of the modified REMS and annually thereafter, instead of every three years as per the previous requirement.

***Reviewer's Comment**: We agree with the Sponsors' proposal. With the addition of new pharmacy stakeholders and removal of the in-person dispensing requirement, more frequent assessment after this REMS modification is needed to ensure REMS processes are being followed and that the REMS is meeting its goal. The requirement can be revisited at a later date if assessment data shows that the modified REMS is meeting its goal. The NDA applicant is required to submit assessment reports as outlined in the timetable for submission of assessments. These reports address requirements for the Mifepristone REMS Program. The Sponsors have indicated that some data will be submitted as separate reports when Sponsor-specific information is needed to address the assessment metrics.*

4. Supporting Document

The Sponsors' REMS Supporting Document was substantially updated to include information regarding the proposed modification under review. Background and rationale from the 12/16/21 REMS Modification Notification letters was included. An updated description of the REMS goal and the ETASU was also included to align with the changes in the REMS Document and provide further clarification. Further explanation of prescriber requirements and rationale for various pharmacy requirements was also included.

Regarding implementation of the modified REMS, the Sponsors additionally proposed that pharmacies that received and shipped mifepristone during the Agency's exercise of enforcement discretion during the COVID-19 PHE, that wish to continue to dispense mifepristone, will be required to comply with the pharmacy certification requirements within 120 days of approval of the modified REMS.

The communication strategy to alert current and future prescriber and pharmacy stakeholders was outlined. Distributors, certified prescribers that purchased mifepristone in the last twelve months, and various professional organizations will receive information about REMS changes within 120 days of modification approval. The Sponsors proposed to list pharmacies that agree to be publicly disclosed on their respective product websites but disclosure of this nature is not a requirement of the REMS. The Sponsors indicated that they anticipate certified pharmacies that do not agree to public disclosure will communicate with the certified prescribers they wish to work with.

The REMS Assessment Plan is discussed in the following section.

***Reviewer's Comment**: We agree with the Sponsors' proposal. The Supporting Document addresses all REMS requirements and provides sufficient clarification of implementation and maintenance of the REMS. The implementation requirements for pharmacies currently dispensing mifepristone under FDA's exercise of enforcement discretion during the COVID-19 PHE provide for continued use of these pharmacies without breaks in service. The communication strategy is also adequate given the efforts to reach both established certified prescribers and potentially new prescribers through professional organizations.*

The Sponsors' plan to communicate which pharmacies are certified to certified prescribers is adequate. For the reasons listed in section 3.3.2.3, confidentiality is a concern for REMS stakeholders. Disclosure of pharmacy certification status should be a choice made by individual certified pharmacies. The Sponsors have indicated that there will be some certified pharmacies that have agreed to publicly disclose their status, making this information available to certified prescribers who wish to use a pharmacy to dispense mifepristone.

5. REMS Assessment Plan

The REMS Assessment Plan is summarized in the REMS Supporting Document and will be included in the REMS Modification Approval letter.

The REMS Assessment Plan was revised to align with the modified REMS goal and objectives.

The goal of the Mifepristone REMS Program is to mitigate the risk of serious complications associated with mifepristone by:

a. Requiring healthcare providers who prescribe mifepristone to be certified in the Mifepristone REMS Program.
    - This objective will be assessed using REMS Certification Statistics and REMS Compliance metrics.

b. Ensuring that mifepristone is only dispensed by or under the supervision of certified prescribers, or by certified pharmacies on prescriptions issued by certified prescribers.
    - This objective will be assessed using REMS Certification Statistics and REMS Compliance metrics.

c. Informing patients about the risk of serious complications associated with mifepristone.
    - This objective will be indirectly assessed using REMS Certification Statistics to avoid compromising patient and prescriber confidentiality. As part of the certification process, healthcare providers agree to:
        - Ensure that the *Patient Agreement Form* is reviewed with the patient and the risks of the mifepristone treatment regimen are fully explained
        - Ensure that the *Patient Agreement Form* is signed by the healthcare provider and the patient
        - Ensure that the patient is provided with a copy of the *Patient Agreement Form* and the Medication Guide
        - Ensure that the signed *Patient Agreement Form* is placed in the patient's medical record

The following revisions were made from the Mifepristone REMS Assessment Plan in the April 11, 2019, Supplement Approval letter:

The Assessment Plan Categories of 1) Program Implementation and Operations and 2) Overall Assessment of REMS Effectiveness were added.

REMS Certification Statistics metrics were added to capture certification numbers for program stakeholders to assess the first objective of requiring healthcare providers who prescribe mifepristone to be certified and the second objective of ensuring that mifepristone is only dispensed by or under the supervision of certified prescribers, or by certified pharmacies on prescriptions issued by certified prescribers. The total number of certified prescribers who certified with the wholesaler/distributor and the total number of certified prescribers who submitted a *Prescriber Agreement Form* to certified pharmacies were added to capture the additional method of prescriber certification. The number of newly certified prescribers and the number of active certified prescribers (i.e., those who ordered mifepristone or submitted a prescription during the reporting period) were added. Metrics were also added to capture the total number of certified, newly certified, and active certified pharmacies as well as the total number of authorized, newly authorized, and active authorized wholesaler/distributors.

Drug Utilization Data metrics were added to obtain information on shipment and dispensing of mifepristone. Metrics were added to capture the total number of tablets shipped by the wholesaler/distributor and the number of prescriptions dispensed.

REMS Compliance Data metrics were added to assess the first objective of requiring healthcare providers who prescribe mifepristone to be certified and the second objective of ensuring that mifepristone is only dispensed by or under the supervision of certified prescribers, or by certified pharmacies on prescriptions issued by certified prescribers. These metrics capture program deviations and evaluate overall if the REMS is operating as intended. Metrics include certified pharmacies and wholesaler/distributor audit results and a summary of instances of non-compliance and actions taken to address non-compliance. Prescriber compliance metrics were added to assess if prescribers are decertified along with reasons why. Pharmacy compliance metrics were added to assess if prescriptions were dispensed that were written by non-certified prescribers or if mifepristone tablets were dispensed by non-certified pharmacies as well as the number of pharmacies that were decertified along with reasons why. Wholesaler/distributor metrics were added to assess if shipments were sent to non-certified prescribers and non-certified pharmacies and corrective actions taken. The audit plan and non-compliance plans will be submitted for FDA review within 60 days after the REMS modification approval.

The Sponsors were asked to develop an assessment of prescription delivery timelines to determine what percentage of prescriptions were delivered on time (within four calendar days) and what percentage were delivered late (more than four calendar days) along with the length of the delay and reasons for the delay (e.g., mifepristone is out of stock shipment issues, other). The protocol for this assessment will be submitted for FDA review within 60 days after the REMS modification approval.

The revised REMS Assessment Plan is in the Appendix.

Reviewer's Comment*: We agree with the Sponsors' proposed REMS Assessment Plan.*

6. Discussion

The Sponsors submitted changes to the REMS to remove the requirement that mifepristone be dispensed only in certain healthcare settings (i.e., the "in-person dispensing requirement") and to add that certified pharmacies can dispense the drug in order to minimize the burden on the healthcare delivery system of complying with the REMS and to ensure that the benefits of the drug outweigh the risks. The REMS goal was updated to this effect. Changes were required for prescriber requirements and Sponsors to support the change in ETASU, and new pharmacy requirements were introduced.

The qualifications to become a certified prescriber have not changed as a result of the modification to the Mifepristone REMS Program; however, clarification has been provided for certain prescriber requirements and new prescriber requirements have been added to support pharmacy dispensing. Although certain responsibilities may be conducted by staff under the supervision of a certified prescriber, the certified prescriber remains responsible for ensuring compliance with the requirements of the Mifepristone REMS Program. In order to clarify this, revisions were made throughout the prescriber requirements and REMS materials to reflect that the certified prescriber is responsible for ensuring that the prescriber requirements are met. Additionally, the review team finds it acceptable that certified prescribers who wish to use a certified pharmacy to dispense mifepristone submit their *Prescriber Agreement Form* to the dispensing certified pharmacy (b) (4) . The burden to prescriber and

pharmacy stakeholders of having certified prescribers submit the form directly to the certified pharmacy that will be dispensing the mifepristone is not unreasonable and has been minimized to the extent possible; it does not impact the safe use of the product. Prescriber requirements necessitated by the addition of some pharmacy requirements were added as well and include prescriber responsibilities in deciding whether or not mifepristone should be dispensed if the patient will receive the drug from the certified pharmacy more than four days after the pharmacy receives the prescription, and prescriber adverse event reporting requirements if a prescriber becomes aware of a patient death and the mifepristone was dispensed from a certified pharmacy. The addition of the latter requirements will ensure consistent adverse event data is relayed to the relevant Mifepristone Sponsor.

Changes were made to the *Patient Agreement Form.* Changes to the form were added to improve clarity of the safety messages. After further consideration, the patient's agreement to take the Medication Guide with them if they visit an emergency room or HCP who did not give them mifepristone so the emergency room or HCP will understand that the patient is having a medical abortion has been removed from the *Patient Agreement Form*. The Medication Guide is not typically carried by patients and this information can be obtained at the point of care. Changes align with updates to labeling submitted with this modification.[13, 14]

The Agency and Sponsors agreed during this modification to focus on certification of pharmacies that can receive *Prescriber Agreement Forms* via email or fax to complete the prescriber certification process. The proposed pharmacy certification requirements also support timely dispensing of mifepristone. If the mifepristone is shipped to the patient, the REMS requires that it must be delivered within four calendar days from the receipt of the prescription by the pharmacy; if the patient will receive the mifepristone more than four calendar days from pharmacy receipt of prescription, the REMS requires the pharmacist to confirm with the certified prescriber that it is still appropriate to dispense the drug to the patient. This allows prescribers to make treatment decisions based on individual patient situations. A requirement to maintain confidentiality was also added to avoid unduly burdening patient access since patients and prescribers may not utilize pharmacy dispensing if they believe their personal information is at risk. Ultimately, the addition of pharmacy distribution with the proposed requirements will offer another option for dispensing mifepristone, alleviating burden associated with the REMS.

(b) (4)

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The Agency reviewed the REMS in 2021, and per the review team's conclusions, a REMS modification was necessary to remove the in-person dispensing requirement and add a requirement that pharmacies that dispense the drug be specially certified; the review team concluded that these changes could occur without compromising patient safety. There have been no new safety concerns identified relevant to the REMS ETASUs that the applicants proposed modifying in their June 22, 2022 submissions since the REMS Modification Notification letters dated 12/16/2021. It is still the position of the review team that the proposed modification is acceptable.

Because the modification proposed include changes to the ETASU of the Mifepristone REMS Program, the assessment plan and timetable of assessments were changed. The assessment plan will capture information on pharmacy dispensing and provide valuable insight as to whether the program is operating as intended Annual assessments are consistent with other approved REMS modifications for major modifications necessitating extensive assessment plan changes.

As part of the REMS Assessment Plan, the REMS goal and objectives are assessed using Program Implementation and Operations Metrics, including REMS Certification Statistics and REMS Compliance Data. The metrics will provide information on the number of certified prescribers, certified pharmacies, and authorized wholesalers/distributors as well as if mifepristone is dispensed by non-certified prescribers or pharmacies. The Sponsors will use the indirect measure of healthcare provider certification to address the objective of informing patients of the risk of serious complications of mifepristone, due to concerns with prescriber and patient confidentiality. Although we typically assess whether patients are informed of the risks identified in a REMS through patient surveys and/or focus groups, we agree that the Sponsors' continued use of the indirect measure of healthcare provider certification adequately addresses the Mifepristone REMS Program objective of informing patients. In addition, because of these prescriber and patient confidentiality concerns, we believe it is unlikely that the Agency would be able to use the typical methods of assessment of patient knowledge and understanding of the risks and safe use of mifepristone.

7. Conclusions and Recommendations

The review team finds the proposed REMS modification for the Mifepristone REMS Program, as submitted on June 22, 2022, and amended on October 19, 2022 (Danco) and October 20, 2022 (GBP), November 30, 2022 (both), December 9 (both), and December 16 (both) acceptable. The REMS materials were amended to be consistent with the revised REMS document. The review team recommends approval of the Mifepristone REMS Program, received on June 22, 2022, and last amended on December 16, 2022, and appended to this review.

8. References

1. (b) (6) Clinical Review of SE-2 Efficacy Supplement for mifepristone, NDA 020687. March 29, 2016. DARRTS Reference ID: 3909590.

2. (b) (6) Summary Review for Regulatory Action for mifepristone, NDA 020687. March 29, 2016. DARRTS Reference ID: 3909594.

3. (b) (6) REMS Review for mifepristone, NDA 020687. March 29, 2016. DARRTS Reference ID: 3909588.

4. (b) (6) REMS Review for mifepristone, NDA 020687. March 29, 2016. DARRTS Reference ID: 3909587.

5. Approval Letter for SE-2 Efficacy Supplement for mifepristone, NDA 020687. March 29, 2016. DARRTS Reference ID: 3909592.

6. (b) (6) REMS Review for mifepristone, NDA 020687. February 22, 2018. DARRTS Reference ID: 4224674.

7. Approval Letter for SE-20 REMS Supplement for mifepristone, NDA 020687. March 29, 2016. DARRTS Reference ID: 4418041.

8. *Am. Coll. of Obstetricians & Gynecologists v. FDA*, 472 F. Supp. 3d 183, 233 (D. Md. July 13, 2020), order clarified, 2020 WL 8167535 (D. Md. Aug. 19, 2020) (preliminarily enjoining FDA from enforcing the in-person dispensing requirement and any other in-person requirements of the

Mifepristone SSS REMS); *FDA v. Am. Coll. of Obstetricians & Gynecologists*, 141 S. Ct. 578 (Jan. 12, 2021) (staying the preliminary injunction imposed by the District Court).

9. (b) (6) REMS Modification Rationale Review for mifepristone, NDA 020687. December 16, 2021. DARRTS Reference ID: 4905882.

10. General Advice Letter for the single, shared system Risk Evaluation and Mitigation Strategy (REMS) for mifepristone, NDA 020687, April 15, 2022. DARRTS ID 4969358.

11. Format and Content of a REMS Document Guidance for Industry https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM184128.pdf. Accessed on December 18, 2022.

12. Grossman D, Raifman S, Morris N, et.al. Mail-order pharmacy dispensing of mifepristone for medication abortion after in-person clinical assessment. Contraception 2022; 107:36-41. https://doi.org/10.1016/j.contraception.2021.09.008. This article was included in the literature review for the December 16, 2021 REMS Modification Rationale Review, while the article was still in press.

9. Appendices

REMS Document

Prescriber Agreement Form for Danco Laboratories, LLC

Prescriber Agreement Form for GenBioPro, Inc.

Patient Agreement Form

Pharmacy Agreement Form for Danco Laboratories, LLC

Pharmacy Agreement Form for GenBioPro, Inc.

Mifepristone REMS Assessment Plan

Initial Shared System REMS approval: 04/2019
Most Recent Modification: 01/2023

Mifepristone Tablets, 200 mg
Progestin Antagonist

RISK EVALUATION AND MITIGATION STRATEGY (REMS)
SINGLE SHARED SYSTEM FOR MIFEPRISTONE 200 MG

I. GOAL

The goal of the REMS for mifepristone is to mitigate the risk of serious complications associated with mifepristone by:

a) Requiring healthcare providers who prescribe mifepristone to be certified in the Mifepristone REMS Program.

b) Ensuring that mifepristone is only dispensed by or under the supervision of certified prescribers, or by certified pharmacies on prescriptions issued by certified prescribers.

c) Informing patients about the risk of serious complications associated with mifepristone.

II. REMS ELEMENTS

A. Elements to Assure Safe Use

1. Healthcare providers who prescribe mifepristone must be specially certified.
   a. To become specially certified to prescribe mifepristone, healthcare providers must:
      i. Review the Prescribing Information for mifepristone.
      ii. Complete a *Prescriber Agreement Form*. By signing[1] a *Prescriber Agreement Form*, prescribers agree that:
         1) They have the following qualifications:
            a) Ability to assess the duration of pregnancy accurately
            b) Ability to diagnose ectopic pregnancies
            c) Ability to provide surgical intervention in cases of incomplete abortion or severe bleeding, or to have made plans to provide such care through others, and ability to assure patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary
         2) They will follow the guidelines for use of mifepristone (see b.i-vii below).
   b. As a condition of certification, prescribers must follow the guidelines for use of mifepristone described below:
      i. Ensure that the *Patient Agreement Form* is reviewed with the patient and the risks of the mifepristone treatment regimen are fully explained. Ensure any questions the patient may have prior to receiving mifepristone are answered.
      ii. Ensure that the healthcare provider and patient sign the *Patient Agreement Form.*

[1] In this REMS, the terms "sign" and "signature" include electronic signatures.

Reference ID: 5103819

iii. Ensure that the patient is provided with a copy of the *Patient Agreement Form* and Medication Guide.

iv. Ensure that the signed *Patient Agreement Form* is placed in the patient's medical record.

v. Ensure that any deaths are reported to the Mifepristone Sponsor that provided the mifepristone, identifying the patient by a non-identifiable reference and including the NDC and lot number from the package of mifepristone that was dispensed to the patient.

vi. If mifepristone will be dispensed by a certified pharmacy:

1) Provide the certified pharmacy a signed *Prescriber Agreement Form*.

2) Assess appropriateness of dispensing mifepristone when contacted by a certified pharmacy about patients who will receive mifepristone more than 4 calendar days after the prescription was received by the certified pharmacy.

3) Obtain the NDC and lot number of the package of mifepristone the patient received in the event the prescriber becomes aware of the death of the patient.

vii. The certified prescriber who dispenses mifepristone or who supervises the dispensing of mifepristone must:

1) Provide an authorized distributor with a signed *Prescriber Agreement Form*.

2) Ensure that the NDC and lot number from each package of mifepristone dispensed are recorded in the patient's record.

3) Ensure that healthcare providers under their supervision follow guidelines i.-v.

c. Mifepristone Sponsors must:

i. Ensure that healthcare providers who prescribe their mifepristone are specially certified in accordance with the requirements described above and de-certify healthcare providers who do not maintain compliance with certification requirements.

ii. Ensure prescribers previously certified in the Mifepristone REMS Program complete the new *Prescriber Agreement Form*:

1) Within 120 days after approval of this modification, for those previously certified prescribers submitting prescriptions to certified pharmacies.

2) Within one year after approval of this modification, if previously certified and ordering from an authorized distributor.

iii. Ensure that healthcare providers can complete the certification process by email or fax to an authorized distributor and/or certified pharmacy.

iv. Provide the Prescribing Information and their *Prescriber Agreement Form* to healthcare providers who inquire about how to become certified.

v. Ensure annually with each certified prescriber that their locations for receiving mifepristone are up to date.

The following materials are part of the Mifepristone REMS Program:

- *Prescriber Agreement Form for Danco Laboratories, LLC*
- *Prescriber Agreement Form for GenBioPro, Inc.*
- *Patient Agreement Form*

Reference ID: 5103819

2. Pharmacies that dispense mifepristone must be specially certified
   a. To become specially certified to dispense mifepristone, pharmacies must:
      i. Be able to receive *Prescriber Agreement Forms* by email and fax.
      ii. Be able to ship mifepristone using a shipping service that provides tracking information.
      iii. Designate an authorized representative to carry out the certification process on behalf of the pharmacy.
      iv. Ensure the authorized representative oversees implementation and compliance with the Mifepristone REMS Program by doing the following:
         1) Review the Prescribing Information for mifepristone.
         2) Complete a *Pharmacy Agreement Form*. By signing a *Pharmacy Agreement Form*, the authorized representative agrees that the pharmacy will put processes and procedures in place to ensure the following requirements are completed:
            a) Verify that the prescriber is certified by confirming their completed *Prescriber Agreement Form* was received with the prescription or is on file with the pharmacy.
            b) Dispense mifepristone such that it is delivered to the patient within 4 calendar days of the date the pharmacy receives the prescription, except as provided in c) below.
            c) Confirm with the prescriber the appropriateness of dispensing mifepristone for patients who will receive the drug more than 4 calendar days after the date the pharmacy receives the prescription and document the prescriber's decision.
            d) Record in the patient's record the NDC and lot number from each package of mifepristone dispensed.
            e) Track and verify receipt of each shipment of mifepristone.
            f) Dispense mifepristone in its package as supplied by the Mifepristone Sponsor.
            g) Report any patient deaths to the prescriber, including the NDC and lot number from the package of mifepristone dispensed to the patient, and remind the prescriber of their obligation to report the deaths to the Mifepristone Sponsor that provided the mifepristone. Notify the Mifepristone Sponsor that provided the dispensed mifepristone that the pharmacy submitted a report of death to the prescriber, including the name and contact information for the prescriber and the NDC and lot number of the dispensed product.
            h) Not distribute, transfer, loan or sell mifepristone except to certified prescribers or other locations of the pharmacy.
            i) Maintain records of *Prescriber Agreement Forms*.
            j) Maintain records of dispensing and shipping.
            k) Maintain records of all processes and procedures including compliance with those processes and procedures.
            l) Maintain the identity of the patient and prescriber as confidential, including limiting access to patient and prescriber identity only to those personnel necessary to dispense mifepristone in accordance with the Mifepristone REMS Program requirements, or as necessary for payment and/or insurance purposes.
            m) Train all relevant staff on the Mifepristone REMS Program requirements.

Reference ID: 5103819

n) Comply with audits carried out by the Mifepristone Sponsors or a third party acting on behalf of the Mifepristone Sponsors to ensure that all processes and procedures are in place and are being followed.

b. Mifepristone Sponsors must:

i. Ensure that pharmacies are specially certified in accordance with the requirements described above and de-certify pharmacies that do not maintain compliance with certification requirements.

ii. Ensure that pharmacies can complete the certification process by email and fax to an authorized distributor.

i. Verify annually that the name and contact information for the pharmacy's authorized representative corresponds to that of the current designated authorized representative for the certified pharmacy, and if different, require the pharmacy to recertify with the new authorized representative.

The following materials are part of the Mifepristone REMS Program:

- *Pharmacy Agreement Form for Danco Laboratories, LLC*
- *Pharmacy Agreement Form for GenBioPro, Inc.*

3. Mifepristone must be dispensed to patients with evidence or other documentation of safe use conditions as ensured by the certified prescriber in signing the *Prescriber Agreement Form*.

a. The patient must sign a *Patient Agreement Form* indicating that the patient has:

i. Received, read and been provided a copy of the *Patient Agreement Form*.

ii. Received counseling from the healthcare provider regarding the risk of serious complications associated with mifepristone.

B. Implementation System

1. Mifepristone Sponsors must ensure that their mifepristone is only distributed to certified prescribers and certified pharmacies by:

a. Ensuring that distributors who distribute their mifepristone comply with the program requirements for distributors.

i. The distributors must put processes and procedures in place to:

1) Complete the certification process upon receipt of a *Prescriber Agreement Form* or *Pharmacy Agreement Form*.

2) Notify healthcare providers and pharmacies when they have been certified by the Mifepristone REMS Program.

3) Ship mifepristone only to certified pharmacies or locations identified by certified prescribers.

4) Not ship mifepristone to pharmacies or prescribers who become de-certified from the Mifepristone REMS Program.

5) Provide the Prescribing Information and their Prescriber Agreement Form to healthcare providers who (1) attempt to order mifepristone and are not yet certified, or (2) inquire about how to become certified.

ii. Put processes and procedures in place to maintain a distribution system that is secure,

confidential and follows all processes and procedures, including those for storage, handling, shipping, tracking package serial numbers, NDC and lot numbers, proof of delivery and controlled returns of mifepristone.

iii. Train all relevant staff on the Mifepristone REMS Program requirements.

iv. Comply with audits by Mifepristone Sponsors or a third party acting on behalf of Mifepristone Sponsors to ensure that all processes and procedures are in place and are being followed for the Mifepristone REMS Program. In addition, distributors must maintain appropriate documentation and make it available for audits.

b. Ensuring that distributors maintain secure and confidential distribution records of all shipments of mifepristone.

2. Mifepristone Sponsors must monitor their distribution data to ensure compliance with the Mifepristone REMS Program.

3. Mifepristone Sponsors must ensure that adequate records are maintained to demonstrate that the Mifepristone REMS Program requirements have been met, including, but not limited to records of mifepristone distribution; certification of prescribers and pharmacies; and audits of pharmacies and distributors. These records must be readily available for FDA inspections.

4. Mifepristone Sponsors must audit their new distributors within 90 calendar days and annually thereafter after the distributor is authorized to ensure that all processes and procedures are in place and functioning to support the requirements of the Mifepristone REMS Program. Mifepristone Sponsors will take steps to address their distributor compliance if noncompliance is identified.

5. Mifepristone Sponsors must audit their certified pharmacies within 180 calendar days after the pharmacy places its first order of mifepristone, and annually thereafter audit certified pharmacies that have ordered mifepristone in the previous 12 months, to ensure that all processes and procedures are in place and functioning to support the requirements of the Mifepristone REMS Program. Mifepristone Sponsors will take steps to address their pharmacy compliance if noncompliance is identified.

6. Mifepristone Sponsors must take reasonable steps to improve implementation of and compliance with the requirements of the Mifepristone REMS Program based on monitoring and assessment of the Mifepristone REMS Program.

7. Mifepristone Sponsors must report to FDA any death associated with mifepristone whether or not considered drug-related, as soon as possible but no later than 15 calendar days from the initial receipt of the information by the Mifepristone Sponsor. This requirement does not affect the sponsors' other reporting and follow-up requirements under FDA regulations.

C. Timetable for Submission of Assessments

The NDA Sponsor must submit REMS assessments to FDA one year from the date of the approval of the modified REMS (1/3/2023) and annually thereafter. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 90 calendar days before the submission date for that assessment. The NDA Sponsor must submit each assessment so that it will be received by the FDA on or before the due date.

MIFEPREX® (Mifepristone) Tablets, 200 mg

PRESCRIBER AGREEMENT FORM

Mifeprex* (Mifepristone) Tablets, 200 mg, is indicated, in a regimen with misoprostol, for the medical termination of intrauterine pregnancy through 70 days gestation. Please see Prescribing Information and Medication Guide for complete safety information.

To ***become a certified prescriber***, you must:

- **If you submit Mifeprex prescriptions for dispensing from certified pharmacies**:
  - Submit this form to each certified pharmacy to which you intend to submit Mifeprex prescriptions. The form must be received by the certified pharmacy before any prescriptions are dispensed by that pharmacy.
- **If you order Mifeprex for dispensing by you or healthcare providers under your supervision:**
  - Submit this form to the distributor. This form must be received by the distributor before the first order will be shipped to the healthcare setting.
  - Healthcare settings, such as medical offices, clinics, and hospitals, where Mifeprex will be dispensed by or under the supervision of a certified prescriber in the Mifepristone REMS Program do not require pharmacy certification.

Prescriber Agreement: By signing this form, you agree that you meet the qualifications below and will follow the guidelines for use. You are responsible for overseeing implementation and compliance with the Mifepristone REMS Program. You also understand that if the guidelines below are not followed, the distributor may stop shipping mifepristone to the locations that you identify and certified pharmacies may stop accepting your mifepristone prescriptions.

Mifepristone must be provided by or under the supervision of a certified prescriber who meets the following qualifications:

- Ability to assess the duration of pregnancy accurately.
- Ability to diagnose ectopic pregnancies.
- Ability to provide surgical intervention in cases of incomplete abortion or severe bleeding, or have made plans to provide such care through others, and be able to assure patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary.
- Has read and understood the Prescribing Information for mifepristone. The Prescribing Information is available by calling 1-877-4 EARLY OPTION (1-877-432-7596 toll-free), or by visiting www.earlyoptionpill.com.

In addition to meeting these qualifications, you also agree to follow these guidelines for use:

- Ensure that the *Patient Agreement Form* is reviewed with the patient and the risks of the mifepristone treatment regimen are fully explained. Ensure any questions the patient may have prior to receiving mifepristone are answered.
- Ensure the healthcare provider and patient sign the *Patient Agreement Form*.
- Ensure that the patient is provided with a copy of the *Patient Agreement Form* and Medication Guide.
- Ensure that the signed *Patient Agreement Form* is placed in the patient's medical record.
- Ensure that any deaths of patients who received Mifeprex are reported to Danco Laboratories, LLC, identifying the patient by a non-identifiable reference and including the NDC and lot number from the package of Mifeprex that was dispensed to the patient.

Ensure that healthcare providers under your supervision follow the guidelines listed above.

- If Mifeprex will be dispensed through a certified pharmacy:
  - Assess appropriateness of dispensing Mifeprex when contacted by a certified pharmacy about patients who will receive Mifeprex more than 4 calendar days after the prescription was received by the certified pharmacy.
  - Obtain the NDC and lot number of the package of Mifeprex the patient received in the event the prescriber becomes aware of the death of a patient.
- If Mifeprex will be dispensed by you or by healthcare providers under your supervision:
  - Ensure the NDC and lot number from each package of Mifeprex are recorded in the patient's record.

I understand that a certified pharmacy may dispense mifepristone made by a different manufacturer than that stated on this Prescriber Agreement Form.

Print Name: _____ Title: _____

Signature: _____ Date: _____

Medical License # _____ State _____

NPI # _____

Practice Setting Address: _____

Return completed form to Mifeprex@dancodistributor.com or fax to 1-866-227-3343.

Approved 01/2023 [Doc control ID]

PRESCRIBER AGREEMENT FORM Mifepristone Tablets, 200 mg

Mifepristone Tablets, 200 mg, is indicated, in a regimen with misoprostol, for the medical termination of intrauterine pregnancy through 70 days gestation. Please see Prescribing Information and Medication Guide for complete safety information.

To ***become a certified prescriber***, you must:

- **If you submit mifepristone prescriptions for dispensing from certified pharmacies**:
  - Submit this form to each certified pharmacy to which you intend to submit mifepristone prescriptions. The form must be received by the certified pharmacy before any prescriptions are dispensed by that pharmacy.
- **If you order mifepristone for dispensing by you or healthcare providers under your supervision:**
  - Submit this form to the distributor. This form must be received by the distributor before the first order will be shipped to the healthcare setting.
  - Healthcare settings, such as medical offices, clinics, and hospitals, where mifepristone will be dispensed by or under the supervision of a certified prescriber in the Mifepristone REMS Program do not require pharmacy certification.

Prescriber Agreement: By signing this form, you agree that you meet the qualifications below and will follow the guidelines for use. You are responsible for overseeing implementation and compliance with the Mifepristone REMS Program. You also understand that if the guidelines below are not followed, the distributor may stop shipping mifepristone to the locations that you identify and certified pharmacies may stop accepting your mifepristone prescriptions.

Mifepristone must be provided by or under the supervision of a certified prescriber who meets the following qualifications:

- Ability to assess the duration of pregnancy accurately.
- Ability to diagnose ectopic pregnancies.
- Ability to provide surgical intervention in cases of incomplete abortion or severe bleeding, or have made plans to provide such care through others, and be able to assure patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary.
- Has read and understood the Prescribing Information for mifepristone. The Prescribing Information is available by calling 1-855-MIFE-INFO (1-855—643-3463 toll-free), or by visiting www.MifeInfo.com.

In addition to meeting these qualifications, you also agree to follow these guidelines for use:

- Ensure that the *Patient Agreement Form* is reviewed with the patient and the risks of the mifepristone treatment regimen are fully explained. Ensure any questions the patient may have prior to receiving mifepristone are answered.
- Ensure the healthcare provider and patient sign the *Patient Agreement Form*.
- Ensure that the patient is provided with a copy of the *Patient Agreement Form* and Medication Guide.
- Ensure that the signed *Patient Agreement Form* is placed in the patient's medical record.
- Ensure that any deaths of patients who received mifepristone are reported to GenBioPro, Inc. that provided the mifepristone, identifying the patient by a non-identifiable reference and including the NDC and lot number from the package of mifepristone that was dispensed to the patient.

Ensure that healthcare providers under your supervision follow the guidelines listed above.

- If mifepristone will be dispensed through a certified pharmacy:
  - Assess appropriateness of dispensing mifepristone when contacted by a certified pharmacy about patients who will receive mifepristone more than 4 calendar days after the prescription was received by the certified pharmacy.
  - Obtain the NDC and lot number of the package of mifepristone the patient received in the event the prescriber becomes aware of the death of a patient.
- If mifepristone will be dispensed by you or by healthcare providers under your supervision:
  - Ensure the NDC and lot number from each package of mifepristone are recorded in the patient's record.

I understand that a certified pharmacy may dispense mifepristone made by a different manufacturer than that stated on this Prescriber Agreement Form.

Print Name: _____ Title: _____

Signature: _____ Date: _____

Medical License # _____ State _____

NPI # _____

Practice Setting Address: _____

Return completed form to **RxAgreements@GenBioPro.com** or fax to 1-877-239-8036

Approved 01/2023 [Doc control ID]

PATIENT AGREEMENT FORM Mifepristone Tablets, 200 mg

Healthcare Providers: *Counsel the patient on the risks of mifepristone. Both you and the patient must provide a written or electronic signature on this form.*

Patient Agreement:

1. I have decided to take mifepristone and misoprostol to end my pregnancy and will follow my healthcare provider's advice about when to take each drug and what to do in an emergency.
2. I understand:
   - **a.** I will take mifepristone on Day 1.
   - **b.** I will take the misoprostol tablets 24 to 48 hours after I take mifepristone.
3. My healthcare provider has talked with me about the risks, including:
   - heavy bleeding
   - infection
4. I will contact the clinic/office/provider right away if in the days after treatment I have:
   - a fever of 100.4°F or higher that lasts for more than four hours
   - heavy bleeding (soaking through two thick full-size sanitary pads per hour for two hours in a row)
   - severe stomach area (abdominal) pain or discomfort, or I am “feeling sick,” including weakness, nausea, vomiting, or diarrhea, more than 24 hours after taking misoprostol
     — these symptoms may be a sign of a serious infection or another problem (including an ectopic pregnancy, a pregnancy outside the womb).

   My healthcare provider has told me that these symptoms listed above could require emergency care. If I cannot reach the clinic/office/provider right away, my healthcare provider has told me who to call and what to do.
5. I should follow up with my healthcare provider about 7 to 14 days after I take mifepristone to be sure that my pregnancy has ended and that I am well.
6. I know that, in some cases, the treatment will not work. This happens in about 2 to 7 out of 100 women who use this treatment. If my pregnancy continues after treatment with mifepristone and misoprostol, I will talk with my provider about a surgical procedure to end my pregnancy.
7. If I need a surgical procedure because the medicines did not end my pregnancy or to stop heavy bleeding, my healthcare provider has told me whether they will do the procedure or refer me to another healthcare provider who will.
8. I have the MEDICATION GUIDE for mifepristone.
9. My healthcare provider has answered all my questions.

Patient Signature: _____ **Patient Name** (print): _____ **Date**: _____

Provider Signature: _____ **Provider Name** (print): _____ **Date**: _____

Patient Agreement Forms may be provided, completed, signed, and transmitted in paper or electronically.

01/2023

Reference ID: 5103819

MIFEPREX®(Mifepristone) Tablets, 200mg

PHARMACY AGREEMENT FORM

Pharmacies must designate an authorized representative to carry out the certification process and oversee implementation and compliance with the Mifepristone REMS Program on behalf of the pharmacy.

Healthcare settings, such as medical offices, clinics, and hospitals, where mifepristone will be dispensed by or under the supervision of a certified prescriber in the Mifepristone REMS Program do not require pharmacy certification.

By signing this form, as the Authorized Representative I certify that:

- Each location of my pharmacy that will dispense Mifeprex is able to receive *Prescriber Agreement Forms* by email and fax.
- Each location of my pharmacy that will dispense Mifeprex is able to ship Mifeprex using a shipping service that provides tracking information.
- I have read and understood the Prescribing Information for Mifeprex. The Prescribing Information is available by calling 1-877-4 EARLY OPTION (1-877-432-7596 toll-free) or online at www.earlyoptionpill.com; and
- Each location of my pharmacy that will dispense Mifeprex will put processes and procedures in place to ensure the following requirements are completed. I also understand that if my pharmacy does not complete these requirements, the distributor may stop accepting Mifeprex orders.
  - Verify that the prescriber is certified in the Mifepristone REMS Program by confirming their completed *Prescriber Agreement Form* was received with the prescription or is on file with your pharmacy.
  - Dispense Mifeprex such that it is delivered to the patient within 4 calendar days of the date the pharmacy receives the prescription, except as provided in the following bullet.
  - Confirm with the prescriber the appropriateness of dispensing Mifeprex for patients who will receive the drug more than 4 calendar days after the date the pharmacy receives the prescription and document the prescriber's decision.
  - Record in the patient's record the NDC and lot number from each package of Mifeprex dispensed.
  - Track and verify receipt of each shipment of Mifeprex.
  - Dispense mifepristone in its package as supplied by Danco Laboratories, LLC.
  - Report any patient deaths to the prescriber, including the NDC and lot number from the package of Mifeprex dispensed to the patient, and remind the prescriber of their obligation to report the deaths to Danco Laboratories, LLC. Notify Danco that your pharmacy submitted a report of death to the prescriber, including the name and contact information for the prescriber and the NDC and lot number of the dispensed product.
  - Not distribute, transfer, loan or sell mifepristone except to certified prescribers or other locations of the pharmacy.
  - Maintain records of *Prescriber Agreement Forms*, dispensing and shipping, and all processes and procedures including compliance with those processes and procedures.
  - Maintain the identity of Mifeprex patients and prescribers as confidential and protected from disclosure except to the extent necessary for dispensing under this REMS or as necessary for payment and/or insurance.
  - Train all relevant staff on the Mifepristone REMS Program requirements.
  - Comply with audits carried out by the Mifepristone Sponsors or a third party acting on behalf of the Mifepristone Sponsors to ensure that all processes and procedures are in place and are being followed.

Any new authorized representative must complete and submit the *Pharmacy Agreement Form*.

Authorized Representative Name: _____ Title: _____

Signature: _____ Date: _____

Email: _____ Phone: _____ Preferred __ email __ phone

Pharmacy Name: _____

Pharmacy Address: _____

Return completed form to Mifeprex@dancodistributor.com or fax to 1-866-227-3343.

PHARMACY AGREEMENT FORM **Mifepristone Tablets, 200 mg**

Pharmacies must designate an authorized representative to carry out the certification process and oversee implementation and compliance with the Mifepristone REMS Program on behalf of the pharmacy.

Healthcare settings, such as medical offices, clinics, and hospitals, where mifepristone will be dispensed by or under the supervision of a certified prescriber in the Mifepristone REMS Program do not require pharmacy certification.

By signing this form, as the Authorized Representative I certify that:

- Each location of my pharmacy that will dispense mifepristone is able to receive *Prescriber Agreement Forms* by email and fax.
- Each location of my pharmacy that will dispense mifepristone is able to ship mifepristone using a shipping service that provides tracking information.
- I have read and understood the Prescribing Information for mifepristone. The Prescribing Information is available by calling 1-855-MIFE-INFO (1-855-643-3463 toll-free) or online at www.MifeInfo.com; and
- Each location of my pharmacy that will dispense mifepristone will put processes and procedures in place to ensure the following requirements are completed. I also understand that if my pharmacy does not complete these requirements, the distributor may stop accepting mifepristone orders.
  - Verify that the prescriber is certified in the Mifepristone REMS Program by confirming their completed *Prescriber Agreement Form* was received with the prescription or is on file with your pharmacy.
  - Dispense mifepristone such that it is delivered to the patient within 4 calendar days of the date the pharmacy receives the prescription, except as provided in the following bullet.
  - Confirm with the prescriber the appropriateness of dispensing mifepristone for patients who will receive the drug more than 4 calendar days after the date the pharmacy receives the prescription and document the prescriber's decision.
  - Record in the patient's record the NDC and lot number from each package of mifepristone dispensed.
  - Track and verify receipt of each shipment of mifepristone.
  - Dispense mifepristone in its package as supplied by GenBioPro, Inc.
  - Report any patient deaths to the prescriber, including the NDC and lot number from the package of mifepristone dispensed to the patient, and remind the prescriber of their obligation to report the deaths to GenBioPro, Inc. Notify GenBioPro that your pharmacy submitted a report of death to the prescriber, including the name and contact information for the prescriber and the NDC and lot number of the dispensed product.
  - Not distribute, transfer, loan or sell mifepristone except to certified prescribers or other locations of the pharmacy.
  - Maintain records of *Prescriber Agreement Forms*, dispensing and shipping, all processes and procedures including compliance with those processes and procedures.
  - Maintain the identity of mifepristone patients and prescribers as confidential and protected from disclosure except to the extent necessary for dispensing under this REMS or as necessary for payment and/or insurance purposes.
  - Train all relevant staff on the Mifepristone REMS Program requirements.
  - Comply with audits carried out by the Mifepristone Sponsors or a third party acting on behalf of the Mifepristone Sponsors to ensure that all processes and procedures are in place and are being followed.

Any new authorized representative must complete and submit the *Pharmacy Agreement Form*.

Authorized Representative Name: _____ Title: _____

Signature: _____ Date: _____

Email: _____ Phone: _____ Preferred __ email __ phone

Pharmacy Name: _____

Pharmacy Address: _____

Return completed form to **RxAgreements@GenBioPro.com** or fax to **1-877-239-8036.**

The REMS Assessment Plan must include but is not limited to the following items.

Program Implementation and Operations

1. REMS Certification Statistics
   a. Prescribers
      i. Number of certified prescribers who have certified with the Sponsor's distributor(s) and number who have submitted *Prescriber Agreement Forms* to Certified Pharmacies
      ii. Number and percentage of newly certified prescribers
      iii. Number and percentage of active certified prescribers (i.e., who ordered mifepristone or submitted a prescription during the reporting period)

   b. Pharmacies
      i. Number of certified pharmacies
      ii. Number and percentage of newly certified pharmacies
      iii. Number and percentage of active certified pharmacies (i.e., that dispensed mifepristone during the reporting period)
   c. Wholesalers/Distributors
      i. Number of authorized wholesalers/distributors
      ii. Number and percentage of newly authorized wholesalers/distributors
      iii. Number and percentage of active authorized wholesalers/distributors (i.e. that shipped mifepristone during the reporting period)

2. Utilization Data
   a. Total number of tablets shipped by wholesalers/distributors, stratified by Certified Prescriber or Certified Pharmacy location
   b. Number of prescriptions dispensed from pharmacies

3. REMS Compliance Data
   a. Audits: Summary of audit activities for each stakeholder (i.e., certified pharmacies and wholesalers/distributors) including but not limited to:
      i. A copy of the final audit plan for each stakeholder type (provide for the current reporting period)
      ii. The number of audits expected, and the number of audits performed
      iii. The number and type of deficiencies noted
      iv. For those with deficiencies noted, report the corrective and preventive actions (CAPAs) required, if any, to address the deficiencies, including the status (e.g., completed, not completed, in progress) (provide for the current reporting period)
      v. For any stakeholders that did not complete the CAPA within the timeframe specified in the audit plan, describe actions taken (provide for the current reporting period)

vi. A summary report of all resulting changes to processes and procedures necessary to ensure compliance with the REMS requirements (provide for the current reporting period)

b. A summary report of non-compliance, associated corrective action plans (CAPAs), and the status of CAPAs including but not limited to:

i. A copy of the final non-compliance plans for Pharmacies and Distributors (provide for the current reporting period)

ii. For each instance of noncompliance below (iii-v), report the following information (provide for the current reporting period):

1. A unique, anonymized ID for the stakeholder(s) associated with the non-compliance event to enable tracking over time
2. The source of the non-compliance data (e.g., self-reported, audit, other)
3. A root cause analysis of the non-compliance
4. Actions to prevent future occurrences and outcomes of such actions

iii. Prescriber compliance

1. Number and percentage of certified prescribers who became decertified as a result of non- compliance
   - Provide a summary of reasons for decertification (provide for the current reporting period)
2. Summary and analysis of any program deviations and corrective actions taken (provide for the current reporting period)

iv. Pharmacy compliance

1. Number and percentage of prescriptions dispensed that were written by prescriber(s) who did not submit a Prescriber Agreement to the dispensing Certified Pharmacy
2. Number and percentage of mifepristone tablets dispensed by non-certified pharmacies
3. Number and percentage of pharmacies that became decertified as a result of non-compliance
   - Provide a summary of reasons for decertification (provide for the current reporting period)
4. An assessment of prescription delivery timelines, including percentage delivered more than four days after receipt of the prescription, duration and causes for delay. A proposal for this assessment will be submitted within 60 days of the approval of the REMS Modification.
5. Summary and analysis of any program deviations and corrective actions taken (provide for the current reporting period)

v. Wholesaler/distributor compliance

1. Number of healthcare providers who successfully ordered mifepristone who were not certified
2. Number of non-certified pharmacies that successfully ordered mifepristone
3. Number of shipments sent to non-certified prescriber receiving locations
4. Number of shipments sent to non-certified pharmacy receiving locations

5. Summary and analysis of any program deviations and corrective actions taken (provide for the current reporting period)

The requirements for assessments of an approved REMS under section 505-1(g)(3) include with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether one or more such goals or such elements should be modified.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

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Center for Drug Evaluation and Research (CDER)

(b) (6)

Application Type	NDA and ANDA
Application Number	020687 and 91178
Reviewer Names	(b) (6)
	(b) (6)
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Review Completion Date	December 16, 2021

Subject	REMS Modification Rationale Review
Established Name	Mifepristone REMS
Name of Applicants	Danco Laboratories, LLC and GenBioPro, Inc.
Therapeutic Class	Progestin antagonist
Formulation	Oral tablets

Table of Contents

EXECUTIVE SUMMARY 4

1. Introduction 5
2. Background 5
   - 2.1. PRODUCT AND REMS INFORMATION 5
   - 2.2. REGULATORY HISTORY AND EVENTS RELEVANT TO THIS REMS MODIFICATION RATIONALE REVIEW 7
3. Rationale for Proposed REMS Modification 9
   - 3.1. CURRENT REQUIREMENTS FOR THE APPROVED REMS 10
   - 3.2. EVALUATION OF THE EVIDENCE 10
   - 3.2.1. Evaluation of the requirement for healthcare providers who prescribe the drug to be specially certified (ETASU A) 12
   - 3.2.2. Evaluation of the requirement for the drug to be dispensed with evidence or other documentation of safe-use conditions (ETASU D) 14
   - 3.2.3. Evaluation of the requirement for drug to be dispensed only in certain healthcare settings (ETASU C) 19
4. Discussion 36
5. Conclusions and Recommendations 41
6. References 42
7. Appendix 45

EXECUTIVE SUMMARY

This review provides the [redacted] rationale and conclusions regarding modifications to the single, shared system Risk Evaluation and Mitigation Strategy (REMS) for mifepristone 200 mg (Mifepristone REMS Program) for new drug application (NDA) 20687 and abbreviated new drug application (ANDA) 91178.

ANDA 91178 was approved with the approval of the Mifepristone REMS Program on April 11, 2019 to mitigate the risk of serious complications associated with mifepristone 200 mg. The most recent REMS modification was approved on May 14, 2021. The REMS consists of elements to assure safe use (ETASU) under ETASU A, C and D, an implementation system, and a timetable for submission of assessments. To determine whether a modification to the REMS was warranted, FDA undertook a comprehensive review of the published literature; safety information collected during the COVID-19 public health emergency (PHE); the one-year REMS assessment report of the Mifepristone REMS Program; adverse event data; and information provided by advocacy groups, individuals and the Applicants. Our review also included an examination of literature references provided by plaintiffs in the *Chelius v. Becerra* litigation discussed below.

The modifications to the REMS will consist of:

- Removing the requirement under ETASU C that mifepristone be dispensed only in certain healthcare settings, specifically clinics, medical offices, and hospitals (referred to here as the "in-person dispensing requirement" for brevity)
- Adding a requirement under ETASU B that pharmacies that dispense the drug be specially certified

A REMS Modification Notification letter will be sent to both Applicants in the Single Shared System.

1. Introduction

In connection with the *Chelius v. Becerra* litigation, FDA agreed to undertake a full review of the Mifepristone REMS Program, in accordance with the REMS assessment provisions of the Federal Food, Drug, and Cosmetic Act (FD&C Act).[a] This review provides the analysis of the (b) (6) ((b) (6) and the (b) (6) ((b) (6) regarding whether any changes are warranted to the single, shared system Risk Evaluation and Mitigation Strategy (REMS) for mifepristone (hereafter referred to as the Mifepristone REMS Program) for new drug application (NDA) 20687 and abbreviated new drug application (ANDA) 91178. The Mifeprex REMS was initially approved in 2011; the single, shared system REMS for mifepristone 200 mg, known as the Mifepristone REMS Program, was approved in 2019.

The last time the existing REMS elements to assure safe use (under ETASU A, C and D) were reviewed was in the context of our review of supplement S-020 to NDA 20687; these ETASU were updated following review and approval of supplement S-020 on March 29, 2016. The key changes approved in 2016 are summarized below.

Changes to labeling included:

- Changing the dosing of Mifeprex to 200 mg orally x 1
- Extension of maximum gestational age through 70 days
- Inclusion of misoprostol in the indication statement
- Replacing the term “physician” with “licensed healthcare provider”
- Removal of the phrase “Under Federal Law”

The Mifeprex REMS and REMS materials were updated to reflect the changes above, and additional changes were made including:

- Removing the Medication Guide as part of the REMS but retaining it as part of labeling.

2. Background

2.1. PRODUCT AND REMS INFORMATION

[a] Section 505-1(g)(2) of the FD&C Act (21 U.S.C. § 355-1(g)(2)).

Mifepristone is a progestin antagonist indicated, in a regimen with misoprostol, for the medical termination of intrauterine pregnancy (IUP) through 70 days gestation. Mifepristone is available as 200 mg tablets for oral use.

Mifeprex (mifepristone) was approved on September 28, 2000 with a restricted distribution program under 21 CFR 314.520 (subpart H)[b] to ensure that the benefits of the drug outweighed the risk of serious complications associated with mifepristone when used for medical abortion. Mifeprex was deemed to have a REMS under section 505-1 of the Federal Food, Drug, and Cosmetic Act with the passage of the Food and Drug Administration Amendments Act (FDAAA) of 2007, and the Mifeprex REMS was approved on June 8, 2011. On March 29, 2016, as noted above, a supplemental application and REMS modification was approved for Mifeprex. On April 11, 2019, ANDA 091178 was approved, and the Mifepristone REMS Program was approved. The Mifepristone REMS Program is a single, shared system REMS that includes NDA 020687 and ANDA 91178.

The goal of the REMS for mifepristone is to mitigate the risk of serious complications associated with mifepristone by:

a. Requiring healthcare providers who prescribe mifepristone to be certified in the Mifepristone REMS Program (under ETASU A).
b. Ensuring that mifepristone is only dispensed in certain healthcare settings, by or under the supervision of a certified prescriber (under ETASU C).
c. Informing patients about the risk of serious complications associated with mifepristone (under ETASU D).

Under ETASU A, to become specially certified to prescribe mifepristone, a healthcare provider must review the prescribing information, complete and sign the *Prescriber Agreement Form,* and follow the guidelines for use of mifepristone. Under ETASU C, mifepristone must be dispensed to patients only in certain healthcare settings, specifically clinics, medical offices, and hospitals, by or under the supervision of a certified prescriber. Under ETASU D, mifepristone must be dispensed to patients with evidence or other documentation of safe use conditions (i.e., the patient must sign a *Patient Agreement Form*). The Mifepristone REMS Program also includes an implementation system, and a timetable for assessments (one year from the date of the initial approval of the REMS on April 11, 2019, and every three years thereafter).

[b] NDA approval letter Mifeprex (NDA 020687) dated September 28, 2000.

2.2. REGULATORY HISTORY AND EVENTS RELEVANT TO THIS REMS MODIFICATION RATIONALE REVIEW

The following is a summary of significant regulatory history since approval of the REMS modification on March 29, 2016:

- 03/29/2016: FDA approved an efficacy supplement (S-020) that, among other things, provided a new dosing regimen (200 mg mifepristone, followed in 24 to 48 hours by 800 mcg buccal misoprostol), increased the gestational age (GA) to which mifepristone may be used (through 70 days gestation), and modified the REMS.

- 03/29/2019: A Citizen Petition was received requesting that FDA revise the product labeling to reflect pre-2016 provisions (including limiting GA to 49 days and requiring patients to make 3 office visits) and that FDA maintain the REMS.

- 04/11/2019: ANDA 91178 was approved along with the Single Shared System REMS for Mifepristone 200 mg (Mifepristone REMS Program) for NDA 20687 and ANDA 91178.

- 01/31/2020: the COVID-19 public health emergency (PHE) was declared by the Secretary of Health and Human Services (HHS) as having existed since January 27, 2020.[c]

- 7/13/2020: The United States (US) District Court of Maryland granted a preliminary injunction in the *ACOG v. FDA* litigation to temporarily bar enforcement of the Mifepristone REMS Program in-person dispensing requirement during the COVID-19 PHE.

- 1/12/2021: US Supreme Court granted a stay of that injunction.

- 04/12/2021: FDA issued a General Advice Letter to both the NDA and ANDA Applicants, stating that provided that all other requirements of the Mifepristone REMS Program are met, and given that in-person dispensing of mifepristone for medical termination of early pregnancy may present additional COVID-related risks to patients and healthcare

[c] *See* Secretary of Health and Human Services, Determination that a Public Health Emergency Exists (originally issued January 31, 2020, and subsequently renewed), available at https://www.phe.gov/emergency/news/healthactions/phe/Pages/default.aspx

personnel because it may involve a clinical visit solely for this purpose, FDA intends to exercise enforcement discretion during the COVID-19 PHE with respect to the in-person dispensing requirement in the Mifepristone REMS Program, including any in-person requirements that may be related to the *Patient Agreement Form.* FDA further stated that to the extent all of the other requirements of the Mifepristone REMS Program are met, FDA intends to exercise enforcement discretion during the COVID-19 PHE with respect to the dispensing of mifepristone through the mail, either by or under the supervision of a certified prescriber, or through a mail-order pharmacy when such dispensing is done under the supervision of a certified prescriber.

- 05/07/2021: FDA stated that it would be reviewing the elements of the Mifepristone REMS Program in accordance with the REMS assessment provisions of section 505-1 of the FD&C Act.

- 05/14/2021: A modification was approved for the Mifepristone REMS Program. This modification was to revise the *Patient Agreement Form* to include gender-neutral language.

- 06/30/2021: An Information Request (IR) was sent to the Applicants for additional information on shipments and any program deviations, adverse events, or noncompliance with the REMS that occurred during the period from April 1, 2021 through September 30, 2021.

- 7/15/2021: An IR was sent to the Applicants to provide the total number of shipments during the period from April 1, 2021 to September 30, 2021 and details on whether any of those shipments were involved in any program deviation or non-compliance.

- 8/5/2021: An IR was sent to the Applicants for additional clinical and other information (e.g., adverse events and units of mifepristone shipped) for the period of March 29, 2016 through June 30, 2021, to be provided by August 31, 2021. This IR also requested information covering the period of July 1, 2021 through September 30, 2021 and an

aggregate summary (for the period of March 29, 2016 through September 30, 2021), to be provided by October 12, 2021.[d]

- 8/26/2021: The ANDA Applicant submitted a response to the IR issued on 8/5/2021.
- 08/27/2021: The NDA Applicant submitted a response to the IR issued on 8/5/2021.
- 10/08/2021: The NDA Applicant submitted a response to the June 30 and July 15, 2021 IRs as well as an aggregate summary for the period March 29, 2016 through September 30, 2021 in response to the August 5, 2021 IR. The NDA Applicant also included a follow-up to their initial response provided on August 27, 2021 to the August 5, 2021 IR.
- 10/12/2021: The ANDA Applicant submitted a response to the June 30 and July 15, 2021 IRs as well as an aggregate summary for the period March 29, 2016 through September 30, 2021 in response to the August 5, 2021 IR.
- 10/16/2021: The ANDA Applicant revised their Oct 12, 2012 response to provide a correction to the number of mifepristone tablets.
- (b) (4) .
- 11/02/2021: A (b) (6) ((b) (6) meeting was convened to obtain CDER concurrence on the removal of the in-person dispensing requirement and the addition of a certification requirement for pharmacies. The (b) (6) (b) (6) and senior CDER leadership concurred with removing the in-person dispensing and adding pharmacy certification.

3. Rationale for Proposed REMS Modification

[d] Multiple Information Requests were issued to obtain additional information on drug shipments, any program deviations or noncompliance, and use of alternative methods for drug distribution during the COVID-19 PHE. These IRs are referenced as appropriate in this document and the one-year REMS Assessment Review of the Mifepristone REMS Program, December 16, 2021.

3.1. CURRENT REQUIREMENTS FOR THE APPROVED REMS

The Mifepristone REMS Program includes elements to assure safe use (ETASU), an implementation system, and a timetable for submission of assessments. Elements to assure safe use in the current REMS include a prescriber certification requirement (ETASU A), a requirement that mifepristone be dispensed only in certain healthcare settings by or under the supervision of a certified prescriber (ETASU C), and a requirement that mifepristone be dispensed only with documentation of safe use conditions (ETASU D). Documentation of safe use conditions under ETASU D consists of a *Patient Agreement Form* between the prescriber and the patient indicating that the patient has received counseling from the prescriber regarding the risk of serious complications associated with mifepristone 200 mg for medical termination of early pregnancy.

3.2. EVALUATION OF THE EVIDENCE

We reviewed multiple different sources of information, including published literature, safety information submitted to the Agency during the COVID-19 PHE, FDA Adverse Event Reporting System (FAERS) reports, the first REMS assessment report for the Mifepristone REMS Program, and information provided by advocacy groups, individuals, and the Applicants. Our review also included an examination of literature references provided by plaintiffs in the *Chelius v. Becerra* litigation. Below is an overview of how information relevant to the current Mifepristone REMS Program was retrieved, analyzed, and applied to each of the individual ETASUs to determine if further changes should be considered.

Methods for the literature search

(b) (6) conducted a literature search in PubMed and Embase to retrieve publications relevant to this review. The time period used for this literature search was between March 29, 2016 (when the Mifeprex labeling and REMS were last substantially revised) through July 26, 2021. The search terms used were “medical abortion” and “mifepristone” and “pregnancy termination and mifepristone.”

The search retrieved 306 publications from PubMed and 613 from Embase, respectively; the search yielded 646 unique publications after eliminating duplications between the two databases. The result of our literature search was also supplemented by an examination of literature references provided by advocacy groups, individuals, plaintiffs in the *Chelius* litigation, and the Applicants, as well as letters from healthcare providers and researchers.

References included in these letters were considered for inclusion in this review using identical selection criteria to the (b) (6) literature search (outlined below).

For this review of the REMS, (b) (6) focused on publications containing safety data related to outcomes of medical abortion (objective safety data) obtained from our literature search and from the references provided to us relevant to the REMS ETASUs. We excluded systematic reviews and meta-analyses because these publications did not include original safety data related to the outcomes of medical abortion. The following are examples of materials that were excluded from our literature search:

- Information from survey studies or qualitative studies that evaluated perspectives on and/or satisfaction with medical abortion procedures from patients, pharmacists, clinic staff, or providers, even if the study assessed REMS ETASUs. These surveys or qualitative studies did not include objective safety data related to outcomes of medical abortion.

- Opinions, commentaries, or policy/advocacy statements. These publications did not include objective safety data related to outcomes of medical abortion.

- Safety data related to mifepristone use for second trimester medical abortion. These publications reported data not applicable to the approved indication for medical abortion up to 70 days gestation.

- Safety data related to mifepristone use for spontaneous first trimester abortion (i.e., miscarriages). These publications reported data not applicable to the approved indication for medical abortion up to 70 days gestation.

- Safety data that pertained only to surgical abortion or did not separate out medical abortion from surgical abortion.

- Other safety information unrelated to the REMS elements (e.g., articles limited to case reports or those discussing unrelated gynecologic or medical issues)

- Publications for which it was not possible to conduct a full review of the methods or results, i.e., the references were limited to an abstract of the study methods and results.

- Publications that provided only general statistics on abortion care in the United States.

- Information pertinent to molecular or other basic science aspects of mifepristone.

- Data on the logistics of accessing abortion care in general, such as time to appointment or the distance traveled to obtain care.

- Publications that provided data not related specifically to abortion care or the REMS (e.g., references focused on federal poverty guidelines, poverty data, or the financial impact of the COVID-19 pandemic).

One exception to the above literature search criteria was the inclusion in Section 3.2.2 of this review, which discusses the *Patient Agreement Form*, of publications that discussed changes in provider volume. The data discussed in relation to provider volume was obtained from surveys. This data was included because changes in provider volume could only be obtained from well-conducted survey studies.

Regarding medical/scientific references submitted with letters from the plaintiffs in the *Chelius* litigation, we applied the same criteria as for the literature search, as described above.

Letters from the plaintiffs in the *Chelius* litigation included several references that preceded our 2016 review of the REMS. Two of those pre-2016 studies were not captured in our 2016 literature search. These two studies were assessed as part of our current review; their results are consistent with the existing safety profile of the approved medical abortion regimen, and therefore, support our current conclusions regarding the REMS. See Appendix A.

3.2.1. Evaluation of the requirement for healthcare providers who prescribe the drug to be specially certified (ETASU A)

In order to become specially certified, prescribers must: 1) review the prescribing information for mifepristone and 2) complete the *Prescriber Agreement Form*. In signing the *Prescriber Agreement Form*, prescribers agree they meet the qualifications listed below:

- Ability to assess the duration of pregnancy accurately
- Ability to diagnose ectopic pregnancies
- Ability to provide surgical intervention in cases of incomplete abortion or severe bleeding, or to have made plans to provide such care through others, and ability to

ensure patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary.
- Has read and understood the Prescribing Information of mifepristone (which the provider can access by phone or online).

In addition to meeting these qualifications, as a condition of certification the healthcare provider also agrees to follow the guidelines for use below:

- Review the *Patient Agreement Form* with the patient and fully explain the risks of the mifepristone treatment regimen. Answer any questions the patient may have prior to receiving mifepristone.
- Sign and obtain the patient's signature on the *Patient Agreement Form*.
- Provide the patient with a copy of the *Patient Agreement Form* and the Medication Guide.
- Place the signed *Patient Agreement Form* in the patient's medical record.
- Record the serial number from each package of mifepristone in each patient's record.
- Report deaths to the Applicant, identifying the patient by a non-identifiable patient reference and the serial number from each package of mifepristone.

The literature review was the primary source of information that contributed to our reassessment of ETASU A.

We continue to be concerned that absent these provider qualifications, serious and potentially fatal complications associated with medical abortion, including missed ectopic pregnancy and heavy bleeding from incomplete abortion, would not be detected or appropriately managed. Our review of the literature did not identify any studies comparing providers who met these qualifications with providers who did not. In the absence of such studies, there is no evidence to contradict our previous finding that prescribers' ability to accurately date pregnancies, diagnose ectopic pregnancies, and provide surgical intervention or arrange for such care through others if needed, is necessary to mitigate the serious risks associated with the use of mifepristone in a regimen with misoprostol. Therefore, our review continues to support the conclusion that a healthcare provider who prescribes mifepristone should meet the above qualifications. We conclude it is reasonable to maintain the requirement for a one-time prescriber certification where prescribers attest to having the ability to diagnose an intrauterine

pregnancy, to diagnose an ectopic pregnancy,[e] and to either manage serious complications themselves or arrange for other providers to provide the needed care in a timely manner.

In addition, in signing the *Prescriber Agreement Form* and placing it in the patient's medical record, the prescribers acknowledge the requirement to report patient deaths associated with mifepristone to the manufacturer. Such a requirement ensures that the manufacturer receives all reports of patient deaths and, in turn, fulfills its regulatory obligations to report those deaths to the FDA.

As discussed in Section 3.2.2 below, there is a potential for doubling of the number of prescribers of mifepristone if the in-person dispensing requirement in ETASU C is removed from the Mifepristone REMS Program. Given the potential addition of new prescribers, in addition to the considerations described above, we conclude that we should maintain the requirement for prescriber certification, to ensure that providers meet the necessary qualifications and adhere to the guidelines for use. Our literature review supports that these requirements are still necessary, and the potential increase in new prescribers under the REMS is a further reason to maintain prescriber certification. Healthcare provider certification continues to be a necessary component of the REMS to ensure the benefits of mifepristone for medical abortion outweigh the risks. The burden of prescriber certification has been minimized to the extent possible by requiring prescribers to certify only one time for each applicant.

3.2.2. Evaluation of the requirement for the drug to be dispensed with evidence or other documentation of safe-use conditions (ETASU D)

In order to receive mifepristone for medical termination of pregnancy through 70 days gestation, the patient must sign a *Patient Agreement Form* indicating that the patient has received, read, and been provided a copy of the *Patient Agreement Form* and received counseling from the prescriber regarding the risk of serious complications associated with mifepristone for this indication. The *Patient Agreement Form* ensures that patients are informed of the risks of serious complications associated with mifepristone for this indication.

[e] American College of Obstetricians and Gynecologists (ACOG) Practice Bulleting Number 191, February 2018. Tubal Ectopic Pregnancy. https://www.acog.org/clinical/clinical-guidance/practice-bulletin/articles/2018/03/tubal-ectopic-pregnancy. Mifepristone is not effective for terminating ectopic pregnancy. Some of the expected symptoms experienced with a medical abortion (abdominal pain, uterine bleeding) may be similar to those of a ruptured ectopic pregnancy. A missed ectopic pregnancy that ruptures is a medical emergency that requires immediate surgical intervention.

In a number of approved REMS, *Patient Agreement Forms* or *Patient Enrollment Forms* ensure that patients are counseled about the risks of the product and/or informed of appropriate safe use conditions.[f]

As a condition of certification under the Mifepristone REMS Program, healthcare providers must follow the guidelines for use of mifepristone, including reviewing the *Patient Agreement Form* with the patient, fully explaining the risks of the treatment regimen, and answering any questions the patient may have before receiving the medication. With this form, the patient acknowledges that they have received and read the form, and that they have received the counseling regarding when to take mifepristone, the risk of serious complications associated with mifepristone and what to do if they experience adverse events (e.g., fever, heavy bleeding). Both the healthcare provider and patient must sign the document and the patient must receive a copy of the signed form. In addition to the counseling described in the *Patient Agreement Form*, patients also receive a copy of the Medication Guide for mifepristone. Ultimately, the *Patient Agreement Form* serves as an important counseling component, and documentation that the safe use conditions of the Mifepristone REMS Program have been satisfied, as the prescriber is required to place the signed *Patient Agreement Form* in the patient's medical record.

Prior to the March 29, 2016 approval of the S-020 efficacy supplement for Mifeprex, FDA undertook a review of all elements of the REMS. At that time, the (b) (6) ((b) (6)), along with the (b) (6) ((b) (6)), recommended removal of the *Patient Agreement Form* (ETASU D). This recommendation received concurrence from the (b) (6) on February 23, 2016. The rationale for this recommendation in the 2016 review[g] is summarized here as follows:

- The safety profile of Mifeprex is well-characterized over 15 years of experience, with known risks occurring rarely; the safety profile has not changed over the period of surveillance.
- Established clinical practice includes patient counseling and documentation of informed consent and evidence shows that practitioners are providing appropriate patient

[f] REMS@FDA, https://www.accessdata fda.gov/scripts/cder/rems/index.cfm, Accessed November 15, 2021.
[g] (b) (6) Clinical Review, NDA 020687/S20, dated March 29, 2016. https://darrts fda.gov/darrts/faces/ViewDocument?documentId=090140af803dc7bd&_afrRedirect=386175573203745

counseling and education; the *Patient Agreement Form* is duplicative of these established practices.

- Medical abortion with Mifeprex is provided by a small group of organizations and their associated providers. Their documents and guidelines are duplicated in the *Patient Agreement Form*.
- ETASUs A and C remain in place: The *Prescriber Agreement Form* and the requirement that Mifeprex be dispensed to patients only in certain healthcare settings, specifically, clinics, medical offices, and hospitals under the supervision of a certified prescriber, remain in place.

In light of a memorandum from the Director of the Center for Drug Evaluation and Research, an addendum to the (b) (6) March 29, 2016 review and a memorandum from the signatory authority in (b) (6) indicated that the *Patient Agreement Form* would be retained in the REMS.[h,i]

The current review of literature from March 29, 2016 to July 26, 2021, is relevant to our assessment of the necessity of the *Patient Agreement Form* as part of the REMS. While our literature search yielded no publications which directly addressed this element of the REMS, we identified the following literature that focused on the informed consent process. These studies were reviewed for their potential relevance on this topic, though the articles do not directly assess the need for the *Patient Agreement Form* as a condition necessary to assure safe use of Mifepristone under ETASU D.

- Two studies[1,2] (both authored by Dr. Grossman in 2021) used the *Patient Agreement Form* and additional clinic-specific written informed consent forms as part of the study methodology. One study evaluated medical abortion with pharmacist dispensing of mifepristone and another evaluated mail-order pharmacy dispensing. Safety and efficacy outcomes were not assessed regarding the element of consent in isolation or the *Patient Agreement Form*.
- Several studies included use of electronic or verbal consent. Two studies were conducted using signed electronic consent (Chong[3], Kerestes[4]). Aiken[5] reported that patients had the option of providing consent verbally and the discussion had to be recorded in the notes. Rocca[6] described obtaining verbal informed consent from patients seeking medical abortion provided in pharmacies or government-certified

h (b) (6) Review of proposed REMS modifications to Mifeprex. March 29, 2106.
i (b) (6) Summary of Regulatory Action for Mifeprex. March 29, 2016.

public health facilities by auxiliary nurse midwives (ANMs) in Nepal. Outcomes were not assessed regarding the single element of consent and its role in the efficacy of medical abortion.

- A retrospective chart review (Wiebe[7]) was conducted in Canada. This study included telemedicine abortions between January 31, 2017 and January 31, 2019 and a similar group of controls seen in the clinic during the same time frame, matched by date of initial appointment. As part of the telemedicine process, patients read a consent form (not specified whether they could view an electronic version) and gave verbal consent "witnessed by the counselor". Again, outcomes were not assessed regarding the single element of consent and its role in the efficacy of medical abortion.

After review, we conclude that there are no outcome data from these studies that address the need for the *Patient Agreement Form* as a condition necessary to assure safe use of mifepristone. Nor do any of these studies provide evidence of whether the patient's informed consent has been adequately documented under the process set out in the study protocol. Therefore, these studies do not provide evidence that would support removing ETASU D.

Although (b) (6) agrees that informed consent in medicine is an established practice, the National Abortion Federation's 2020 Clinical Policy Guidelines for Abortion Care[8] continue to include a detailed section on patient education, counseling, and informed consent. The guidelines state that these steps are essential parts of the abortion process; that they should be conducted by appropriate personnel, with accurate information, including about alternatives and potential risks and benefits; and that the patients must have an opportunity to have any questions answered to their satisfaction prior to any intervention. Under these guidelines, documentation must show that the patient affirms that they understand all the information provided and that the decision to undergo an abortion is voluntary. The guidelines specifically list the risks that must be addressed at a minimum, including those pertinent to medical abortion: hemorrhage, infection, continuing pregnancy, and death. Additionally, Practice Bulletins from ACOG[9] and the Society of Family Planning also support detailed patient counseling.

In addition, trends in US clinical practice are developing which could negatively impact adequate patient counseling about the risks of medical abortion. One survey by Jones 2017[10] of abortion providers in the United States and Canada prior to the COVID-19 pandemic did reveal strong adherence to evidence-based guidelines. However, this same survey noted continued increasing uptake of medical abortion by US providers. Grossman[11] conducted a US survey in

2019 which suggested that the number of obstetrician/gynecologists providing medical abortion care may be increasing and that uptake might increase if mifepristone were dispensed by pharmacies instead of being dispensed in-person. A subsequent survey of US obstetricians/ gynecologists by Daniel in 2021[12] evaluated a subsample (n = 868) from a prior national survey of providers and found that 164 (19%) reported providing medical abortion in the previous year. Of those obstetrician/gynecologists not providing medical abortion, 171 (24%) said they would offer the method to their patients if the in-person dispensing requirement for mifepristone were removed. This indicates a potential doubling of providers (+ 104%, 95% confidence interval (CI): 97% −112%). There were geographical variations, with the largest potential increases being in the Midwest (+ 189%, 95% CI: 172% −207%) and the South (+ 118%, 95% CI: 103% −134%).

Based on the articles discussed above, removal of the in-person dispensing requirement from the Mifepristone REMS Program (as discussed below in section 3.2.3) could significantly increase the number of providers to a larger group of practitioners. The *Patient Agreement Form* is an important part of standardizing the medication information on the use of mifepristone that prescribers communicate to their patients, and also provides the information in a brief and understandable format for patients. The requirement to counsel the patient, to provide the patient with the *Patient Agreement Form*, and to have the healthcare provider and patient sign the *Patient Agreement Form*, ensures that each provider, including new providers, informs each patient of the appropriate use of mifepristone, risks associated with treatment, and what to do if the patient experiences symptoms that may require emergency care. The single-page *Patient Agreement Form* is in line with other elements of this REMS, in that it supports the requirement that certified prescribers be able to accurately assess a patient, counsel a patient appropriately and recognize and manage potential complications. The form is placed in the patient's medical record to document the patient's acknowledgment of receiving the information from the prescriber and a copy is provided to the patient. We determined, consistent with section 505-1(f)(2) of the FD&C Act, that this does not impose an unreasonable burden on providers or patients, and that the *Patient Agreement Form* remains necessary to assure the safe use of Mifepristone.

After considering potential burden on healthcare providers and patients and considering the available data discussed above, including the potential for increased prescribing of mifepristone if in-patient dispensing is removed from the REMS, we conclude that the *Patient Agreement Form* should remain a safe use condition in the REMS.

3.2.3. Evaluation of the requirement for drug to be dispensed only in certain healthcare settings (ETASU C)

Mifepristone applicants must ensure that mifepristone is available to be dispensed to patients only in clinics, medical offices, and hospitals by or under the supervision of a certified prescriber. This creates what we refer to in this document as an in-person dispensing requirement under the REMS; i.e., the patient must be present in person in the clinic, medical office or hospital when the drug is dispensed. The mifepristone REMS document states that mifepristone may not be distributed to or dispensed through retail pharmacies or settings other than these.

The following information contributed to our analysis of this requirement: Mifepristone REMS Program year-one assessment data, postmarketing safety information and literature review.

REMS Assessment Data

Reporting period for the Mifepristone REMS Program - April 11, 2019 through February 29, 2020

We evaluated information included in the one-year (1st)[j] REMS assessment reports for the Mifepristone REMS Program, which included healthcare provider certification data, program utilization data, compliance data, audit results and patient exposure data.[13] The assessment reports were submitted on April 10, 2020 by the NDA Applicant and April 15, 2020 by the ANDA Applicant and cover a reporting period from April 11, 2019 through February 29, 2020. During this reporting period, the NDA Applicant reported (b) (4) newly certified healthcare providers, and the ANDA Applicant reported (b) (4) newly certified healthcare providers in the Mifepristone REMS Program. The NDA Applicant reported a total of (b) (4) certified healthcare providers (includes new and previously certified) ordered mifepristone during the assessment reporting period, and the ANDA Applicant reported a total of (b) (4) certified healthcare providers ordered mifepristone during the assessment reporting period. The NDA Applicant estimated that a total of (b) (4) patients were exposed to mifepristone during the assessment reporting period. The ANDA Applicant reported an estimated total of (b) (4) patients were exposed to mifepristone during the reporting period.

During the reporting period, a small number of non-compliance events were reported. The authorized distributor for the NDA applicant reported to the NDA Applicant that they experienced deviations with scanning of the product serial numbers which were confirmed during the February 2020 audit. The authorized distributor conducted a root cause analysis and developed a corrective and preventive action (CAPA) on February 12, 2020. The CAPA was

[j] This REMS assessment report was the first to be submitted following the approval of the single, shared system REMS for mifepristone.

validated and deployed with monitoring of the system through April 10, 2020. The corrective action will prevent similar events from occurring in the future.

January 27, 2020 through September 30, 2021

During the timeframe from January 27, 2020 through September 30, 2021, there were periods when the in-person dispensing requirement was not being enforced.

- On July 13, 2020, the United States District Court for the District of Maryland granted a preliminary injunction in the *ACOG* case to temporarily bar enforcement of the in-person dispensing requirement during the COVID-19 PHE.
- On January 12, 2021, the United States Supreme Court issued a stay of the injunction.
- On April 12, 2021, the FDA issued a General Advice Letter informing the applicants of the Agency's intent to exercise enforcement discretion during the COVID-19 public health emergency regarding the in-person dispensing requirement in the Mifepristone REMS Program.[k,l]

To better understand whether there was any impact on safety or noncompliance during the periods when the in-person dispensing requirement was not being enforced, we requested additional information from the Applicants to provide for more comprehensive assessment of the REMS for the time period from January 27, 2020 (the effective date of the COVID-19 PHE) to September 30, 2021. We requested the Applicants provide a summary and analysis of any program deviation or noncompliance events from the REMS requirements and any adverse events that occurred during this time period that had not already been submitted to FDA. As part of an additional request for information for the REMS assessment report, the Applicants were also asked to submit the adverse events to FAERS and to notify FDA that the reports were submitted.

Between January 27, 2020 and September 30, 2021, the NDA Applicant distributed (b) (4) shipments representing (b) (4) tablets. The NDA Applicant reported that there were (b) (4) shipments representing a total of (b) (4) tablets sent to (b) (4) non-certified healthcare providers.[m,n] (b) (4) of these healthcare providers subsequently became certified while (b) (4) did not. Of the (b) (4) healthcare providers who were not subsequently certified, (b) (4) returned a total of (b) (4)

[k] FDA General Advice Letter for NDA 20687, April 12, 2021.
[l] FDA General Advice Letter for ANDA 091178, April 12, 2021.

[m] NDA 020687 September 9, 2021 response to the FDA's September 2, 2021 Information Request.
[n] NDA 020687 October 8, 2021 response to the FDA's June 30, 2021 Information Request.

Mifeprex tablets to the distributor. (b) (4) non-certified healthcare provider dispensed (b) (4) to a patient; no adverse events were reported. The NDA Applicant attributed the non-compliance observed to the authorized distributor's transition to a new platform. The NDA Applicant implemented a corrective and preventative action to address this issue, which we found to be acceptable.

The ANDA Applicant distributed (b) (4) shipments representing (b) (4) tablets of mifepristone from January 27, 2020 to September 30, 2021 and reported no instances of shipments to non-certified healthcare providers during this timeframe.

The NDA and the ANDA applicants reported a total of eight cases reporting adverse events between January 27, 2020 and September 30, 2021. These eight cases were also identified in the FAERS database and are described in the section below.

The number of adverse events reported to FDA during the COVID-19 PHE with mifepristone use for medical termination of pregnancy is small, and the data provide no indication that any program deviation or noncompliance with the Mifepristone REMS Program contributed to these reported adverse events. Further analysis of the adverse events is included below in the section on Pharmacovigilance Data.

Pharmacovigilance Data

The (b) (6) ((b) (6) conducted a search of the FAERS database and the published medical literature to identify U.S. postmarketing adverse events that reportedly occurred from January 27, 2020 through September 30, 2021 with mifepristone use for medical termination of pregnancy.[o,p]

The data for this time period were then further divided into date ranges when the in-person dispensing requirement was being enforced per the REMS (January 27, 2020 - July 12, 2020 & January 13, 2021 - April 12, 2021) versus when the in-person dispensing requirement was not being enforced (July 13, 2020 - January 12, 2021 (in-person dispensing requirement was temporarily enjoined) & April 13, 2021 - September 30, 2021 (in-person dispensing requirement was not being enforced because of the COVID-19 PHE)).

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[o] (b) (6). Pharmacovigilance Memorandum: Mifepristone and All Adverse Events. NDA 020687 and ANDA 091178. (b) (6) # 2007-525. Finalized April 12, 2021.

[p] (b) (6) Pharmacovigilance Memorandum: Mifepristone and All Adverse Events. NDA 020687 and ANDA 091178. (b) (6) # 2007-525. Finalized December 16, 2021.

A total of eight cases that met the search criteria were identified in FAERS and no additional case reports were identified in the medical literature. Two of the eight cases reported adverse events that occurred when the in-person dispensing requirement in the REMS was being enforced (i.e., January 27, 2020 - July 12, 2020 & January 13, 2021 - April 12, 2021). These two cases reported the occurrence of uterine/vaginal bleeding (case 1) and uterine/vaginal bleeding and sepsis (case 2). Of note, uterine/vaginal bleeding and sepsis are labeled adverse events. Five of the eight cases reported adverse events that occurred when the in-person dispensing requirement was not being enforced (i.e., July 13, 2020 - January 12, 2021 & April 13, 2021 - September 30, 2021). These five cases reported the occurrence of ongoing pregnancy (case 3), drug intoxication and death approximately 5 months after ingestion of mifepristone (case 4), death [cause of death is currently unknown] (case 5), sepsis and death (case 6), and pulmonary embolism (case 7). Although these adverse events occurred during the period when the in-person dispensing requirement was not being enforced, the narratives provided in the FAERS reports for cases 5, 6, and 7 explicitly stated that mifepristone was dispensed in-person. Of note, ongoing pregnancy, and sepsis, including the possibility of fatal septic shock, are labeled adverse events. The remaining case from July 2021 reported the occurrence of oral pain/soreness (case 8) but did not provide sufficient information to determine the exact date of the adverse event. Based upon the U.S. postmarketing data reviewed, no new safety concerns were identified by (b) (6)

In addition to the FAERS data provided above, (b) (6) routinely monitors adverse events reported to FAERS and published in the medical literature for mifepristone for medical termination of pregnancy. (b) (6) has not identified any new safety concerns with the use of mifepristone for medical termination of pregnancy.

To enable additional review of adverse events, the Applicants were requested[q] to provide a summary and analysis of adverse events reported with incomplete medical abortion requiring surgical intervention to complete abortion, blood transfusion following heavy bleeding or hemorrhage, ectopic pregnancies, sepsis, infection without sepsis, hospitalization related to medical abortion, and emergency department (ED)/urgent care encounter related to medical abortion. The Applicant for Mifeprex provided a summary of postmarketing safety information from March 29, 2016, when S-020 was approved, through September 30, 2021, on August 27 and October 8, 2021. During the time period in question, (b) (4) tablets were shipped, and

[q] On August 5, 2021, an IR was sent to the Applicants requesting a summary and analysis of adverse events from March 29, 2016 through June 30, 2021 and from July 1, 2021 through September 30, 2021.

48 adverse events were received. The 48 adverse events included 4 deaths (one of which occurred in 2010 but was reported in 2017), 25 incomplete abortions requiring surgical intervention, 17 blood transfusions following heavy vaginal bleeding, 2 ectopic pregnancies, 7 infections (1 sepsis and 6 infection without sepsis), 13 hospitalizations, and 43 ED or urgent care visits related to medical abortion. For the period between January 27, 2020 and September 30, 2021, a time frame that includes the entire period when the COVID-19 public health emergency (PHE) has been in effect, there were three adverse events reported corresponding to the above cases from FAERS identified by (b) (6) case 1 (uterine/vaginal bleeding), case 2 (uterine/vaginal bleeding and sepsis), and case 4 (drug intoxication and death).

The ANDA Applicant provided a summary of postmarketing safety information from April 11, 2019 (date of ANDA approval) through September 30, 2021. On August 26, 2021, the Applicant provided distribution and adverse event information from April 11, 2019 through June 30, 2021. During this time period, a total of (b) (4) tablets were shipped. There were 7 adverse events including 3 deaths (1 from sepsis, 1 from bilateral pulmonary artery thromboemboli, 1 in a patient who complained of not being able to breathe), 1 ongoing pregnancy treated with uterine aspiration, 2 blood transfusions, 1 sepsis (with death), 1 hospitalization, and 3 ED or urgent care visits related to medical abortion. On October 12, 2021 the Applicant provided information from July 1, 2021 to September 30, 2021; there were no additional adverse events. For the period between January 27, 2020 and September 30, 2021, there were four adverse events reported corresponding to the above cases from FAERS identified by (b) (6) case 3 (ongoing pregnancy), case 5 (death unknown cause), case 6 (sepsis and death), and case 7 (pulmonary embolism).[r]

The postmarketing data from FAERS were analyzed by (b) (6) to determine if there was a difference in adverse events between periods when the in-person dispensing requirement was being enforced and periods when the in-person dispensing requirement was not being enforced. Based on this review, we conclude that there does not appear to be a difference in adverse events between periods when the in-person dispensing requirement was being enforced and periods when the in-person dispensing requirement was not being enforced. This suggests that mifepristone may be safely used without an in-person dispensing requirement.

[r] The eighth FAERS case, oral pain/soreness, was not within the scope of the August 5, 2021 IR and was not considered for this review of postmarketing safety information submitted by the Applicants in response to the IRs.

(b) (6) review of the Applicants' IR responses, which included the same cases identified by (b) (6) from FAERS, did not change our conclusion.[s]

Literature Review

Published studies have described alternatives in location and method for dispensing mifepristone by a certified prescriber (or an equivalent healthcare provider in countries other than the US). Some studies have examined replacing in-person dispensing in certain health care settings with dispensing at retail pharmacies (Grossman[2], Wiebe[7], Rocca[6]) and dispensing mifepristone from pharmacies by mail (Grossman[1], Upadhyay[14], Hyland[15]). Other studies have evaluated two modes of dispensing by prescribers: (1) prescribers mailing the medications to women (Gynuity study [Raymond[16], Chong[3], Anger[17]], Kerestes[4], Aiken[5] (2021)) and (2) prescribers using couriered delivery of medications (Reynolds-Wright[18]). Other studies have evaluated dispensing mifepristone by mail by an entity described as "a partner organization" (Aiken[19] (2017), Norton[20], Endler[21]). For ease of review, in the sections below that describe these studies, we have separated relevant references by the methodology used to dispense mifepristone.

Retail pharmacy dispensing

Three studies report medical abortion outcomes for retail pharmacy dispensing of mifepristone after clinical evaluation. Grossman[2] conducted a US-based study in which mifepristone and misoprostol were dispensed from a pharmacy partnered with the clinic where the participant had an evaluation by ultrasound and counseling. Of the 266 participants enrolled, 260 had known abortion outcomes. Complete abortion without additional procedure occurred in 243 participants (93.5% of those with known outcomes). Seventeen participants (6.5% of those with known outcomes) were diagnosed with incomplete abortion and underwent uterine aspiration. The reported proportion of complete abortion is within the range described in the approved mifepristone labeling. However, the finding represents a lower-than-expected efficacy based on the cohort's GA (84% of participants were at ≤ 56 days GA, a cohort for which the labeled success rate is 96.8%). No participants experienced a serious adverse event, were hospitalized, or required transfusion. Three participants had ED visits with treatment (intravenous hydration, pain medication, pelvic infection after uterine aspiration for incomplete abortion). The study's

[s] The reporting period of (b) (6) assessment of the adverse events in FAERS is not identical to the time period for summaries of adverse events in the IRs to the Applicants. Therefore, the numbers of cases and adverse events summarized in (b) (6) assessment may differ from the numbers of cases and adverse events summarized by the Applicants in their responses to IRs (note that each case report may include more than one adverse event).

safety and efficacy outcomes are consistent with labeled frequencies. The majority of participants (65%) were very satisfied with the experience. There were some complaints from participants about not receiving all prescribed medications at the initial pharmacy visit, privacy not being adequately maintained, and perceived negative pharmacist attitude.

Overall, we conclude that this study has limited generalizability because it was conducted in two US states and involved partnered pharmacies, some of which were in the same building as the clinic. Additionally, all participating pharmacies in this study were required to have a pharmacist on duty during clinic hours who had been trained in the study protocol and was willing to dispense mifepristone. The study conditions may not be generalizable to US retail pharmacies; there is insufficient information to assess this. Rocca[6] conducted an observational study evaluating 605 participants at ≤63 days GA who obtained medical abortions in Nepal by comparing the provision of medical abortion service by newly trained nurse midwives in pharmacies to medical abortion provided in government-certified clinics. Participants who presented to pharmacy study sites underwent clinical screening including a pelvic exam by trained nurse midwives at the pharmacy (which was equipped with an examination room) and if eligible for medical abortion, were dispensed mifepristone and misoprostol in the pharmacy at the time of their visit. Participants who presented to public health facilities underwent clinical screening including pelvic examination by abortion providers including trained nurse midwives and if eligible for medical abortion were dispensed mifepristone and misoprostol in the clinic at the time of their visit. The authors reported that, with respect to complete abortion (>97%) and complications (no hospitalizations or transfusions), evaluation and dispensing in pharmacy was non-inferior to in-clinic evaluation and dispensing.

Wiebe,[7] in a retrospective, chart review study conducted in Canada, compared abortion outcomes of 182 women at ≤ 70 days GA who underwent medical abortion with telemedicine consult, and either received medications by courier or picked them up at a local pharmacy, with outcomes of a matched control cohort of 199 women who received the medications at a pharmacy after an in-clinic visit. The groups had similar documented complete medical abortion outcomes (90%, calculated maintaining subjects with unknown outcomes in the denominator; ≥ 95% calculated with known outcomes only). The telemedicine group had one case of hemorrhage (0.5%) and one case of infection requiring antibiotics (0.5%) compared with no cases of hemorrhage or infection requiring antibiotics in the in-clinic cohort. The telemedicine group had more ED visits (3.3% compared to 1.5% in-clinic cohort). Both models of dispensing mifepristone resulted in efficacy and safety outcomes within labeled frequency.

None of the three studies described above allow a determination regarding differences in safety between in-person dispensing by a certified prescriber in a health care setting and dispensing through a retail pharmacy, due to limitations on the generalizability of the studies to the current retail pharmacy environment in the US. The outcome findings from the one US study (Grossman[2]), in which the pharmacies were partnered with prescribers, may not be generalizable to much of the US as they do not reflect typical prescription medication availability with use of retail pharmacy dispensing. Although retail pharmacy dispensing of mifepristone and misoprostol in Canada has been described in the literature, there are important differences in healthcare systems between Canada and the US that render the findings from studies in Canada (Wiebe[7]) not generalizable to the US. In the Wiebe study, timely provision of medication from the retail pharmacy was accomplished by either courier to the woman or faxed prescription to the woman's pharmacy. It is unknown whether conditions that allow timely access to medications for medical abortion would occur in retail pharmacies throughout the US. Canada's federal government has reaffirmed that abortion is an essential health service[t] which may have implications affecting access to medical abortion from retail pharmacies in Canada. The Rocca[6] study evaluated medical abortion provided in Nepali pharmacies and essentially moved the abortion provider and clinical examination into the pharmacy, a scenario that is not, at this time, applicable to the US retail setting.

Mail order pharmacy

Grossman[1] published an interim analysis of an ongoing prospective cohort study evaluating medical abortion with mifepristone and misoprostol dispensed by mail-order pharmacy after in-person clinical assessment. All participants were evaluated for eligibility during a clinic visit with GA up to 63 days confirmed with either an ultrasound or examination; instead of receiving medication at the clinic visit, participants received medications from a mail-order pharmacy. A total of 240 participants have been enrolled; three participants did not take either medication. A total of 227 (94.6%) provided some outcome information, of whom 224 provided abortion outcome information. Complete abortion without additional procedures occurred in 217 participants (96.9% of those with known outcomes). Two (0.9%) participants experienced serious adverse events (SAE); one received a blood transfusion, and one was hospitalized overnight. Nine (4%) participants attended 10 ED visits. In this interim analysis, the outcomes are consistent with labeled frequencies. With respect to the time interval between a

[t] As noted in Mark[23] and Martin[24], most provincial and federal health insurance programs in Canada cover medical abortion, and covered services are free at the point of care.

participant's clinic visit and receipt of medications, of the 224 participants with known abortion outcomes, 184 (82.1%) received medication within 3 days. However, 17% received between 4-7 days and one participant waited over 7 days for receipt. Seven of 216 (3.2%) participants who completed the day-3 survey reported compromised confidentiality (e.g., someone found their medication, privacy concerns).

Upadhyay[14] reports findings from a retrospective cohort study of 141 women undergoing medical abortion in the US without a consultation or visit. Eligibility was assessed based on a participant-completed online form collecting pregnancy and medical history. Participants who were considered eligible received medication delivered by a mail-order pharmacy. Three interactions via text, messaging or telephone occurred to confirm medication administration, assessment of expulsion and pregnancy symptoms, and results of a 4-week home pregnancy test. Abortion outcome was determined by either the day 3 assessment or the 4-week pregnancy test. The investigators reported a complete abortion rate without additional procedures of 95% (105 participants out of 110 for whom outcomes were known) and stated that no participants had any major adverse events. The proportion of abortion outcomes assessed at 3 days versus 4 weeks is not reported. Regardless, determining outcomes at 3 days is insufficient to determine outcome rates or safety findings because a 3-day follow-up period is too short. Additionally, a substantial number of participants (31) provided no outcomes information. Among the 141 participants enrolled, 128 had any follow-up contact with the study staff, and 110 provided outcomes information. Excluding outcomes of 22% of the cohort is a limitation of this study. This study used a model with numerous deviations from standard provision of medical abortion in the US, such as no synchronous interaction with the prescriber during informed consent or prior to prescribing medication, no confirmation of self-reported medical, surgical, and menstrual history. Further, follow-up information based on a 3-day period is insufficient to determine outcome rates or safety findings. These deviations, limited follow-up information, and small sample size limit the usefulness of this study.

Hyland[15] describes findings from a cohort study in Australia evaluating medical abortion outcomes utilizing telemedicine and a central mail order pharmacy. All participants obtained screening tests including ultrasound confirmation of GA. A total of 1010 participants completed the screening process and were provided mifepristone and misoprostol. Abortion outcomes were determined for 754 (75%) of the 1010. Outcomes for the remaining 256 participants (25%) were not included because 31 provided no relevant information after shipment, 14 reported not taking misoprostol, and 211 did not have "full follow up" (i.e., known outcome of either complete medical abortion, uterine evacuation, or ongoing pregnancy with plan to continue).

Complete abortions without additional procedures occurred in 727 participants (96% of those with definitively documented outcomes) and is consistent with labeled efficacy. Of the 754 participants included in the analysis 717 (95%) had no face-to-face clinical encounters after medications were mailed while 21 (3%) were admitted to the hospital and 16 (2%) had an outpatient encounter. One participant who was hospitalized and underwent a surgical uterine evacuation received a transfusion. Not included in the findings are 7 hospitalizations occurring in 7 participants who did not have "full follow up". The authors do not report any other adverse events and conclude use of the telemedicine medical abortion service is safe. The reasons for hospitalization are not discussed by the authors; therefore, it is unknown why the patients were hospitalized. Although the reported number of hospitalizations (3%) is higher than the less than 1% in the FDA-approved mifepristone labeling, conclusions regarding the safety findings in this study cannot be made in the absence of information about the reasons for hospitalization. Other limitations of this study include incomplete information about outcomes with face-to-face encounters, and not reporting outcomes of 25% of the enrolled cohort.

Overall, the three studies evaluating mail order pharmacy dispensing suggest that the efficacy of medical abortion is maintained with mail order pharmacy dispensing. In the Grossman[1] study, the interim analysis, although small, does not raise serious safety concerns. We note that 18% of participants did not receive medications within 3 days; the potential for delay in receiving medication by mail could limit the GA eligible for medical abortion through mail order pharmacy dispensing, because women at GA closer to 70 days might not receive medication in time. A small proportion (3%) of participants raised concerns regarding the issues of confidentiality and privacy. Safety findings from the Hyland[15] study are difficult to interpret. Although only one transfusion is reported, and the authors state the findings demonstrate safety, the higher hospitalization rates, and lack of information on the reasons for hospitalization do not allow any conclusions about safety findings. Lastly, the Upadhyay[14] study had no reported adverse events, but the findings are less useful because of the limited follow-up, and because medical abortions were provided using a model with numerous deviations from standard provision of medical abortion in the US.

Clinic dispensing by mail

A total of five studies evaluated clinic dispensing by mail.[3,4,5,16,17] Gynuity Health Projects conducted a prospective cohort study (the "TelAbortion" study) evaluating use of telemedicine for remote visits and mifepristone being dispensed from clinics via overnight or regular tracked mail. Three publications reviewed have reported outcomes for the Gynuity population

exclusively: Raymond[16] from May 2016 to December 2018, Chong[3] from May 2016 to September 2020 and Anger[17] from March 2020 to September 2020. Due to the pandemic, the Gynuity study deviated from the protocol requirement of confirmation of GA by examination or ultrasound for many participants treated from March 2020 onward (although none of the three publications reported on the single element of dispensing mifepristone from the healthcare setting by mail). A fourth study, Kerestes,[4] reports outcomes of medical abortion at the University of Hawai'i from April 2020 to November 2020: seventy-five (of whom 71 were enrolled in the Gynuity study) of the 334 participants in Kerestes were dispensed mifepristone by mail after a telemedicine consult. The section below discusses these four studies from the US as well as a large UK study by Aiken[5] (2021).

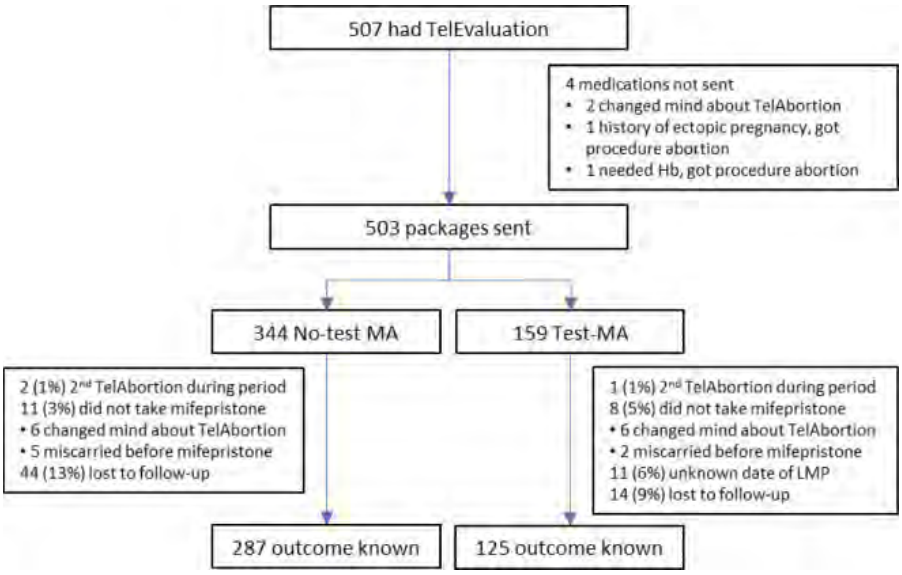
Raymond [16] (2019) reported outcomes from the Gynuity study prior to the pandemic. In the TelAbortion study, participants were not required to have an in-person clinic visit; rather, they obtained screening tests at laboratories and radiology offices and then communicated with the abortion provider by videoconference. If the participant was eligible for treatment, the provider dispensed the medications by mail. Of 433 women screened, 165 (38%) either declined to schedule the videoconference or did not keep the videoconference appointment. Among the 268 participants evaluated via videoconference, medication packages were sent to 248. Abortion outcomes were determined for 190 (77%) of the 248; outcomes for 58 (23%) participants were unknown. Complete abortion without additional procedures occurred in 177 participants (93% of those with known outcomes). The investigators obtained follow-up information from 217 participants after package shipment; there were two hospitalizations (one received a transfusion for severe anemia despite having had a complete abortion), and 16 other participants (7%) had clinical encounters in ED and urgent care centers. The reported outcomes in Raymond[16] (2019) are similar to outcomes described in approved labeling except the combined ED/urgent care center encounters (7%) exceeded the ED visits in approved labeling (2.9-4.6%). The authors note that half of the ED/urgent care visits did not entail any medical treatment and opine that the increased number of visits may have been due to the study participants living farther from the abortion providers.[16] All participants received medications within 8 days.

Chong[3] updated the findings from the Gynuity study described in Raymond[16] and reported on 1157 medical abortion outcomes, of which approximately 50% occurred during the period of the COVID-19 PHE. Although a screening ultrasound was required per the protocol, sites determined in 52% (346/669) of abortions that occurred during the period of the COVID-19 PHE that, in order to avoid potential exposure to COVID-19 at a health care facility, those

participants were not required to obtain a screening ultrasound. Use of urine pregnancy test to confirm abortion completion also increased from 67% (144/214) in the 6 months prior to the pandemic to 90% (602/669) in the 6 months during the pandemic. Of the 1390 participants to whom medicine packages (containing both mifepristone and misoprostol) were mailed, 1157 (83.2%) had known abortion outcomes. Complete abortion without a procedure occurred in 1103 participants (95% of the those with a known outcome). Ten women experienced an SAE (5 transfusions (0.4%) and 7 hospitalizations (0.7%)) and 70 (6%) participants had unplanned clinical encounters in ED/urgent care. Surgical interventions were required in 47 participants (4.1% of 1390) to complete abortion. The reported outcomes in this study are similar to outcomes described in approved labeling, except that the combined ED/urgent care center encounters (6%) exceeded the ED visits in approved labeling (2.9-4.6%).

Anger[17] compared outcomes among participants enrolled in the Gynuity study who did versus did not have confirmation of GA/intrauterine location with an examination or ultrasound from 10 jurisdictions across the US. These participants were screened for enrollment from March 25 through September 15, 2020. All participants had a telemedicine consultation and received mifepristone and misoprostol by mail from the healthcare facility. Determination of which participants did not require confirmation of GA by examination or ultrasound to be eligible depended on the study clinician's assessment of eligibility for "no-test medication abortion"[u] based on a sample protocol published by Raymond[22] (2020). There were two key differences between the two groups. Participants for whom the study clinician determined a pre-abortion ultrasound was required were more likely than the participants who had no ultrasound or examination to live further than 150 miles from the clinic (51.2% vs. 31.7%) and were more likely to have a GA above 63 days (12.0% vs. 1.7%). The study sites shipped 503 medication packages during the analysis period; 344 packages went to the "no test" group while 159 went to the "test" medical abortion cohort (see figure below). However, because the two cohorts were not randomized in this study, they had different baseline characteristics. Consequently, findings based on the comparisons between the two cohorts should be interpreted carefully.

[u] "No-test medication abortion" refers to medical abortion provided without a pretreatment ultrasound, pelvic examination, or laboratory tests when, in the judgment of the provider, doing so is medically appropriate (appropriateness based on history and symptoms); "no-test medication abortion" does include post-abortion follow up. A sample protocol is described by Raymond et al.[22]



Source: Figure 1 in this publication. MA= medical abortion.

The investigators' analyses excluded 91 (18% of 503; 57 in the no-test group and 34 in the test group) participants because they did not provide a date of the last menstrual period (LMP), did not take mifepristone, or did not have a recorded abortion outcome. Overall, 410 participants (81.5% of 503) provided outcomes data. There were no reported ectopic pregnancies in either group. The number of ED/urgent care visits and the proportion of unplanned clinical encounters that led to medical treatment were not reported. In the no-test group, complete medical abortion was confirmed in 271 participants who took medications (94% among those with known outcome). In the no-test cohort, two participants were "hospitalized and/or blood transfusion," and 36 (12.5%) had an unplanned clinical encounter (participant sought in-person medical care related to abortion and the visit was not planned prior to abortion).

In the test medical abortion group, complete abortion was confirmed in 123 participants (of 125 with known outcomes); the completion rate was 98% among those with known outcomes. In the test medical abortion group, one participant was "hospitalized and/or blood transfusion," and 10 (8.0%) had an unplanned clinical encounter. The authors concluded that, compared to participants who had an ultrasound prior to medical abortion, those without an examination prior to medical abortion were more likely to require procedural interventions and had more unplanned clinical encounters.

Kerestes[4] was the only publication that linked outcomes of medical abortion with different delivery models. Participants included in the report had GA up to 77 days and received

medications in Hawaii between April 2020 and January 2020. A total of 334 medication packages (to 330 unique participants) were dispensed containing mifepristone and misoprostol; three different delivery models were used concurrently: 110 (32.9%) had traditional in-person visits, 149 (44.6%) had telemedicine consultation with in-person pick-up of medications, and 75 (22.5%) were sent medications by mail (71 of these were enrolled through Gynuity's TelAbortion study). Seven participants of the 330 participants who received 334 medication packages reported that they did not take them and were excluded from analysis of the outcomes. Among participants with follow-up data, the rates of successful medical abortion without surgery were 93.6%, 96.8%, and 97.1% in the in-clinic group, telemedicine + in-person pickup group, and telemedicine + mail group, respectively; these were consistent with outcomes in approved labeling. Blood transfusion was given to two participants (both in the telemedicine + in-person pickup group). Eleven participants went to an ED. Although ED visits occurred the most frequently in the telemedicine + mail group (four participants or 5.8%) and the least in the in-person group (two participants or 2.1%), the study reported no increases in other serious adverse events.

Taken together, the three Gynuity study reports[3,16,17] and Kerestes[4] support dispensing mifepristone and misoprostol by mail after a telemedicine visit. Efficacy was maintained in all four studies. All of the studies reported SAEs frequencies comparable to labeled rates, except two of the Gynuity study reports (Raymond[16], Chong[3]) and Kerestes[4] report a higher frequency of ED/urgent care visits than the labeled frequency of ED visits. We do not know whether the reporting of combined ED and urgent care visits represents an increased rate of ED visits compared to the labeled rate of ED visits (2.9-4.6%). Other labeled SAEs (e.g., transfusion) occur infrequently (< 1%).

Aiken[5] (2021) reports outcomes of medical abortion up to 70 days GA in the UK before and during the pandemic in a retrospective cohort study. In the UK, prior to the COVID-19 pandemic, all patients attended an in-clinic visit where they received an ultrasound, were administered mifepristone in the clinic, and given misoprostol in-clinic for use at home (traditional model). During the pandemic, medical abortion consultations were performed remotely by telephone or video. Based on the consultation and questionnaire (including date of last menstrual period; menstrual, contraceptive and medical history; symptoms; risk for ectopic pregnancy), an assessment of eligibility for treatment via telemedicine was made. If eligible, medications were delivered to participants via mail or were made available for collection from the clinic for use at home. If the participant was assessed to be ineligible for treatment via

telemedicine, an in-person assessment with ultrasound was performed and medications were provided from the clinic for home use (hybrid model).

The study compared the two cohorts: 22,158 obtained medical abortion before the pandemic and had in-person visits and dispensing (traditional model) and 29,984 obtained medical abortion during the pandemic with either in-person visit and in-person dispensing, or a telemedicine visit and dispensing by mail or picked up from the clinic (hybrid model). Outcomes were obtained from electronic records and incident databases. Outcomes of all hospitalizations related to abortion, ED visits, infection without sepsis, and hemorrhage without transfusion were not reported. The investigators' analysis for non-inferiority determined the efficacy and safety were comparable between both cohorts. Complete abortion occurred in > 98% in both cohorts. Hemorrhage requiring transfusion was reported in 0.04% and 0.02% of the traditional and hybrid cohorts, respectively; this is lower than the labeled 0.5% transfusion rate. There were no severe infections requiring hospitalization, major surgery or deaths reported.

A secondary analysis of the hybrid cohort was reported. Within the 29,984-person hybrid model cohort, 11,549 (39%) abortions were conducted in-person (in-person assessment with ultrasound was performed and medications provided from the clinic for home use) and 18,435 (61%) abortions were provided by telemedicine visit, without tests or confirmation of GA/intrauterine position by ultrasound, and medications either mailed or picked up from the clinic. Outcomes stratified by type of mifepristone dispensing were not reported. The rate of complete abortion was slightly higher in the telemedicine group (99.2%) than that in the in-person group (98.1%). There were no significant differences in the rates of reported SAEs. Adjustments for clinical and demographic characteristics were made because the two groups differed in baseline characteristics, including a higher proportion of pregnancies with GA over 6 weeks in the in-person group (68.2% compared with 55.1%). The authors conclude a hybrid model for medical abortion that includes no-test medical abortion[u] (no ultrasound, no pelvic exam, no pregnancy test) is effective and safe.

We conclude that although the Aiken[5] (2021) study has a large sample size and includes 85% of all medical abortions performed in England and Wales during the study period, the study has limitations. The authors acknowledge the main limitation of their study was that analysis was based on deidentified information in the NHS database and the investigators were unable to verify the outcomes extracted. Other limitations included that their search only captured

outcomes in electronic records and incident databases that met the authors' defined threshold for SAE reporting, and that the labeled abortion outcomes considered serious, such as hospitalizations related to abortion, infection without sepsis, hemorrhage without transfusion, or ED/urgent care visits, were not all included in the authors' definition of serious adverse event.

Data from the mail order dispensing studies with telemedicine visits from Gynuity (Raymond, Chong and Anger),[3,16,17] Kerestes[4], and Aiken[5] (2021) support that efficacy of medical abortion was maintained. The Aiken[5] study appears to be of sufficient sample size to determine whether safety outcomes with mail dispensing differ from in-person dispensing; however, the study's design did not capture all serious safety outcomes, thus limiting the certainty of the findings. Study reports of Raymond[16] Chong[3], and Kerestes[4] all suggest there may be an increase in ED/urgent care visits with telemedicine visits and dispensing by mail without increases in other adverse events. Anger's[17] comparative analysis suggests a pre-abortion examination may decrease the occurrence of procedural intervention and decrease the number of unplanned visits for postabortion care. Overall, despite the limitations noted, these studies support that dispensing by mail is safe and effective. Although the literature suggests there may be more frequent ED/urgent care visits related to the use of mifepristone when dispensed by mail from the clinic, there are no apparent increases in other SAEs related to mifepristone use. One reason for the increase in frequent ED/urgent care visits in the Raymond[16] publication, according to its authors, may have been that a substantial proportion of participants lived significant distances from their providers and increased distances have been associated with higher use of ED following treatment. Raymond[16] reported that half of the participants who had an ED/urgent care visit did not require medical treatment.

Clinic dispensing by courier

Reynolds-Wright[18] reported findings from a prospective cohort study of 663 women at less than 12 weeks' GA in Scotland undergoing medical abortion at home with use of telemedicine during the pandemic (from April 1 to July 9, 2020). The majority of medical abortions (78.7%) used telemedicine visits, eliminated pre-abortion ultrasound, and provided mifepristone for pick up at the service or by couriered delivery to woman's home. The number of couriered deliveries was not reported; thus, this study does not provide abortion outcomes separately for couriered delivery of mifepristone and misoprostol. With access to NHS regional hospital databases, the investigators were able to verify pregnancy outcomes and complications. Of the 663 participants, 642 (98.2%) were under 10 weeks GA, 21 (1.8%) were between 10 and 12 weeks

GA, and one participant was never pregnant. A total of 650 participants had complete abortion without requiring surgical intervention (98%), 5 (0.8%) an ongoing pregnancy and 4 (0.6%) an incomplete abortion. The outcomes from this study in Scotland are consistent with labeled mifepristone outcomes. The study shares the same limitations as the Aiken[5] (2021) study.

Partner organization dispensing by mail

Women on Web (WoW), an internet group, connects patients and providers outside of the US and provides medical abortion globally, dispensing mifepristone through "a partner organization" by mail.[v] Medical abortion eligibility is determined using an online questionnaire with asynchronous physician review. If eligible, medications are mailed to the women. WoW provides help and support by email or instant messaging.

Aiken[19] (2017) conducted a population-based study analyzing findings from 1,636 women in the Republic of Ireland and Northern Ireland who were sent medications between 2010 and 2012. Receipt of medications was confirmed for 1,181 women, among whom 1,023 confirmed use of mifepristone and misoprostol; outcome information was available for 1,000 (61% of women sent medications). Of the 1,000 women, the majority (781, 78%) were less than 7 weeks GA and 219 (22%) were at 7-9 weeks. Complete abortion without surgical intervention occurred in 947 (94.7% of 1,000 with known outcome); 7 (0.7%) women received a blood transfusion, 26 (2.6%) received antibiotics (route of administration undetermined) and 87 (8.7%) sought medical care at a hospital or clinic for symptoms related to medical abortion. Hospitalizations related to abortion were not reported. The reported proportion of complete abortion is within the range labeled for medical abortion up to 70 days (92.7-98.1%). However, the finding of 94.7% complete abortion represents a lower-than-expected efficacy based on the cohort's GA (almost 80% less than 7 weeks, labeled success for medical abortion ≤ 49 days is 98.1%). This study has limitations, including outcomes based on self-report without validation of completed abortion by examination or laboratory testing, and no known outcomes for 39% of study cohort. Additionally, the authors noted medical abortion was provided in a legally-restrictive setting, where the law provided a maximum penalty of life imprisonment for the woman undergoing the abortion, which may affect participants' self-reporting.

[v] In March 2019, FDA sent a WL to Aidaccess.org, a group affiliated with WoW. Aidaccess.org received this WL because it was introducing misbranded and unapproved new drugs into the U.S. In the context of this REMS review, studies involving WoW are included solely for purposes of evaluating of data regarding the methods of dispensing mifepristone.

Endler[21] and Norten[20] have reported outcomes from WoW cohorts but do not provide relevant information on mifepristone dispensing by mail, because neither provide meaningful outcomes data for consideration. Endler[21] compared the outcomes of self-reported heavy bleeding and clinical visits occurring during the "first or second day of abortion" that occurred in women undergoing medical abortion at 9 weeks GA or less, with outcomes from women at more than 9 weeks GA. Outcome data from day 1 or 2 is of limited usefulness. Norten[20] describes findings from a survey of women who were sent medical abortion medication through WoW and provided self-reported outcomes. Results were based on surveys returned from only 37% of participants, a return rate that is too low for the study to be considered valid.

WoW uses a model with numerous deviations from the standard provision of medical abortion in the US. For example, this model has no synchronous interaction with the prescriber during informed consent or prior to prescribing medication and no confirmation of self-reported medical, surgical, and menstrual history or confirmed pregnancy testing. Further, although Aiken[19] (2017) is a large cohort study, the outcomes are self-reported with no verification of complete abortion by laboratory or clinical evaluation and 39% of outcomes are unaccounted for. These limitations in the Aiken study result in the data being insufficient to determine the safety of dispensing mifepristone by mail through a partner organization.

4. Discussion

After review of the published literature, safety information collected during the COVID-19 PHE, postmarketing data, information from the first Mifepristone REMS Program assessment report, responses to information requests to the Applicants, and information provided by advocacy groups, individuals and the plaintiffs in the *Chelius v. Becerra* litigation, we conclude that the REMS can be modified to reduce burden without compromising patient safety.

Prescriber Certification

None of the publications we reviewed would support a conclusion that a healthcare provider who prescribes mifepristone does not need to meet the qualifications included in the Mifepristone REMS Program as described above in section 3.2.1. Absent these provider qualifications, serious complications associated with medical abortion, including missed ectopic pregnancy and heavy bleeding from incomplete abortion, would not be detected or appropriately managed.

We conclude that prescriber certification (ETASU A) should be maintained. The current process requires the prescriber to agree to the requirements of the Mifepristone REMS Program and to attest that they meet the qualifications described in section 3.2.1 above. The REMS has been structured to minimize burden to prescribers by requiring only a one-time certification by the prescriber for each Applicant. We have determined that healthcare provider certification continues to be necessary to ensure the benefits outweigh the risks, especially considering that, if the in-person dispensing requirement is removed from the Mifepristone REMS Program, the number of new providers may increase (see discussion in section 3.2.2 above).

Drug to be dispensed with evidence or other documentation of safe use conditions

The requirement to counsel the patient and provide them with the *Patient Agreement Form* ensures that each patient is informed of the appropriate use of mifepristone, the risks associated with treatment, and what to do if they experience symptoms that may require emergency care.

In 2016, we initially recommended eliminating the *Patient Agreement Form* (see section 3.2.2), though the form was ultimately maintained as part of the REMS. As discussed above, our current literature review has indicated that there is no basis to remove the *Patient Agreement Form* from the REMS. In addition, surveys we reviewed suggest that if the in-person dispensing requirement for mifepristone is removed, there could be a potential doubling of medical abortion providers. This potential doubling of medical abortion providers supports the continued need to ensure that patients are consistently provided patient education under the Mifepristone REMS Program regarding the use and risks of mifepristone. The *Patient Agreement Form* is an important part of standardizing the medication information that prescribers communicate to their patients, including new prescribers, and also provides the information in a brief and understandable format to patients. We determined, in accordance with section 505-1(f)(2) of the FD&C Act, that this does not impose an unreasonable burden on providers or patients.[w]

Given the likelihood of a potential increase in new prescribers if the in-person dispensing requirement is removed from the Mifepristone REMS Program, we conclude that maintaining the *Patient Agreement Form* remains necessary to assure safe use at this time.

[w] *The Patient Agreement Form* can be signed in person or through other means.

Drug to be dispensed only in certain healthcare settings

As discussed above in section 3.2.3, our evaluation of information submitted by the applicants in the one-year (1st) REMS assessment report for the Mifepristone REMS Program and in response to follow-up requests from the Agency indicates that the number of adverse events reported to FDA during the COVID-19 PHE with mifepristone use is small, and the data provide no indication that any program deviation or noncompliance with the Mifepristone REMS Program contributed to these adverse events. We further conclude, based our review of the postmarketing safety data from FAERS during the COVID-19 PHE and information submitted by the applicants for the timeframe of January 27, 2020 through September 30, 2021, that there does not appear to be a difference in adverse events between periods during the COVID-19 PHE when the in-person dispensing requirement was being enforced and periods when the in-person dispensing requirement was not being enforced; nor have we identified any new safety concerns with the use of mifepristone for medical termination of early pregnancy.

Alternatives to in-person dispensing of mifepristone have been investigated in several studies and countries. The literature review identified 15 publications[x] that assessed safety outcomes from various medication delivery models (US, UK, Canada, Ireland, Australia, Nepal), including dispensing by retail and mail order pharmacies, prescribers mailing medications or using couriered service to deliver medications, and dispensing by "partner organizations". The ability to generalize the results of these studies to the US population is hampered by differences in pre-abortion care (e.g., telemedicine versus in-person, testing), and the usefulness of the studies is limited in some instances by small sample sizes and lack of follow-up information on outcomes with regard to both safety and efficacy.

In addition, there are factors which complicate the analysis of the dispensing element alone. Some of these factors are: (1) only a few studies have evaluated alternatives for in-person dispensing of mifepristone in isolation; for example, most studies on mail dispensing of mifepristone also include telemedicine consultation, and (2) because most SAEs with medical abortion are infrequent, though they can be life threatening, further evaluation of changes in dispensing would require studies with larger numbers of participants. We did not find any large clinical studies that were designed to collect safety outcomes in healthcare systems similar to the US.

[x] The 15 publications correspond to endnote numbers: 1-7, 14-21.

Based on the literature identified by our review, dispensing mifepristone by mail from the clinic or from a mail order pharmacy does not appear to jeopardize the efficacy of medical abortion. The studies we reviewed are not adequate on their own to establish the safety of the model of dispensing mifepristone by mail, although the safety and efficacy outcomes reported in these studies remain within the ranges described in mifepristone labeling except for increased numbers of ED/urgent care visits and hospitalizations.

Four publications (Raymond[16], Chong[3], Anger[17] and Kerestes[4]), describe a relevant US cohort where dispensing mifepristone from the clinic by mail was paired with telemedicine visits. These studies showed that efficacy was maintained and there was no increased frequency of SAEs except for higher ED/urgent care visits. The increased ED/urgent care visits were not associated with increases of other SAEs, and in the view of one study's authors (Raymond[16]), may be associated with participants being located significant distances from their providers. The Aiken[5] (2021) study of a large UK cohort where the clinics mailed mifepristone report small (lower than labeled) occurrences of transfusion and no significant infections requiring hospitalization. In Grossman[1] and Hyland[15], where the pharmacies mailed mifepristone after prescribers confirmed GA, efficacy is maintained. Grossman's[1] interim analysis found no increases in SAEs. Hyland[15] reported higher numbers of hospitalizations but did not report increases of other SAEs. Overall, while the studies assessing mifepristone dispensing by mail suggest more frequent encounters with healthcare providers, they generally support a conclusion that dispensing by mail is safe. Despite the limitations of the studies we reviewed, we conclude that overall, the outcomes of these studies are not inconsistent with our conclusion that, based on the 1st year REMS assessment report and postmarketing safety data, mifepristone will remain safe, and efficacy will be maintained if the in-person dispensing requirement is removed from the Mifepristone REMS Program.

Based on the REMS assessment data, FAERS data from the time period when the in-person dispensing requirement was not being enforced, our review of the literature, and information provided by advocacy groups, individuals, the Applicants, and the plaintiffs in the *Chelius v. Becerra* litigation, we conclude that mifepristone will remain safe and effective for medical abortion if the in-person dispensing requirement is removed, provided all the other requirements of the REMS are met, and pharmacy certification is added as described below.

Removing the in-person dispensing requirement will render the REMS less burdensome to healthcare providers and patients and provided all other requirements of the REMS are met, including the additional requirement for pharmacy certification, the REMS will continue to

ensure that the benefits of mifepristone for medical abortion outweigh the risks. Therefore, to reduce the burden imposed by the REMS, the Mifepristone REMS Program should be modified to remove the in-person dispensing requirement, which would allow, for example, dispensing of mifepristone by mail via certified prescribers or pharmacies, in addition to in-person dispensing in clinics, medical offices and hospitals as currently outlined in ETASU C.

New requirement to be added for pharmacy certification

The current distribution model requires the certified prescriber to dispense mifepristone directly to the patient in a clinic, medical office, or hospital. During the periods when the in-person dispensing requirement was not being enforced, both applicants used mail order pharmacies to receive and hold mifepristone on behalf of the certified healthcare providers who had purchased the product.[j,y,z] Pursuant to a prescription for mifepristone, the mail order pharmacy would ship the product to a named patient.

The Mifepristone REMS Program continues to require that mifepristone be prescribed only by certified prescribers. With the removal of the in-person dispensing requirement, however, the drug is no longer required to be dispensed only in a clinic, medical office or hospital. Under the REMS as modified, mifepristone can be dispensed through a pharmacy, provided the product is prescribed by a certified prescriber and all other requirements of the REMS are met. Given this modification to the dispensing requirements in the REMS, it is necessary to add a requirement for certification of pharmacies under ETASU B. Adding the pharmacy certification requirement incorporates pharmacies into the REMS, ensures that pharmacies are aware of and agree to follow applicable REMS requirements, and ensures that mifepristone is only dispensed pursuant to prescriptions that are written by certified prescribers. Without pharmacy certification, a pharmacy might dispense product that was not prescribed by a certified prescriber. Adding pharmacy certification ensures that ETASU A is met prior to dispensing the product to a patient; certified prescribers, in turn, have agreed to meet all the conditions of the REMS, including ensuring that the *Patient Agreement Form* (ETASU D) is completed. In addition, wholesalers and distributors can only ship to certified pharmacies. Based on our review of the safety data and our consideration of the distribution model implemented by the Applicants during the periods

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y ANDA 091178: September 23, 2021 response to the September 15, 2021 information request; October 11 and 16, 2021 responses to the June 30, 2021 and July 15, 2021 information requests; October 26, 2021 response to the October 22, 2021 information request; October 29, 2021 response to the October 27 information request.
z NDA 020687: September 20, 2021 response to the September 15, 2021 information request; October 26, 2021 response to the October 22 information request.

when the in-person dispensing requirement was not being enforced, as well as REMS assessment data and published literature, we conclude that provided all other requirements of the REMS are met, the REMS program, with the removal of the in-person dispensing requirement and the addition of a requirement for pharmacy certification, will continue to ensure the benefits of mifepristone for medical abortion outweigh the risks while minimizing the burden imposed by the REMS on healthcare providers and patients. As modified, the REMS would allow, for example, dispensing by mail order or specialty pharmacies, similar to the distribution model used by applicants during the periods when the in-person dispensing requirement was not being enforced.[aa]

The above recommendations were discussed with the (b) (6) ((b) (6) and senior leadership from CDER on November 2, 2021. The (b) (6) (b) (4) along with senior CDER leadership, concurred with removing the in-person dispensing requirement provided that all of the remaining REMS requirements are met, including but not limited to prescriber certification where prescribers need to attest to having certain qualifications, and maintaining the *Patient Agreement Form*. The (b) (6) (b) (4) and senior leadership from CDER were also in favor of adding pharmacy certification to assure the safe use of mifepristone.

5. Conclusions and Recommendations

Based on the results of REMS assessments; our review of safety data collected during the PHE as well as data from FAERS; our literature search; and information provided by advocacy groups, individuals, the Applicants, and the plaintiffs in the *Chelius v. Becerra* litigation, (b) (6) and (b) (6) have concluded that a REMS modification is necessary and should include the following changes:

- Removing the requirement under ETASU C that mifepristone be dispensed only in certain healthcare settings, specifically clinics, medical offices, and hospitals.
- Adding a requirement under ETASU B that pharmacies that dispense the drug be specially certified.

[aa] Our current conclusion that the REMS would allow dispensing by mail order or specialty pharmacies is based on data received from Applicants relating to the periods when the in-person dispensing requirement was not enforced and mail-order pharmacies were used to dispense the product, as well as our analysis of postmarketing safety data and available literature. At this time we do not have data (from the Applicants or from other sources) to assess the certification of retail pharmacies under the REMS. We have not yet determined the details of pharmacy certification requirements, including whether any limitations on the types of pharmacies that may dispense the product are necessary.

(b) (6) and (b) (6) recommend the Applicants be issued a REMS Modification Notification Letter that requests submission within 120 days from the date of the letter.

6. References

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7. Appendix A

References Cited in Letters from Plaintiffs

References cited in letter from *Chelius v. Becerra* Plaintiffs (September 29, 2021)	
References included in the REMS review	
Aiken A et al. BJOG 2021: 128 (9): 1464-1474	
Chong, et al. Contraception 2021; 104(1) 43-48	
Daniel S. et al. Contraception 2021; 104(1): 73-76	
References excluded from the REMS review	**Rationale for Exclusion**
Am. Coll. of Obstetricians & Gynecologists, *Position Statement: Improving Access to Mifepristone for Reproductive Health Indications* (June 2018), https://www.acog.org/clinical-information/policy-and-position-statements/position-statements/2018/improving-access-to-mifepristone-for-reproductive-health-indications	Policy/advocacy statement
House of Delegates, Am. Med. Ass'n., *Memorial Resolutions Adopted Unanimously No. 504 (2018)* https://www.ama-assn.org/sites/ama-assn.org/files/corp/media-browser/public/hod/a18-resolutions.pdf	Policy/advocacy statement
Cong. Of Delegates, Am. Acad. Of Fam. Physicians, *Resolution No. 506 (CoSponsored C) Removing Risk Evaluation and Mitigation Strategy (REMS) Categorization of Mifepristone* (May 24, 2018) https://www.reproductiveaccess.org/wp-content/uploads/2019/02/Resolution-No.-506-REMS.pdf	Policy/advocacy statement
Schummers L et al, Contraception 2020; 102(4): 273	Abstract
Upadhyay UD et al.) Obstet & Gynecol 2015; 125: 175	Published prior to March 29, 2016-July 26, 2021 timeframe for current literature review. We note that the extensive literature review conducted as part of the 2016 review, which was consistent with the division's standard approach for reviewing an efficacy supplement

	and encompassed 90 references, did not capture this publication. However, the authors' conclusion in this publication is consistent with our review of the safety data in 2016.
Kapp N et al. Best Pract Clin Obstet Gynaecol. 2020;63:37-44	Abstract. Also outside the scope of first trimester medical abortion.
Fuentes L et al. J Women's Health 2019; 28 (12): 1623, 1625 Bearak JM, Lancet Pub Health 2017 Nov;2(11): e493, e495-96 Cartwright A et al 20 J Med Internet Res 2018 20(5):e10235 Barr-Walker J, et al PLoS One 2019;14(4): e0209991 Grossman et al JAMA Network 2017;317(4):437, 437-438 Dobie S et al 31 Fam Plan Persp 1999; 31(5): 241-244 Shelton JD 8 Fam Plan Persp 1976; 8(6):260, 260-262 Norris AH et al Am J Pub Health 2020; 110 (8): 1228,1232 Upadhyay UD et al Am J Pub Health 2014; 104(9):1687, 1689	Focused on the logistics of accessing abortion care.
CDC MMWR Abortion Surveillance – United States, 2018 https://www.cdc.gov/mmwr/volumes/69/ss/ss6907a1.htm#T5_down	Contains primarily general statistics on abortion care by state.

References cited in appendix from *Chelius v. Becerra* Plaintiffs (September 29, 2021)
References included in the REMS review
None

Reference ID: 4905882

References excluded from the REMS review	Rationale for Exclusion
Jones RK et al Guttmacher Institute Abortion Incidence and Service Availability in the United States, 2017 (2019) Guttmacher Inst, Induced Abortion in the United States (2019)	Contains primarily general statistics on abortion care and logistics of accessing abortion care.
University of Minnesota Healthy Youth Dev. Prevention Rsch Ctr, 2019 Minnesota Adolescent Sexual Health Report 3 (2019)	Not related specifically to abortion care.
Jerman J et al Guttmacher Inst, Characteristics of U.S. Abortion Patients in 2014 and Changes since 2008 (2016)	Contains figures on patient characteristics from 2008-2014.
Roberts CM et al Women's Health Issues 2014; 24:e211, e215	Focused on cost of abortion.
CDC MMWR Abortion Surveillance 2018 https://www.cdc.gov/mmwr/volumes/69/ss/ss6907a1.htm#T7 down (last updated Nov. 7, 2020)	Contains primarily statistics on number of abortions in the US.
Jones RK Persp on Sexual & Reprod Health 2017; 49:17, 20	Focused on abortion incidence and service availability.
Fuentes L et al (as above) Bearak JM et al (as above) Cartwright A et al (as above) Johns NE et al. BMC Health Serv Res 2017; 17: 287, 294	Focused on logistics of accessing abortion care.

References cited in letter from Society of Family Planning (August 11, 2021)
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Grossman D et al. Obstet Gynecol 2021; 137 (4): 613-622.	
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Chen MJ et al. Obstet Gynecol 2015;126(1):12-21 reviewed in 2016 memo	
Chong et al. Contraception 2021;104(1): 43-48	
Aiken A et al. BJOG 2021; 128 (9): 1464 -1474	
Hyland 2018 et al. Aust New Zeal J Obstet Gynaecol 2018; 58 (3): 335-340	
References excluded from the REMS review	**Rationale for Exclusion**
Schummers L et al. BMJ Sex Reprod Heal 2021;47(e1)	Abstract
Kapp et al. 2020 (as above)	Abstract
Upadhyay et al. 2015 (as above)	(See rationale above)
Srinivasulu et al. Contraception 2021; 104(1):92-97	Survey on clinician perspectives on access to mifepristone.
Calloway D et al. Contraception 2021; 104(1): 24-28	Primarily addresses provider stigma around abortion care.
Rasmussen et al. Contraception; 104(1): 98-103	Opinion/commentary
Cleland et al. Obstet Gynecol 2013;121(1):166-171	Published prior to March 29, 2016 - July 26, 2021 timeframe for current literature review. We note that the extensive literature search conducted as part of the 2016 clinical review, which was consistent with the division's standard approach for reviewing an efficacy supplement and encompassed 90 references, did not capture this publication. However, the authors' conclusion in this publication is consistent with our review of the safety data in 2016.
National Academy of Sciences, Engineering, and Medicine. Safety and Quality of Abortion Care in the US 2018	General information about abortion care in the US. Did not provide safety data relevant to the elements of the REMS
Raymond EG. Obstet Gynecol 2012: 119(2): 215-219	Does not separate out medical and surgical abortion.

Bartlett LA et al. Obstet Gynecol 2004; 103(4): 729-737	Focused on surgical abortion.
Jones RK, Jerman J. Time to appointment and delays in accessing care among U.S. abortion patients, Guttmacher 2016	Focused on logistics of accessing abortion care.
Foster DG et al. Perspect Sex Reprod Health 2013; 45(4):210-218	Focused on second trimester abortion.
Ely G et al. Heal Soc Work 2019;44(1):13-21	Focused on logistics of accessing abortion care.
Munro S et al. Ann Fam Med 2020; 18(5):413-421.	Survey on physician perspectives on implementing medical abortion with mifepristone.

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EXHIBIT

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Center for Drug Evaluation and Research (CDER)

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Application Type	NDA and ANDA
Application Number	020687 and 91178
Reviewer Names	(b) (6)
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Review Completion Date	December 16, 2021

Subject	REMS Modification Rationale Review
Established Name	Mifepristone REMS
Name of Applicants	Danco Laboratories, LLC and GenBioPro, Inc.
Therapeutic Class	Progestin antagonist
Formulation	Oral tablets

Table of Contents

EXECUTIVE SUMMARY 4

1. Introduction 5
2. Background 5
   - 2.1. PRODUCT AND REMS INFORMATION 5
   - 2.2. REGULATORY HISTORY AND EVENTS RELEVANT TO THIS REMS MODIFICATION RATIONALE REVIEW 7
3. Rationale for Proposed REMS Modification 9
   - 3.1. CURRENT REQUIREMENTS FOR THE APPROVED REMS 10
   - 3.2. EVALUATION OF THE EVIDENCE 10
   - 3.2.1. Evaluation of the requirement for healthcare providers who prescribe the drug to be specially certified (ETASU A) 12
   - 3.2.2. Evaluation of the requirement for the drug to be dispensed with evidence or other documentation of safe-use conditions (ETASU D) 14
   - 3.2.3. Evaluation of the requirement for drug to be dispensed only in certain healthcare settings (ETASU C) 19
4. Discussion 36
5. Conclusions and Recommendations 41
6. References 42
7. Appendix 45

EXECUTIVE SUMMARY

This review provides the [redacted] rationale and conclusions regarding modifications to the single, shared system Risk Evaluation and Mitigation Strategy (REMS) for mifepristone 200 mg (Mifepristone REMS Program) for new drug application (NDA) 20687 and abbreviated new drug application (ANDA) 91178.

ANDA 91178 was approved with the approval of the Mifepristone REMS Program on April 11, 2019 to mitigate the risk of serious complications associated with mifepristone 200 mg. The most recent REMS modification was approved on May 14, 2021. The REMS consists of elements to assure safe use (ETASU) under ETASU A, C and D, an implementation system, and a timetable for submission of assessments. To determine whether a modification to the REMS was warranted, FDA undertook a comprehensive review of the published literature; safety information collected during the COVID-19 public health emergency (PHE); the one-year REMS assessment report of the Mifepristone REMS Program; adverse event data; and information provided by advocacy groups, individuals and the Applicants. Our review also included an examination of literature references provided by plaintiffs in the *Chelius v. Becerra* litigation discussed below.

The modifications to the REMS will consist of:

- Removing the requirement under ETASU C that mifepristone be dispensed only in certain healthcare settings, specifically clinics, medical offices, and hospitals (referred to here as the "in-person dispensing requirement" for brevity)
- Adding a requirement under ETASU B that pharmacies that dispense the drug be specially certified

A REMS Modification Notification letter will be sent to both Applicants in the Single Shared System.

1. Introduction

In connection with the *Chelius v. Becerra* litigation, FDA agreed to undertake a full review of the Mifepristone REMS Program, in accordance with the REMS assessment provisions of the Federal Food, Drug, and Cosmetic Act (FD&C Act).[a] This review provides the analysis of the (b) (6) ((b) (6) and the (b) (6) ((b) (6) regarding whether any changes are warranted to the single, shared system Risk Evaluation and Mitigation Strategy (REMS) for mifepristone (hereafter referred to as the Mifepristone REMS Program) for new drug application (NDA) 20687 and abbreviated new drug application (ANDA) 91178. The Mifeprex REMS was initially approved in 2011; the single, shared system REMS for mifepristone 200 mg, known as the Mifepristone REMS Program, was approved in 2019.

The last time the existing REMS elements to assure safe use (under ETASU A, C and D) were reviewed was in the context of our review of supplement S-020 to NDA 20687; these ETASU were updated following review and approval of supplement S-020 on March 29, 2016. The key changes approved in 2016 are summarized below.

Changes to labeling included:

- Changing the dosing of Mifeprex to 200 mg orally x 1
- Extension of maximum gestational age through 70 days
- Inclusion of misoprostol in the indication statement
- Replacing the term “physician” with “licensed healthcare provider”
- Removal of the phrase “Under Federal Law”

The Mifeprex REMS and REMS materials were updated to reflect the changes above, and additional changes were made including:

- Removing the Medication Guide as part of the REMS but retaining it as part of labeling.

2. Background

2.1. PRODUCT AND REMS INFORMATION

[a] Section 505-1(g)(2) of the FD&C Act (21 U.S.C. § 355-1(g)(2)).

Mifepristone is a progestin antagonist indicated, in a regimen with misoprostol, for the medical termination of intrauterine pregnancy (IUP) through 70 days gestation. Mifepristone is available as 200 mg tablets for oral use.

Mifeprex (mifepristone) was approved on September 28, 2000 with a restricted distribution program under 21 CFR 314.520 (subpart H)[b] to ensure that the benefits of the drug outweighed the risk of serious complications associated with mifepristone when used for medical abortion. Mifeprex was deemed to have a REMS under section 505-1 of the Federal Food, Drug, and Cosmetic Act with the passage of the Food and Drug Administration Amendments Act (FDAAA) of 2007, and the Mifeprex REMS was approved on June 8, 2011. On March 29, 2016, as noted above, a supplemental application and REMS modification was approved for Mifeprex. On April 11, 2019, ANDA 091178 was approved, and the Mifepristone REMS Program was approved. The Mifepristone REMS Program is a single, shared system REMS that includes NDA 020687 and ANDA 91178.

The goal of the REMS for mifepristone is to mitigate the risk of serious complications associated with mifepristone by:

a. Requiring healthcare providers who prescribe mifepristone to be certified in the Mifepristone REMS Program (under ETASU A).
b. Ensuring that mifepristone is only dispensed in certain healthcare settings, by or under the supervision of a certified prescriber (under ETASU C).
c. Informing patients about the risk of serious complications associated with mifepristone (under ETASU D).

Under ETASU A, to become specially certified to prescribe mifepristone, a healthcare provider must review the prescribing information, complete and sign the *Prescriber Agreement Form,* and follow the guidelines for use of mifepristone. Under ETASU C, mifepristone must be dispensed to patients only in certain healthcare settings, specifically clinics, medical offices, and hospitals, by or under the supervision of a certified prescriber. Under ETASU D, mifepristone must be dispensed to patients with evidence or other documentation of safe use conditions (i.e., the patient must sign a *Patient Agreement Form*). The Mifepristone REMS Program also includes an implementation system, and a timetable for assessments (one year from the date of the initial approval of the REMS on April 11, 2019, and every three years thereafter).

[b] NDA approval letter Mifeprex (NDA 020687) dated September 28, 2000.

2.2. REGULATORY HISTORY AND EVENTS RELEVANT TO THIS REMS MODIFICATION RATIONALE REVIEW

The following is a summary of significant regulatory history since approval of the REMS modification on March 29, 2016:

- 03/29/2016: FDA approved an efficacy supplement (S-020) that, among other things, provided a new dosing regimen (200 mg mifepristone, followed in 24 to 48 hours by 800 mcg buccal misoprostol), increased the gestational age (GA) to which mifepristone may be used (through 70 days gestation), and modified the REMS.

- 03/29/2019: A Citizen Petition was received requesting that FDA revise the product labeling to reflect pre-2016 provisions (including limiting GA to 49 days and requiring patients to make 3 office visits) and that FDA maintain the REMS.

- 04/11/2019: ANDA 91178 was approved along with the Single Shared System REMS for Mifepristone 200 mg (Mifepristone REMS Program) for NDA 20687 and ANDA 91178.

- 01/31/2020: the COVID-19 public health emergency (PHE) was declared by the Secretary of Health and Human Services (HHS) as having existed since January 27, 2020.[c]

- 7/13/2020: The United States (US) District Court of Maryland granted a preliminary injunction in the *ACOG v. FDA* litigation to temporarily bar enforcement of the Mifepristone REMS Program in-person dispensing requirement during the COVID-19 PHE.

- 1/12/2021: US Supreme Court granted a stay of that injunction.

- 04/12/2021: FDA issued a General Advice Letter to both the NDA and ANDA Applicants, stating that provided that all other requirements of the Mifepristone REMS Program are met, and given that in-person dispensing of mifepristone for medical termination of early pregnancy may present additional COVID-related risks to patients and healthcare

[c] *See* Secretary of Health and Human Services, Determination that a Public Health Emergency Exists (originally issued January 31, 2020, and subsequently renewed), available at https://www.phe.gov/emergency/news/healthactions/phe/Pages/default.aspx

personnel because it may involve a clinical visit solely for this purpose, FDA intends to exercise enforcement discretion during the COVID-19 PHE with respect to the in-person dispensing requirement in the Mifepristone REMS Program, including any in-person requirements that may be related to the *Patient Agreement Form.* FDA further stated that to the extent all of the other requirements of the Mifepristone REMS Program are met, FDA intends to exercise enforcement discretion during the COVID-19 PHE with respect to the dispensing of mifepristone through the mail, either by or under the supervision of a certified prescriber, or through a mail-order pharmacy when such dispensing is done under the supervision of a certified prescriber.

- 05/07/2021: FDA stated that it would be reviewing the elements of the Mifepristone REMS Program in accordance with the REMS assessment provisions of section 505-1 of the FD&C Act.

- 05/14/2021: A modification was approved for the Mifepristone REMS Program. This modification was to revise the *Patient Agreement Form* to include gender-neutral language.

- 06/30/2021: An Information Request (IR) was sent to the Applicants for additional information on shipments and any program deviations, adverse events, or noncompliance with the REMS that occurred during the period from April 1, 2021 through September 30, 2021.

- 7/15/2021: An IR was sent to the Applicants to provide the total number of shipments during the period from April 1, 2021 to September 30, 2021 and details on whether any of those shipments were involved in any program deviation or non-compliance.

- 8/5/2021: An IR was sent to the Applicants for additional clinical and other information (e.g., adverse events and units of mifepristone shipped) for the period of March 29, 2016 through June 30, 2021, to be provided by August 31, 2021. This IR also requested information covering the period of July 1, 2021 through September 30, 2021 and an

aggregate summary (for the period of March 29, 2016 through September 30, 2021), to be provided by October 12, 2021.[d]

- 8/26/2021: The ANDA Applicant submitted a response to the IR issued on 8/5/2021.
- 08/27/2021: The NDA Applicant submitted a response to the IR issued on 8/5/2021.
- 10/08/2021: The NDA Applicant submitted a response to the June 30 and July 15, 2021 IRs as well as an aggregate summary for the period March 29, 2016 through September 30, 2021 in response to the August 5, 2021 IR. The NDA Applicant also included a follow-up to their initial response provided on August 27, 2021 to the August 5, 2021 IR.
- 10/12/2021: The ANDA Applicant submitted a response to the June 30 and July 15, 2021 IRs as well as an aggregate summary for the period March 29, 2016 through September 30, 2021 in response to the August 5, 2021 IR.
- 10/16/2021: The ANDA Applicant revised their Oct 12, 2012 response to provide a correction to the number of mifepristone tablets.
- (b) (4)
- 11/02/2021: A (b) (6) ((b) (6) meeting was convened to obtain CDER concurrence on the removal of the in-person dispensing requirement and the addition of a certification requirement for pharmacies. The (b) (6) (b) (6) and senior CDER leadership concurred with removing the in-person dispensing and adding pharmacy certification.

3. Rationale for Proposed REMS Modification

[d] Multiple Information Requests were issued to obtain additional information on drug shipments, any program deviations or noncompliance, and use of alternative methods for drug distribution during the COVID-19 PHE. These IRs are referenced as appropriate in this document and the one-year REMS Assessment Review of the Mifepristone REMS Program, December 16, 2021.

3.1. CURRENT REQUIREMENTS FOR THE APPROVED REMS

The Mifepristone REMS Program includes elements to assure safe use (ETASU), an implementation system, and a timetable for submission of assessments. Elements to assure safe use in the current REMS include a prescriber certification requirement (ETASU A), a requirement that mifepristone be dispensed only in certain healthcare settings by or under the supervision of a certified prescriber (ETASU C), and a requirement that mifepristone be dispensed only with documentation of safe use conditions (ETASU D). Documentation of safe use conditions under ETASU D consists of a *Patient Agreement Form* between the prescriber and the patient indicating that the patient has received counseling from the prescriber regarding the risk of serious complications associated with mifepristone 200 mg for medical termination of early pregnancy.

3.2. EVALUATION OF THE EVIDENCE

We reviewed multiple different sources of information, including published literature, safety information submitted to the Agency during the COVID-19 PHE, FDA Adverse Event Reporting System (FAERS) reports, the first REMS assessment report for the Mifepristone REMS Program, and information provided by advocacy groups, individuals, and the Applicants. Our review also included an examination of literature references provided by plaintiffs in the *Chelius v. Becerra* litigation. Below is an overview of how information relevant to the current Mifepristone REMS Program was retrieved, analyzed, and applied to each of the individual ETASUs to determine if further changes should be considered.

Methods for the literature search

(b) (6) conducted a literature search in PubMed and Embase to retrieve publications relevant to this review. The time period used for this literature search was between March 29, 2016 (when the Mifeprex labeling and REMS were last substantially revised) through July 26, 2021. The search terms used were “medical abortion” and “mifepristone” and “pregnancy termination and mifepristone.”

The search retrieved 306 publications from PubMed and 613 from Embase, respectively; the search yielded 646 unique publications after eliminating duplications between the two databases. The result of our literature search was also supplemented by an examination of literature references provided by advocacy groups, individuals, plaintiffs in the *Chelius* litigation, and the Applicants, as well as letters from healthcare providers and researchers.

References included in these letters were considered for inclusion in this review using identical selection criteria to the (b) (6) literature search (outlined below).

For this review of the REMS, (b) (6) focused on publications containing safety data related to outcomes of medical abortion (objective safety data) obtained from our literature search and from the references provided to us relevant to the REMS ETASUs. We excluded systematic reviews and meta-analyses because these publications did not include original safety data related to the outcomes of medical abortion. The following are examples of materials that were excluded from our literature search:

- Information from survey studies or qualitative studies that evaluated perspectives on and/or satisfaction with medical abortion procedures from patients, pharmacists, clinic staff, or providers, even if the study assessed REMS ETASUs. These surveys or qualitative studies did not include objective safety data related to outcomes of medical abortion.

- Opinions, commentaries, or policy/advocacy statements. These publications did not include objective safety data related to outcomes of medical abortion.

- Safety data related to mifepristone use for second trimester medical abortion. These publications reported data not applicable to the approved indication for medical abortion up to 70 days gestation.

- Safety data related to mifepristone use for spontaneous first trimester abortion (i.e., miscarriages). These publications reported data not applicable to the approved indication for medical abortion up to 70 days gestation.

- Safety data that pertained only to surgical abortion or did not separate out medical abortion from surgical abortion.

- Other safety information unrelated to the REMS elements (e.g., articles limited to case reports or those discussing unrelated gynecologic or medical issues)

- Publications for which it was not possible to conduct a full review of the methods or results, i.e., the references were limited to an abstract of the study methods and results.

- Publications that provided only general statistics on abortion care in the United States.

- Information pertinent to molecular or other basic science aspects of mifepristone.

- Data on the logistics of accessing abortion care in general, such as time to appointment or the distance traveled to obtain care.

- Publications that provided data not related specifically to abortion care or the REMS (e.g., references focused on federal poverty guidelines, poverty data, or the financial impact of the COVID-19 pandemic).

One exception to the above literature search criteria was the inclusion in Section 3.2.2 of this review, which discusses the *Patient Agreement Form*, of publications that discussed changes in provider volume. The data discussed in relation to provider volume was obtained from surveys. This data was included because changes in provider volume could only be obtained from well-conducted survey studies.

Regarding medical/scientific references submitted with letters from the plaintiffs in the *Chelius* litigation, we applied the same criteria as for the literature search, as described above.

Letters from the plaintiffs in the *Chelius* litigation included several references that preceded our 2016 review of the REMS. Two of those pre-2016 studies were not captured in our 2016 literature search. These two studies were assessed as part of our current review; their results are consistent with the existing safety profile of the approved medical abortion regimen, and therefore, support our current conclusions regarding the REMS. See Appendix A.

3.2.1. Evaluation of the requirement for healthcare providers who prescribe the drug to be specially certified (ETASU A)

In order to become specially certified, prescribers must: 1) review the prescribing information for mifepristone and 2) complete the *Prescriber Agreement Form*. In signing the *Prescriber Agreement Form*, prescribers agree they meet the qualifications listed below:

- Ability to assess the duration of pregnancy accurately
- Ability to diagnose ectopic pregnancies
- Ability to provide surgical intervention in cases of incomplete abortion or severe bleeding, or to have made plans to provide such care through others, and ability to

ensure patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary.
- Has read and understood the Prescribing Information of mifepristone (which the provider can access by phone or online).

In addition to meeting these qualifications, as a condition of certification the healthcare provider also agrees to follow the guidelines for use below:

- Review the *Patient Agreement Form* with the patient and fully explain the risks of the mifepristone treatment regimen. Answer any questions the patient may have prior to receiving mifepristone.
- Sign and obtain the patient's signature on the *Patient Agreement Form*.
- Provide the patient with a copy of the *Patient Agreement Form* and the Medication Guide.
- Place the signed *Patient Agreement Form* in the patient's medical record.
- Record the serial number from each package of mifepristone in each patient's record.
- Report deaths to the Applicant, identifying the patient by a non-identifiable patient reference and the serial number from each package of mifepristone.

The literature review was the primary source of information that contributed to our reassessment of ETASU A.

We continue to be concerned that absent these provider qualifications, serious and potentially fatal complications associated with medical abortion, including missed ectopic pregnancy and heavy bleeding from incomplete abortion, would not be detected or appropriately managed. Our review of the literature did not identify any studies comparing providers who met these qualifications with providers who did not. In the absence of such studies, there is no evidence to contradict our previous finding that prescribers' ability to accurately date pregnancies, diagnose ectopic pregnancies, and provide surgical intervention or arrange for such care through others if needed, is necessary to mitigate the serious risks associated with the use of mifepristone in a regimen with misoprostol. Therefore, our review continues to support the conclusion that a healthcare provider who prescribes mifepristone should meet the above qualifications. We conclude it is reasonable to maintain the requirement for a one-time prescriber certification where prescribers attest to having the ability to diagnose an intrauterine

pregnancy, to diagnose an ectopic pregnancy,[e] and to either manage serious complications themselves or arrange for other providers to provide the needed care in a timely manner.

In addition, in signing the *Prescriber Agreement Form* and placing it in the patient's medical record, the prescribers acknowledge the requirement to report patient deaths associated with mifepristone to the manufacturer. Such a requirement ensures that the manufacturer receives all reports of patient deaths and, in turn, fulfills its regulatory obligations to report those deaths to the FDA.

As discussed in Section 3.2.2 below, there is a potential for doubling of the number of prescribers of mifepristone if the in-person dispensing requirement in ETASU C is removed from the Mifepristone REMS Program. Given the potential addition of new prescribers, in addition to the considerations described above, we conclude that we should maintain the requirement for prescriber certification, to ensure that providers meet the necessary qualifications and adhere to the guidelines for use. Our literature review supports that these requirements are still necessary, and the potential increase in new prescribers under the REMS is a further reason to maintain prescriber certification. Healthcare provider certification continues to be a necessary component of the REMS to ensure the benefits of mifepristone for medical abortion outweigh the risks. The burden of prescriber certification has been minimized to the extent possible by requiring prescribers to certify only one time for each applicant.

3.2.2. Evaluation of the requirement for the drug to be dispensed with evidence or other documentation of safe-use conditions (ETASU D)

In order to receive mifepristone for medical termination of pregnancy through 70 days gestation, the patient must sign a *Patient Agreement Form* indicating that the patient has received, read, and been provided a copy of the *Patient Agreement Form* and received counseling from the prescriber regarding the risk of serious complications associated with mifepristone for this indication. The *Patient Agreement Form* ensures that patients are informed of the risks of serious complications associated with mifepristone for this indication.

[e] American College of Obstetricians and Gynecologists (ACOG) Practice Bulleting Number 191, February 2018. Tubal Ectopic Pregnancy. https://www.acog.org/clinical/clinical-guidance/practice-bulletin/articles/2018/03/tubal-ectopic-pregnancy. Mifepristone is not effective for terminating ectopic pregnancy. Some of the expected symptoms experienced with a medical abortion (abdominal pain, uterine bleeding) may be similar to those of a ruptured ectopic pregnancy. A missed ectopic pregnancy that ruptures is a medical emergency that requires immediate surgical intervention.

In a number of approved REMS, *Patient Agreement Forms* or *Patient Enrollment Forms* ensure that patients are counseled about the risks of the product and/or informed of appropriate safe use conditions.[f]

As a condition of certification under the Mifepristone REMS Program, healthcare providers must follow the guidelines for use of mifepristone, including reviewing the *Patient Agreement Form* with the patient, fully explaining the risks of the treatment regimen, and answering any questions the patient may have before receiving the medication. With this form, the patient acknowledges that they have received and read the form, and that they have received the counseling regarding when to take mifepristone, the risk of serious complications associated with mifepristone and what to do if they experience adverse events (e.g., fever, heavy bleeding). Both the healthcare provider and patient must sign the document and the patient must receive a copy of the signed form. In addition to the counseling described in the *Patient Agreement Form*, patients also receive a copy of the Medication Guide for mifepristone. Ultimately, the *Patient Agreement Form* serves as an important counseling component, and documentation that the safe use conditions of the Mifepristone REMS Program have been satisfied, as the prescriber is required to place the signed *Patient Agreement Form* in the patient's medical record.

Prior to the March 29, 2016 approval of the S-020 efficacy supplement for Mifeprex, FDA undertook a review of all elements of the REMS. At that time, the (b) (6) ((b) (6)), along with the (b) (6) ((b) (6)), recommended removal of the *Patient Agreement Form* (ETASU D). This recommendation received concurrence from the (b) (6) on February 23, 2016. The rationale for this recommendation in the 2016 review[g] is summarized here as follows:

- The safety profile of Mifeprex is well-characterized over 15 years of experience, with known risks occurring rarely; the safety profile has not changed over the period of surveillance.
- Established clinical practice includes patient counseling and documentation of informed consent and evidence shows that practitioners are providing appropriate patient

[f] REMS@FDA, https://www.accessdata fda.gov/scripts/cder/rems/index.cfm, Accessed November 15, 2021.
[g] (b) (6) Clinical Review, NDA 020687/S20, dated March 29, 2016. https://darrts fda.gov/darrts/faces/ViewDocument?documentId=090140af803dc7bd&_afrRedirect=386175573203745

counseling and education; the *Patient Agreement Form* is duplicative of these established practices.

- Medical abortion with Mifeprex is provided by a small group of organizations and their associated providers. Their documents and guidelines are duplicated in the *Patient Agreement Form*.
- ETASUs A and C remain in place: The *Prescriber Agreement Form* and the requirement that Mifeprex be dispensed to patients only in certain healthcare settings, specifically, clinics, medical offices, and hospitals under the supervision of a certified prescriber, remain in place.

In light of a memorandum from the Director of the Center for Drug Evaluation and Research, an addendum to the (b) (6) March 29, 2016 review and a memorandum from the signatory authority in (b) (6) indicated that the *Patient Agreement Form* would be retained in the REMS.[h,i]

The current review of literature from March 29, 2016 to July 26, 2021, is relevant to our assessment of the necessity of the *Patient Agreement Form* as part of the REMS. While our literature search yielded no publications which directly addressed this element of the REMS, we identified the following literature that focused on the informed consent process. These studies were reviewed for their potential relevance on this topic, though the articles do not directly assess the need for the *Patient Agreement Form* as a condition necessary to assure safe use of Mifepristone under ETASU D.

- Two studies[1,2] (both authored by Dr. Grossman in 2021) used the *Patient Agreement Form* and additional clinic-specific written informed consent forms as part of the study methodology. One study evaluated medical abortion with pharmacist dispensing of mifepristone and another evaluated mail-order pharmacy dispensing. Safety and efficacy outcomes were not assessed regarding the element of consent in isolation or the *Patient Agreement Form*.
- Several studies included use of electronic or verbal consent. Two studies were conducted using signed electronic consent (Chong[3], Kerestes[4]). Aiken[5] reported that patients had the option of providing consent verbally and the discussion had to be recorded in the notes. Rocca[6] described obtaining verbal informed consent from patients seeking medical abortion provided in pharmacies or government-certified

h (b) (6) Review of proposed REMS modifications to Mifeprex. March 29, 2106.
i (b) (6) Summary of Regulatory Action for Mifeprex. March 29, 2016.

public health facilities by auxiliary nurse midwives (ANMs) in Nepal. Outcomes were not assessed regarding the single element of consent and its role in the efficacy of medical abortion.

- A retrospective chart review (Wiebe[7]) was conducted in Canada. This study included telemedicine abortions between January 31, 2017 and January 31, 2019 and a similar group of controls seen in the clinic during the same time frame, matched by date of initial appointment. As part of the telemedicine process, patients read a consent form (not specified whether they could view an electronic version) and gave verbal consent "witnessed by the counselor". Again, outcomes were not assessed regarding the single element of consent and its role in the efficacy of medical abortion.

After review, we conclude that there are no outcome data from these studies that address the need for the *Patient Agreement Form* as a condition necessary to assure safe use of mifepristone. Nor do any of these studies provide evidence of whether the patient's informed consent has been adequately documented under the process set out in the study protocol. Therefore, these studies do not provide evidence that would support removing ETASU D.

Although (b) (6) agrees that informed consent in medicine is an established practice, the National Abortion Federation's 2020 Clinical Policy Guidelines for Abortion Care[8] continue to include a detailed section on patient education, counseling, and informed consent. The guidelines state that these steps are essential parts of the abortion process; that they should be conducted by appropriate personnel, with accurate information, including about alternatives and potential risks and benefits; and that the patients must have an opportunity to have any questions answered to their satisfaction prior to any intervention. Under these guidelines, documentation must show that the patient affirms that they understand all the information provided and that the decision to undergo an abortion is voluntary. The guidelines specifically list the risks that must be addressed at a minimum, including those pertinent to medical abortion: hemorrhage, infection, continuing pregnancy, and death. Additionally, Practice Bulletins from ACOG[9] and the Society of Family Planning also support detailed patient counseling.

In addition, trends in US clinical practice are developing which could negatively impact adequate patient counseling about the risks of medical abortion. One survey by Jones 2017[10] of abortion providers in the United States and Canada prior to the COVID-19 pandemic did reveal strong adherence to evidence-based guidelines. However, this same survey noted continued increasing uptake of medical abortion by US providers. Grossman[11] conducted a US survey in

2019 which suggested that the number of obstetrician/gynecologists providing medical abortion care may be increasing and that uptake might increase if mifepristone were dispensed by pharmacies instead of being dispensed in-person. A subsequent survey of US obstetricians/ gynecologists by Daniel in 2021[12] evaluated a subsample (n = 868) from a prior national survey of providers and found that 164 (19%) reported providing medical abortion in the previous year. Of those obstetrician/gynecologists not providing medical abortion, 171 (24%) said they would offer the method to their patients if the in-person dispensing requirement for mifepristone were removed. This indicates a potential doubling of providers (+ 104%, 95% confidence interval (CI): 97% −112%). There were geographical variations, with the largest potential increases being in the Midwest (+ 189%, 95% CI: 172% −207%) and the South (+ 118%, 95% CI: 103% −134%).

Based on the articles discussed above, removal of the in-person dispensing requirement from the Mifepristone REMS Program (as discussed below in section 3.2.3) could significantly increase the number of providers to a larger group of practitioners. The *Patient Agreement Form* is an important part of standardizing the medication information on the use of mifepristone that prescribers communicate to their patients, and also provides the information in a brief and understandable format for patients. The requirement to counsel the patient, to provide the patient with the *Patient Agreement Form*, and to have the healthcare provider and patient sign the *Patient Agreement Form*, ensures that each provider, including new providers, informs each patient of the appropriate use of mifepristone, risks associated with treatment, and what to do if the patient experiences symptoms that may require emergency care. The single-page *Patient Agreement Form* is in line with other elements of this REMS, in that it supports the requirement that certified prescribers be able to accurately assess a patient, counsel a patient appropriately and recognize and manage potential complications. The form is placed in the patient's medical record to document the patient's acknowledgment of receiving the information from the prescriber and a copy is provided to the patient. We determined, consistent with section 505-1(f)(2) of the FD&C Act, that this does not impose an unreasonable burden on providers or patients, and that the *Patient Agreement Form* remains necessary to assure the safe use of Mifepristone.

After considering potential burden on healthcare providers and patients and considering the available data discussed above, including the potential for increased prescribing of mifepristone if in-patient dispensing is removed from the REMS, we conclude that the *Patient Agreement Form* should remain a safe use condition in the REMS.

3.2.3. Evaluation of the requirement for drug to be dispensed only in certain healthcare settings (ETASU C)

Mifepristone applicants must ensure that mifepristone is available to be dispensed to patients only in clinics, medical offices, and hospitals by or under the supervision of a certified prescriber. This creates what we refer to in this document as an in-person dispensing requirement under the REMS; i.e., the patient must be present in person in the clinic, medical office or hospital when the drug is dispensed. The mifepristone REMS document states that mifepristone may not be distributed to or dispensed through retail pharmacies or settings other than these.

The following information contributed to our analysis of this requirement: Mifepristone REMS Program year-one assessment data, postmarketing safety information and literature review.

REMS Assessment Data

Reporting period for the Mifepristone REMS Program - April 11, 2019 through February 29, 2020

We evaluated information included in the one-year (1st)[j] REMS assessment reports for the Mifepristone REMS Program, which included healthcare provider certification data, program utilization data, compliance data, audit results and patient exposure data.[13] The assessment reports were submitted on April 10, 2020 by the NDA Applicant and April 15, 2020 by the ANDA Applicant and cover a reporting period from April 11, 2019 through February 29, 2020. During this reporting period, the NDA Applicant reported (b) (4) newly certified healthcare providers, and the ANDA Applicant reported (b) (4) newly certified healthcare providers in the Mifepristone REMS Program. The NDA Applicant reported a total of (b) (4) certified healthcare providers (includes new and previously certified) ordered mifepristone during the assessment reporting period, and the ANDA Applicant reported a total of (b) (4) certified healthcare providers ordered mifepristone during the assessment reporting period. The NDA Applicant estimated that a total of (b) (4) patients were exposed to mifepristone during the assessment reporting period. The ANDA Applicant reported an estimated total of (b) (4) patients were exposed to mifepristone during the reporting period.

During the reporting period, a small number of non-compliance events were reported. The authorized distributor for the NDA applicant reported to the NDA Applicant that they experienced deviations with scanning of the product serial numbers which were confirmed during the February 2020 audit. The authorized distributor conducted a root cause analysis and developed a corrective and preventive action (CAPA) on February 12, 2020. The CAPA was

[j] This REMS assessment report was the first to be submitted following the approval of the single, shared system REMS for mifepristone.

validated and deployed with monitoring of the system through April 10, 2020. The corrective action will prevent similar events from occurring in the future.

January 27, 2020 through September 30, 2021

During the timeframe from January 27, 2020 through September 30, 2021, there were periods when the in-person dispensing requirement was not being enforced.

- On July 13, 2020, the United States District Court for the District of Maryland granted a preliminary injunction in the *ACOG* case to temporarily bar enforcement of the in-person dispensing requirement during the COVID-19 PHE.
- On January 12, 2021, the United States Supreme Court issued a stay of the injunction.
- On April 12, 2021, the FDA issued a General Advice Letter informing the applicants of the Agency's intent to exercise enforcement discretion during the COVID-19 public health emergency regarding the in-person dispensing requirement in the Mifepristone REMS Program.[k,l]

To better understand whether there was any impact on safety or noncompliance during the periods when the in-person dispensing requirement was not being enforced, we requested additional information from the Applicants to provide for more comprehensive assessment of the REMS for the time period from January 27, 2020 (the effective date of the COVID-19 PHE) to September 30, 2021. We requested the Applicants provide a summary and analysis of any program deviation or noncompliance events from the REMS requirements and any adverse events that occurred during this time period that had not already been submitted to FDA. As part of an additional request for information for the REMS assessment report, the Applicants were also asked to submit the adverse events to FAERS and to notify FDA that the reports were submitted.

Between January 27, 2020 and September 30, 2021, the NDA Applicant distributed (b) (4) shipments representing (b) (4) tablets. The NDA Applicant reported that there were (b) (4) shipments representing a total of (b) (4) tablets sent to (b) (4) non-certified healthcare providers.[m,n] (b) (4) of these healthcare providers subsequently became certified while (b) (4) did not. Of the (b) (4) healthcare providers who were not subsequently certified, (b) (4) returned a total of 12 of the 13

[k] FDA General Advice Letter for NDA 20687, April 12, 2021.
[l] FDA General Advice Letter for ANDA 091178, April 12, 2021.

[m] NDA 020687 September 9, 2021 response to the FDA's September 2, 2021 Information Request.
[n] NDA 020687 October 8, 2021 response to the FDA's June 30, 2021 Information Request.

Mifeprex tablets to the distributor. (b) (4) non-certified healthcare provider dispensed one tablet to a patient; no adverse events were reported. The NDA Applicant attributed the non-compliance observed to the authorized distributor's transition to a new platform. The NDA Applicant implemented a corrective and preventative action to address this issue, which we found to be acceptable.

The ANDA Applicant distributed (b) (4) shipments representing (b) (4) tablets of mifepristone from January 27, 2020 to September 30, 2021 and reported no instances of shipments to non-certified healthcare providers during this timeframe.

The NDA and the ANDA applicants reported a total of eight cases reporting adverse events between January 27, 2020 and September 30, 2021. These eight cases were also identified in the FAERS database and are described in the section below.

The number of adverse events reported to FDA during the COVID-19 PHE with mifepristone use for medical termination of pregnancy is small, and the data provide no indication that any program deviation or noncompliance with the Mifepristone REMS Program contributed to these reported adverse events. Further analysis of the adverse events is included below in the section on Pharmacovigilance Data.

Pharmacovigilance Data

The (b) (6) ((b) (6) conducted a search of the FAERS database and the published medical literature to identify U.S. postmarketing adverse events that reportedly occurred from January 27, 2020 through September 30, 2021 with mifepristone use for medical termination of pregnancy.[o,p]

The data for this time period were then further divided into date ranges when the in-person dispensing requirement was being enforced per the REMS (January 27, 2020 - July 12, 2020 & January 13, 2021 - April 12, 2021) versus when the in-person dispensing requirement was not being enforced (July 13, 2020 - January 12, 2021 (in-person dispensing requirement was temporarily enjoined) & April 13, 2021 - September 30, 2021 (in-person dispensing requirement was not being enforced because of the COVID-19 PHE)).

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[o] (b) (6). Pharmacovigilance Memorandum: Mifepristone and All Adverse Events. NDA 020687 and ANDA 091178. (b) (6) # 2007-525. Finalized April 12, 2021.

[p] (b) (6) Pharmacovigilance Memorandum: Mifepristone and All Adverse Events. NDA 020687 and ANDA 091178. (b) (6) # 2007-525. Finalized December 16, 2021.

A total of eight cases that met the search criteria were identified in FAERS and no additional case reports were identified in the medical literature. Two of the eight cases reported adverse events that occurred when the in-person dispensing requirement in the REMS was being enforced (i.e., January 27, 2020 - July 12, 2020 & January 13, 2021 - April 12, 2021). These two cases reported the occurrence of uterine/vaginal bleeding (case 1) and uterine/vaginal bleeding and sepsis (case 2). Of note, uterine/vaginal bleeding and sepsis are labeled adverse events. Five of the eight cases reported adverse events that occurred when the in-person dispensing requirement was not being enforced (i.e., July 13, 2020 - January 12, 2021 & April 13, 2021 - September 30, 2021). These five cases reported the occurrence of ongoing pregnancy (case 3), drug intoxication and death approximately 5 months after ingestion of mifepristone (case 4), death [cause of death is currently unknown] (case 5), sepsis and death (case 6), and pulmonary embolism (case 7). Although these adverse events occurred during the period when the in-person dispensing requirement was not being enforced, the narratives provided in the FAERS reports for cases 5, 6, and 7 explicitly stated that mifepristone was dispensed in-person. Of note, ongoing pregnancy, and sepsis, including the possibility of fatal septic shock, are labeled adverse events. The remaining case from July 2021 reported the occurrence of oral pain/soreness (case 8) but did not provide sufficient information to determine the exact date of the adverse event. Based upon the U.S. postmarketing data reviewed, no new safety concerns were identified by (b) (6)

In addition to the FAERS data provided above, (b) (6) routinely monitors adverse events reported to FAERS and published in the medical literature for mifepristone for medical termination of pregnancy. (b) (6) has not identified any new safety concerns with the use of mifepristone for medical termination of pregnancy.

To enable additional review of adverse events, the Applicants were requested[q] to provide a summary and analysis of adverse events reported with incomplete medical abortion requiring surgical intervention to complete abortion, blood transfusion following heavy bleeding or hemorrhage, ectopic pregnancies, sepsis, infection without sepsis, hospitalization related to medical abortion, and emergency department (ED)/urgent care encounter related to medical abortion. The Applicant for Mifeprex provided a summary of postmarketing safety information from March 29, 2016, when S-020 was approved, through September 30, 2021, on August 27 and October 8, 2021. During the time period in question, (b) (4) tablets were shipped, and

[q] On August 5, 2021, an IR was sent to the Applicants requesting a summary and analysis of adverse events from March 29, 2016 through June 30, 2021 and from July 1, 2021 through September 30, 2021.

48 adverse events were received. The 48 adverse events included 4 deaths (one of which occurred in 2010 but was reported in 2017), 25 incomplete abortions requiring surgical intervention, 17 blood transfusions following heavy vaginal bleeding, 2 ectopic pregnancies, 7 infections (1 sepsis and 6 infection without sepsis), 13 hospitalizations, and 43 ED or urgent care visits related to medical abortion. For the period between January 27, 2020 and September 30, 2021, a time frame that includes the entire period when the COVID-19 public health emergency (PHE) has been in effect, there were three adverse events reported corresponding to the above cases from FAERS identified by (b) (6) case 1 (uterine/vaginal bleeding), case 2 (uterine/vaginal bleeding and sepsis), and case 4 (drug intoxication and death).

The ANDA Applicant provided a summary of postmarketing safety information from April 11, 2019 (date of ANDA approval) through September 30, 2021. On August 26, 2021, the Applicant provided distribution and adverse event information from April 11, 2019 through June 30, 2021. During this time period, a total of (b) (4) tablets were shipped. There were 7 adverse events including 3 deaths (1 from sepsis, 1 from bilateral pulmonary artery thromboemboli, 1 in a patient who complained of not being able to breathe), 1 ongoing pregnancy treated with uterine aspiration, 2 blood transfusions, 1 sepsis (with death), 1 hospitalization, and 3 ED or urgent care visits related to medical abortion. On October 12, 2021 the Applicant provided information from July 1, 2021 to September 30, 2021; there were no additional adverse events. For the period between January 27, 2020 and September 30, 2021, there were four adverse events reported corresponding to the above cases from FAERS identified by (b) (6) case 3 (ongoing pregnancy), case 5 (death unknown cause), case 6 (sepsis and death), and case 7 (pulmonary embolism).[r]

The postmarketing data from FAERS were analyzed by (b) (6) to determine if there was a difference in adverse events between periods when the in-person dispensing requirement was being enforced and periods when the in-person dispensing requirement was not being enforced. Based on this review, we conclude that there does not appear to be a difference in adverse events between periods when the in-person dispensing requirement was being enforced and periods when the in-person dispensing requirement was not being enforced. This suggests that mifepristone may be safely used without an in-person dispensing requirement.

[r] The eighth FAERS case, oral pain/soreness, was not within the scope of the August 5, 2021 IR and was not considered for this review of postmarketing safety information submitted by the Applicants in response to the IRs.

(b) (6) review of the Applicants' IR responses, which included the same cases identified by (b) (6) from FAERS, did not change our conclusion.[s]

Literature Review

Published studies have described alternatives in location and method for dispensing mifepristone by a certified prescriber (or an equivalent healthcare provider in countries other than the US). Some studies have examined replacing in-person dispensing in certain health care settings with dispensing at retail pharmacies (Grossman[2], Wiebe[7], Rocca[6]) and dispensing mifepristone from pharmacies by mail (Grossman[1], Upadhyay[14], Hyland[15]). Other studies have evaluated two modes of dispensing by prescribers: (1) prescribers mailing the medications to women (Gynuity study [Raymond[16], Chong[3], Anger[17]], Kerestes[4], Aiken[5] (2021)) and (2) prescribers using couriered delivery of medications (Reynolds-Wright[18]). Other studies have evaluated dispensing mifepristone by mail by an entity described as "a partner organization" (Aiken[19] (2017), Norton[20], Endler[21]). For ease of review, in the sections below that describe these studies, we have separated relevant references by the methodology used to dispense mifepristone.

Retail pharmacy dispensing

Three studies report medical abortion outcomes for retail pharmacy dispensing of mifepristone after clinical evaluation. Grossman[2] conducted a US-based study in which mifepristone and misoprostol were dispensed from a pharmacy partnered with the clinic where the participant had an evaluation by ultrasound and counseling. Of the 266 participants enrolled, 260 had known abortion outcomes. Complete abortion without additional procedure occurred in 243 participants (93.5% of those with known outcomes). Seventeen participants (6.5% of those with known outcomes) were diagnosed with incomplete abortion and underwent uterine aspiration. The reported proportion of complete abortion is within the range described in the approved mifepristone labeling. However, the finding represents a lower-than-expected efficacy based on the cohort's GA (84% of participants were at ≤ 56 days GA, a cohort for which the labeled success rate is 96.8%). No participants experienced a serious adverse event, were hospitalized, or required transfusion. Three participants had ED visits with treatment (intravenous hydration, pain medication, pelvic infection after uterine aspiration for incomplete abortion). The study's

[s] The reporting period of (b) (6) assessment of the adverse events in FAERS is not identical to the time period for summaries of adverse events in the IRs to the Applicants. Therefore, the numbers of cases and adverse events summarized in (b) (6) assessment may differ from the numbers of cases and adverse events summarized by the Applicants in their responses to IRs (note that each case report may include more than one adverse event).

safety and efficacy outcomes are consistent with labeled frequencies. The majority of participants (65%) were very satisfied with the experience. There were some complaints from participants about not receiving all prescribed medications at the initial pharmacy visit, privacy not being adequately maintained, and perceived negative pharmacist attitude.

Overall, we conclude that this study has limited generalizability because it was conducted in two US states and involved partnered pharmacies, some of which were in the same building as the clinic. Additionally, all participating pharmacies in this study were required to have a pharmacist on duty during clinic hours who had been trained in the study protocol and was willing to dispense mifepristone. The study conditions may not be generalizable to US retail pharmacies; there is insufficient information to assess this. Rocca[6] conducted an observational study evaluating 605 participants at ≤63 days GA who obtained medical abortions in Nepal by comparing the provision of medical abortion service by newly trained nurse midwives in pharmacies to medical abortion provided in government-certified clinics. Participants who presented to pharmacy study sites underwent clinical screening including a pelvic exam by trained nurse midwives at the pharmacy (which was equipped with an examination room) and if eligible for medical abortion, were dispensed mifepristone and misoprostol in the pharmacy at the time of their visit. Participants who presented to public health facilities underwent clinical screening including pelvic examination by abortion providers including trained nurse midwives and if eligible for medical abortion were dispensed mifepristone and misoprostol in the clinic at the time of their visit. The authors reported that, with respect to complete abortion (>97%) and complications (no hospitalizations or transfusions), evaluation and dispensing in pharmacy was non-inferior to in-clinic evaluation and dispensing.

Wiebe,[7] in a retrospective, chart review study conducted in Canada, compared abortion outcomes of 182 women at ≤ 70 days GA who underwent medical abortion with telemedicine consult, and either received medications by courier or picked them up at a local pharmacy, with outcomes of a matched control cohort of 199 women who received the medications at a pharmacy after an in-clinic visit. The groups had similar documented complete medical abortion outcomes (90%, calculated maintaining subjects with unknown outcomes in the denominator; ≥ 95% calculated with known outcomes only). The telemedicine group had one case of hemorrhage (0.5%) and one case of infection requiring antibiotics (0.5%) compared with no cases of hemorrhage or infection requiring antibiotics in the in-clinic cohort. The telemedicine group had more ED visits (3.3% compared to 1.5% in-clinic cohort). Both models of dispensing mifepristone resulted in efficacy and safety outcomes within labeled frequency.

None of the three studies described above allow a determination regarding differences in safety between in-person dispensing by a certified prescriber in a health care setting and dispensing through a retail pharmacy, due to limitations on the generalizability of the studies to the current retail pharmacy environment in the US. The outcome findings from the one US study (Grossman[2]), in which the pharmacies were partnered with prescribers, may not be generalizable to much of the US as they do not reflect typical prescription medication availability with use of retail pharmacy dispensing. Although retail pharmacy dispensing of mifepristone and misoprostol in Canada has been described in the literature, there are important differences in healthcare systems between Canada and the US that render the findings from studies in Canada (Wiebe[7]) not generalizable to the US. In the Wiebe study, timely provision of medication from the retail pharmacy was accomplished by either courier to the woman or faxed prescription to the woman's pharmacy. It is unknown whether conditions that allow timely access to medications for medical abortion would occur in retail pharmacies throughout the US. Canada's federal government has reaffirmed that abortion is an essential health service[t] which may have implications affecting access to medical abortion from retail pharmacies in Canada. The Rocca[6] study evaluated medical abortion provided in Nepali pharmacies and essentially moved the abortion provider and clinical examination into the pharmacy, a scenario that is not, at this time, applicable to the US retail setting.

Mail order pharmacy

Grossman[1] published an interim analysis of an ongoing prospective cohort study evaluating medical abortion with mifepristone and misoprostol dispensed by mail-order pharmacy after in-person clinical assessment. All participants were evaluated for eligibility during a clinic visit with GA up to 63 days confirmed with either an ultrasound or examination; instead of receiving medication at the clinic visit, participants received medications from a mail-order pharmacy. A total of 240 participants have been enrolled; three participants did not take either medication. A total of 227 (94.6%) provided some outcome information, of whom 224 provided abortion outcome information. Complete abortion without additional procedures occurred in 217 participants (96.9% of those with known outcomes). Two (0.9%) participants experienced serious adverse events (SAE); one received a blood transfusion, and one was hospitalized overnight. Nine (4%) participants attended 10 ED visits. In this interim analysis, the outcomes are consistent with labeled frequencies. With respect to the time interval between a

[t] As noted in Mark[23] and Martin[24], most provincial and federal health insurance programs in Canada cover medical abortion, and covered services are free at the point of care.

participant's clinic visit and receipt of medications, of the 224 participants with known abortion outcomes, 184 (82.1%) received medication within 3 days. However, 17% received between 4-7 days and one participant waited over 7 days for receipt. Seven of 216 (3.2%) participants who completed the day-3 survey reported compromised confidentiality (e.g., someone found their medication, privacy concerns).

Upadhyay[14] reports findings from a retrospective cohort study of 141 women undergoing medical abortion in the US without a consultation or visit. Eligibility was assessed based on a participant-completed online form collecting pregnancy and medical history. Participants who were considered eligible received medication delivered by a mail-order pharmacy. Three interactions via text, messaging or telephone occurred to confirm medication administration, assessment of expulsion and pregnancy symptoms, and results of a 4-week home pregnancy test. Abortion outcome was determined by either the day 3 assessment or the 4-week pregnancy test. The investigators reported a complete abortion rate without additional procedures of 95% (105 participants out of 110 for whom outcomes were known) and stated that no participants had any major adverse events. The proportion of abortion outcomes assessed at 3 days versus 4 weeks is not reported. Regardless, determining outcomes at 3 days is insufficient to determine outcome rates or safety findings because a 3-day follow-up period is too short. Additionally, a substantial number of participants (31) provided no outcomes information. Among the 141 participants enrolled, 128 had any follow-up contact with the study staff, and 110 provided outcomes information. Excluding outcomes of 22% of the cohort is a limitation of this study. This study used a model with numerous deviations from standard provision of medical abortion in the US, such as no synchronous interaction with the prescriber during informed consent or prior to prescribing medication, no confirmation of self-reported medical, surgical, and menstrual history. Further, follow-up information based on a 3-day period is insufficient to determine outcome rates or safety findings. These deviations, limited follow-up information, and small sample size limit the usefulness of this study.

Hyland[15] describes findings from a cohort study in Australia evaluating medical abortion outcomes utilizing telemedicine and a central mail order pharmacy. All participants obtained screening tests including ultrasound confirmation of GA. A total of 1010 participants completed the screening process and were provided mifepristone and misoprostol. Abortion outcomes were determined for 754 (75%) of the 1010. Outcomes for the remaining 256 participants (25%) were not included because 31 provided no relevant information after shipment, 14 reported not taking misoprostol, and 211 did not have "full follow up" (i.e., known outcome of either complete medical abortion, uterine evacuation, or ongoing pregnancy with plan to continue).

Reference ID: 4905882

Complete abortions without additional procedures occurred in 727 participants (96% of those with definitively documented outcomes) and is consistent with labeled efficacy. Of the 754 participants included in the analysis 717 (95%) had no face-to-face clinical encounters after medications were mailed while 21 (3%) were admitted to the hospital and 16 (2%) had an outpatient encounter. One participant who was hospitalized and underwent a surgical uterine evacuation received a transfusion. Not included in the findings are 7 hospitalizations occurring in 7 participants who did not have "full follow up". The authors do not report any other adverse events and conclude use of the telemedicine medical abortion service is safe. The reasons for hospitalization are not discussed by the authors; therefore, it is unknown why the patients were hospitalized. Although the reported number of hospitalizations (3%) is higher than the less than 1% in the FDA-approved mifepristone labeling, conclusions regarding the safety findings in this study cannot be made in the absence of information about the reasons for hospitalization. Other limitations of this study include incomplete information about outcomes with face-to-face encounters, and not reporting outcomes of 25% of the enrolled cohort.

Overall, the three studies evaluating mail order pharmacy dispensing suggest that the efficacy of medical abortion is maintained with mail order pharmacy dispensing. In the Grossman[1] study, the interim analysis, although small, does not raise serious safety concerns. We note that 18% of participants did not receive medications within 3 days; the potential for delay in receiving medication by mail could limit the GA eligible for medical abortion through mail order pharmacy dispensing, because women at GA closer to 70 days might not receive medication in time. A small proportion (3%) of participants raised concerns regarding the issues of confidentiality and privacy. Safety findings from the Hyland[15] study are difficult to interpret. Although only one transfusion is reported, and the authors state the findings demonstrate safety, the higher hospitalization rates, and lack of information on the reasons for hospitalization do not allow any conclusions about safety findings. Lastly, the Upadhyay[14] study had no reported adverse events, but the findings are less useful because of the limited follow-up, and because medical abortions were provided using a model with numerous deviations from standard provision of medical abortion in the US.

Clinic dispensing by mail

A total of five studies evaluated clinic dispensing by mail.[3,4,5,16,17] Gynuity Health Projects conducted a prospective cohort study (the "TelAbortion" study) evaluating use of telemedicine for remote visits and mifepristone being dispensed from clinics via overnight or regular tracked mail. Three publications reviewed have reported outcomes for the Gynuity population

exclusively: Raymond[16] from May 2016 to December 2018, Chong[3] from May 2016 to September 2020 and Anger[17] from March 2020 to September 2020. Due to the pandemic, the Gynuity study deviated from the protocol requirement of confirmation of GA by examination or ultrasound for many participants treated from March 2020 onward (although none of the three publications reported on the single element of dispensing mifepristone from the healthcare setting by mail). A fourth study, Kerestes,[4] reports outcomes of medical abortion at the University of Hawai'i from April 2020 to November 2020: seventy-five (of whom 71 were enrolled in the Gynuity study) of the 334 participants in Kerestes were dispensed mifepristone by mail after a telemedicine consult. The section below discusses these four studies from the US as well as a large UK study by Aiken[5] (2021).

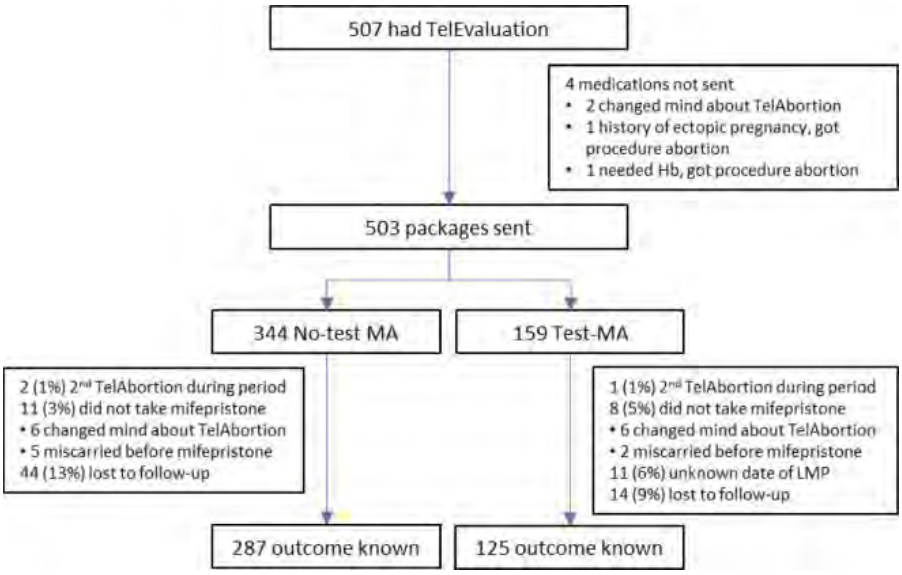
Raymond [16] (2019) reported outcomes from the Gynuity study prior to the pandemic. In the TelAbortion study, participants were not required to have an in-person clinic visit; rather, they obtained screening tests at laboratories and radiology offices and then communicated with the abortion provider by videoconference. If the participant was eligible for treatment, the provider dispensed the medications by mail. Of 433 women screened, 165 (38%) either declined to schedule the videoconference or did not keep the videoconference appointment. Among the 268 participants evaluated via videoconference, medication packages were sent to 248. Abortion outcomes were determined for 190 (77%) of the 248; outcomes for 58 (23%) participants were unknown. Complete abortion without additional procedures occurred in 177 participants (93% of those with known outcomes). The investigators obtained follow-up information from 217 participants after package shipment; there were two hospitalizations (one received a transfusion for severe anemia despite having had a complete abortion), and 16 other participants (7%) had clinical encounters in ED and urgent care centers. The reported outcomes in Raymond[16] (2019) are similar to outcomes described in approved labeling except the combined ED/urgent care center encounters (7%) exceeded the ED visits in approved labeling (2.9-4.6%). The authors note that half of the ED/urgent care visits did not entail any medical treatment and opine that the increased number of visits may have been due to the study participants living farther from the abortion providers.[16] All participants received medications within 8 days.

Chong[3] updated the findings from the Gynuity study described in Raymond[16] and reported on 1157 medical abortion outcomes, of which approximately 50% occurred during the period of the COVID-19 PHE. Although a screening ultrasound was required per the protocol, sites determined in 52% (346/669) of abortions that occurred during the period of the COVID-19 PHE that, in order to avoid potential exposure to COVID-19 at a health care facility, those

participants were not required to obtain a screening ultrasound. Use of urine pregnancy test to confirm abortion completion also increased from 67% (144/214) in the 6 months prior to the pandemic to 90% (602/669) in the 6 months during the pandemic. Of the 1390 participants to whom medicine packages (containing both mifepristone and misoprostol) were mailed, 1157 (83.2%) had known abortion outcomes. Complete abortion without a procedure occurred in 1103 participants (95% of the those with a known outcome). Ten women experienced an SAE (5 transfusions (0.4%) and 7 hospitalizations (0.7%)) and 70 (6%) participants had unplanned clinical encounters in ED/urgent care. Surgical interventions were required in 47 participants (4.1% of 1390) to complete abortion. The reported outcomes in this study are similar to outcomes described in approved labeling, except that the combined ED/urgent care center encounters (6%) exceeded the ED visits in approved labeling (2.9-4.6%).

Anger[17] compared outcomes among participants enrolled in the Gynuity study who did versus did not have confirmation of GA/intrauterine location with an examination or ultrasound from 10 jurisdictions across the US. These participants were screened for enrollment from March 25 through September 15, 2020. All participants had a telemedicine consultation and received mifepristone and misoprostol by mail from the healthcare facility. Determination of which participants did not require confirmation of GA by examination or ultrasound to be eligible depended on the study clinician's assessment of eligibility for "no-test medication abortion"[u] based on a sample protocol published by Raymond[22] (2020). There were two key differences between the two groups. Participants for whom the study clinician determined a pre-abortion ultrasound was required were more likely than the participants who had no ultrasound or examination to live further than 150 miles from the clinic (51.2% vs. 31.7%) and were more likely to have a GA above 63 days (12.0% vs. 1.7%). The study sites shipped 503 medication packages during the analysis period; 344 packages went to the "no test" group while 159 went to the "test" medical abortion cohort (see figure below). However, because the two cohorts were not randomized in this study, they had different baseline characteristics. Consequently, findings based on the comparisons between the two cohorts should be interpreted carefully.

[u] "No-test medication abortion" refers to medical abortion provided without a pretreatment ultrasound, pelvic examination, or laboratory tests when, in the judgment of the provider, doing so is medically appropriate (appropriateness based on history and symptoms); "no-test medication abortion" does include post-abortion follow up. A sample protocol is described by Raymond et al.[22]



Source: Figure 1 in this publication. MA= medical abortion.

The investigators' analyses excluded 91 (18% of 503; 57 in the no-test group and 34 in the test group) participants because they did not provide a date of the last menstrual period (LMP), did not take mifepristone, or did not have a recorded abortion outcome. Overall, 410 participants (81.5% of 503) provided outcomes data. There were no reported ectopic pregnancies in either group. The number of ED/urgent care visits and the proportion of unplanned clinical encounters that led to medical treatment were not reported. In the no-test group, complete medical abortion was confirmed in 271 participants who took medications (94% among those with known outcome). In the no-test cohort, two participants were "hospitalized and/or blood transfusion," and 36 (12.5%) had an unplanned clinical encounter (participant sought in-person medical care related to abortion and the visit was not planned prior to abortion).

In the test medical abortion group, complete abortion was confirmed in 123 participants (of 125 with known outcomes); the completion rate was 98% among those with known outcomes. In the test medical abortion group, one participant was "hospitalized and/or blood transfusion," and 10 (8.0%) had an unplanned clinical encounter. The authors concluded that, compared to participants who had an ultrasound prior to medical abortion, those without an examination prior to medical abortion were more likely to require procedural interventions and had more unplanned clinical encounters.

Kerestes[4] was the only publication that linked outcomes of medical abortion with different delivery models. Participants included in the report had GA up to 77 days and received

medications in Hawaii between April 2020 and January 2020. A total of 334 medication packages (to 330 unique participants) were dispensed containing mifepristone and misoprostol; three different delivery models were used concurrently: 110 (32.9%) had traditional in-person visits, 149 (44.6%) had telemedicine consultation with in-person pick-up of medications, and 75 (22.5%) were sent medications by mail (71 of these were enrolled through Gynuity's TelAbortion study). Seven participants of the 330 participants who received 334 medication packages reported that they did not take them and were excluded from analysis of the outcomes. Among participants with follow-up data, the rates of successful medical abortion without surgery were 93.6%, 96.8%, and 97.1% in the in-clinic group, telemedicine + in-person pickup group, and telemedicine + mail group, respectively; these were consistent with outcomes in approved labeling. Blood transfusion was given to two participants (both in the telemedicine + in-person pickup group). Eleven participants went to an ED. Although ED visits occurred the most frequently in the telemedicine + mail group (four participants or 5.8%) and the least in the in-person group (two participants or 2.1%), the study reported no increases in other serious adverse events.

Taken together, the three Gynuity study reports[3,16,17] and Kerestes[4] support dispensing mifepristone and misoprostol by mail after a telemedicine visit. Efficacy was maintained in all four studies. All of the studies reported SAEs frequencies comparable to labeled rates, except two of the Gynuity study reports (Raymond[16], Chong[3]) and Kerestes[4] report a higher frequency of ED/urgent care visits than the labeled frequency of ED visits. We do not know whether the reporting of combined ED and urgent care visits represents an increased rate of ED visits compared to the labeled rate of ED visits (2.9-4.6%). Other labeled SAEs (e.g., transfusion) occur infrequently (< 1%).

Aiken[5] (2021) reports outcomes of medical abortion up to 70 days GA in the UK before and during the pandemic in a retrospective cohort study. In the UK, prior to the COVID-19 pandemic, all patients attended an in-clinic visit where they received an ultrasound, were administered mifepristone in the clinic, and given misoprostol in-clinic for use at home (traditional model). During the pandemic, medical abortion consultations were performed remotely by telephone or video. Based on the consultation and questionnaire (including date of last menstrual period; menstrual, contraceptive and medical history; symptoms; risk for ectopic pregnancy), an assessment of eligibility for treatment via telemedicine was made. If eligible, medications were delivered to participants via mail or were made available for collection from the clinic for use at home. If the participant was assessed to be ineligible for treatment via

telemedicine, an in-person assessment with ultrasound was performed and medications were provided from the clinic for home use (hybrid model).

The study compared the two cohorts: 22,158 obtained medical abortion before the pandemic and had in-person visits and dispensing (traditional model) and 29,984 obtained medical abortion during the pandemic with either in-person visit and in-person dispensing, or a telemedicine visit and dispensing by mail or picked up from the clinic (hybrid model). Outcomes were obtained from electronic records and incident databases. Outcomes of all hospitalizations related to abortion, ED visits, infection without sepsis, and hemorrhage without transfusion were not reported. The investigators' analysis for non-inferiority determined the efficacy and safety were comparable between both cohorts. Complete abortion occurred in > 98% in both cohorts. Hemorrhage requiring transfusion was reported in 0.04% and 0.02% of the traditional and hybrid cohorts, respectively; this is lower than the labeled 0.5% transfusion rate. There were no severe infections requiring hospitalization, major surgery or deaths reported.

A secondary analysis of the hybrid cohort was reported. Within the 29,984-person hybrid model cohort, 11,549 (39%) abortions were conducted in-person (in-person assessment with ultrasound was performed and medications provided from the clinic for home use) and 18,435 (61%) abortions were provided by telemedicine visit, without tests or confirmation of GA/intrauterine position by ultrasound, and medications either mailed or picked up from the clinic. Outcomes stratified by type of mifepristone dispensing were not reported. The rate of complete abortion was slightly higher in the telemedicine group (99.2%) than that in the in-person group (98.1%). There were no significant differences in the rates of reported SAEs. Adjustments for clinical and demographic characteristics were made because the two groups differed in baseline characteristics, including a higher proportion of pregnancies with GA over 6 weeks in the in-person group (68.2% compared with 55.1%). The authors conclude a hybrid model for medical abortion that includes no-test medical abortion[u] (no ultrasound, no pelvic exam, no pregnancy test) is effective and safe.

We conclude that although the Aiken[5] (2021) study has a large sample size and includes 85% of all medical abortions performed in England and Wales during the study period, the study has limitations. The authors acknowledge the main limitation of their study was that analysis was based on deidentified information in the NHS database and the investigators were unable to verify the outcomes extracted. Other limitations included that their search only captured

outcomes in electronic records and incident databases that met the authors' defined threshold for SAE reporting, and that the labeled abortion outcomes considered serious, such as hospitalizations related to abortion, infection without sepsis, hemorrhage without transfusion, or ED/urgent care visits, were not all included in the authors' definition of serious adverse event.

Data from the mail order dispensing studies with telemedicine visits from Gynuity (Raymond, Chong and Anger),[3,16,17] Kerestes[4], and Aiken[5] (2021) support that efficacy of medical abortion was maintained. The Aiken[5] study appears to be of sufficient sample size to determine whether safety outcomes with mail dispensing differ from in-person dispensing; however, the study's design did not capture all serious safety outcomes, thus limiting the certainty of the findings. Study reports of Raymond[16] Chong[3], and Kerestes[4] all suggest there may be an increase in ED/urgent care visits with telemedicine visits and dispensing by mail without increases in other adverse events. Anger's[17] comparative analysis suggests a pre-abortion examination may decrease the occurrence of procedural intervention and decrease the number of unplanned visits for postabortion care. Overall, despite the limitations noted, these studies support that dispensing by mail is safe and effective. Although the literature suggests there may be more frequent ED/urgent care visits related to the use of mifepristone when dispensed by mail from the clinic, there are no apparent increases in other SAEs related to mifepristone use. One reason for the increase in frequent ED/urgent care visits in the Raymond[16] publication, according to its authors, may have been that a substantial proportion of participants lived significant distances from their providers and increased distances have been associated with higher use of ED following treatment. Raymond[16] reported that half of the participants who had an ED/urgent care visit did not require medical treatment.

Clinic dispensing by courier

Reynolds-Wright[18] reported findings from a prospective cohort study of 663 women at less than 12 weeks' GA in Scotland undergoing medical abortion at home with use of telemedicine during the pandemic (from April 1 to July 9, 2020). The majority of medical abortions (78.7%) used telemedicine visits, eliminated pre-abortion ultrasound, and provided mifepristone for pick up at the service or by couriered delivery to woman's home. The number of couriered deliveries was not reported; thus, this study does not provide abortion outcomes separately for couriered delivery of mifepristone and misoprostol. With access to NHS regional hospital databases, the investigators were able to verify pregnancy outcomes and complications. Of the 663 participants, 642 (98.2%) were under 10 weeks GA, 21 (1.8%) were between 10 and 12 weeks

GA, and one participant was never pregnant. A total of 650 participants had complete abortion without requiring surgical intervention (98%), 5 (0.8%) an ongoing pregnancy and 4 (0.6%) an incomplete abortion. The outcomes from this study in Scotland are consistent with labeled mifepristone outcomes. The study shares the same limitations as the Aiken[5] (2021) study.

Partner organization dispensing by mail

Women on Web (WoW), an internet group, connects patients and providers outside of the US and provides medical abortion globally, dispensing mifepristone through "a partner organization" by mail.[v] Medical abortion eligibility is determined using an online questionnaire with asynchronous physician review. If eligible, medications are mailed to the women. WoW provides help and support by email or instant messaging.

Aiken[19] (2017) conducted a population-based study analyzing findings from 1,636 women in the Republic of Ireland and Northern Ireland who were sent medications between 2010 and 2012. Receipt of medications was confirmed for 1,181 women, among whom 1,023 confirmed use of mifepristone and misoprostol; outcome information was available for 1,000 (61% of women sent medications). Of the 1,000 women, the majority (781, 78%) were less than 7 weeks GA and 219 (22%) were at 7-9 weeks. Complete abortion without surgical intervention occurred in 947 (94.7% of 1,000 with known outcome); 7 (0.7%) women received a blood transfusion, 26 (2.6%) received antibiotics (route of administration undetermined) and 87 (8.7%) sought medical care at a hospital or clinic for symptoms related to medical abortion. Hospitalizations related to abortion were not reported. The reported proportion of complete abortion is within the range labeled for medical abortion up to 70 days (92.7-98.1%). However, the finding of 94.7% complete abortion represents a lower-than-expected efficacy based on the cohort's GA (almost 80% less than 7 weeks, labeled success for medical abortion ≤ 49 days is 98.1%). This study has limitations, including outcomes based on self-report without validation of completed abortion by examination or laboratory testing, and no known outcomes for 39% of study cohort. Additionally, the authors noted medical abortion was provided in a legally-restrictive setting, where the law provided a maximum penalty of life imprisonment for the woman undergoing the abortion, which may affect participants' self-reporting.

[v] In March 2019, FDA sent a WL to Aidaccess.org, a group affiliated with WoW. Aidaccess.org received this WL because it was introducing misbranded and unapproved new drugs into the U.S. In the context of this REMS review, studies involving WoW are included solely for purposes of evaluating of data regarding the methods of dispensing mifepristone.

Endler[21] and Norten[20] have reported outcomes from WoW cohorts but do not provide relevant information on mifepristone dispensing by mail, because neither provide meaningful outcomes data for consideration. Endler[21] compared the outcomes of self-reported heavy bleeding and clinical visits occurring during the "first or second day of abortion" that occurred in women undergoing medical abortion at 9 weeks GA or less, with outcomes from women at more than 9 weeks GA. Outcome data from day 1 or 2 is of limited usefulness. Norten[20] describes findings from a survey of women who were sent medical abortion medication through WoW and provided self-reported outcomes. Results were based on surveys returned from only 37% of participants, a return rate that is too low for the study to be considered valid.

WoW uses a model with numerous deviations from the standard provision of medical abortion in the US. For example, this model has no synchronous interaction with the prescriber during informed consent or prior to prescribing medication and no confirmation of self-reported medical, surgical, and menstrual history or confirmed pregnancy testing. Further, although Aiken[19] (2017) is a large cohort study, the outcomes are self-reported with no verification of complete abortion by laboratory or clinical evaluation and 39% of outcomes are unaccounted for. These limitations in the Aiken study result in the data being insufficient to determine the safety of dispensing mifepristone by mail through a partner organization.

4. Discussion

After review of the published literature, safety information collected during the COVID-19 PHE, postmarketing data, information from the first Mifepristone REMS Program assessment report, responses to information requests to the Applicants, and information provided by advocacy groups, individuals and the plaintiffs in the *Chelius v. Becerra* litigation, we conclude that the REMS can be modified to reduce burden without compromising patient safety.

Prescriber Certification

None of the publications we reviewed would support a conclusion that a healthcare provider who prescribes mifepristone does not need to meet the qualifications included in the Mifepristone REMS Program as described above in section 3.2.1. Absent these provider qualifications, serious complications associated with medical abortion, including missed ectopic pregnancy and heavy bleeding from incomplete abortion, would not be detected or appropriately managed.

We conclude that prescriber certification (ETASU A) should be maintained. The current process requires the prescriber to agree to the requirements of the Mifepristone REMS Program and to attest that they meet the qualifications described in section 3.2.1 above. The REMS has been structured to minimize burden to prescribers by requiring only a one-time certification by the prescriber for each Applicant. We have determined that healthcare provider certification continues to be necessary to ensure the benefits outweigh the risks, especially considering that, if the in-person dispensing requirement is removed from the Mifepristone REMS Program, the number of new providers may increase (see discussion in section 3.2.2 above).

Drug to be dispensed with evidence or other documentation of safe use conditions

The requirement to counsel the patient and provide them with the *Patient Agreement Form* ensures that each patient is informed of the appropriate use of mifepristone, the risks associated with treatment, and what to do if they experience symptoms that may require emergency care.

In 2016, we initially recommended eliminating the *Patient Agreement Form* (see section 3.2.2), though the form was ultimately maintained as part of the REMS. As discussed above, our current literature review has indicated that there is no basis to remove the *Patient Agreement Form* from the REMS. In addition, surveys we reviewed suggest that if the in-person dispensing requirement for mifepristone is removed, there could be a potential doubling of medical abortion providers. This potential doubling of medical abortion providers supports the continued need to ensure that patients are consistently provided patient education under the Mifepristone REMS Program regarding the use and risks of mifepristone. The *Patient Agreement Form* is an important part of standardizing the medication information that prescribers communicate to their patients, including new prescribers, and also provides the information in a brief and understandable format to patients. We determined, in accordance with section 505-1(f)(2) of the FD&C Act, that this does not impose an unreasonable burden on providers or patients.[w]

Given the likelihood of a potential increase in new prescribers if the in-person dispensing requirement is removed from the Mifepristone REMS Program, we conclude that maintaining the *Patient Agreement Form* remains necessary to assure safe use at this time.

[w] *The Patient Agreement Form* can be signed in person or through other means.

Drug to be dispensed only in certain healthcare settings

As discussed above in section 3.2.3, our evaluation of information submitted by the applicants in the one-year (1st) REMS assessment report for the Mifepristone REMS Program and in response to follow-up requests from the Agency indicates that the number of adverse events reported to FDA during the COVID-19 PHE with mifepristone use is small, and the data provide no indication that any program deviation or noncompliance with the Mifepristone REMS Program contributed to these adverse events. We further conclude, based our review of the postmarketing safety data from FAERS during the COVID-19 PHE and information submitted by the applicants for the timeframe of January 27, 2020 through September 30, 2021, that there does not appear to be a difference in adverse events between periods during the COVID-19 PHE when the in-person dispensing requirement was being enforced and periods when the in-person dispensing requirement was not being enforced; nor have we identified any new safety concerns with the use of mifepristone for medical termination of early pregnancy.

Alternatives to in-person dispensing of mifepristone have been investigated in several studies and countries. The literature review identified 15 publications[x] that assessed safety outcomes from various medication delivery models (US, UK, Canada, Ireland, Australia, Nepal), including dispensing by retail and mail order pharmacies, prescribers mailing medications or using couriered service to deliver medications, and dispensing by "partner organizations". The ability to generalize the results of these studies to the US population is hampered by differences in pre-abortion care (e.g., telemedicine versus in-person, testing), and the usefulness of the studies is limited in some instances by small sample sizes and lack of follow-up information on outcomes with regard to both safety and efficacy.

In addition, there are factors which complicate the analysis of the dispensing element alone. Some of these factors are: (1) only a few studies have evaluated alternatives for in-person dispensing of mifepristone in isolation; for example, most studies on mail dispensing of mifepristone also include telemedicine consultation, and (2) because most SAEs with medical abortion are infrequent, though they can be life threatening, further evaluation of changes in dispensing would require studies with larger numbers of participants. We did not find any large clinical studies that were designed to collect safety outcomes in healthcare systems similar to the US.

[x] The 15 publications correspond to endnote numbers: 1-7, 14-21.

Based on the literature identified by our review, dispensing mifepristone by mail from the clinic or from a mail order pharmacy does not appear to jeopardize the efficacy of medical abortion. The studies we reviewed are not adequate on their own to establish the safety of the model of dispensing mifepristone by mail, although the safety and efficacy outcomes reported in these studies remain within the ranges described in mifepristone labeling except for increased numbers of ED/urgent care visits and hospitalizations.

Four publications (Raymond[16], Chong[3], Anger[17] and Kerestes[4]), describe a relevant US cohort where dispensing mifepristone from the clinic by mail was paired with telemedicine visits. These studies showed that efficacy was maintained and there was no increased frequency of SAEs except for higher ED/urgent care visits. The increased ED/urgent care visits were not associated with increases of other SAEs, and in the view of one study's authors (Raymond[16]), may be associated with participants being located significant distances from their providers. The Aiken[5] (2021) study of a large UK cohort where the clinics mailed mifepristone report small (lower than labeled) occurrences of transfusion and no significant infections requiring hospitalization. In Grossman[1] and Hyland[15], where the pharmacies mailed mifepristone after prescribers confirmed GA, efficacy is maintained. Grossman's[1] interim analysis found no increases in SAEs. Hyland[15] reported higher numbers of hospitalizations but did not report increases of other SAEs. Overall, while the studies assessing mifepristone dispensing by mail suggest more frequent encounters with healthcare providers, they generally support a conclusion that dispensing by mail is safe. Despite the limitations of the studies we reviewed, we conclude that overall, the outcomes of these studies are not inconsistent with our conclusion that, based on the 1st year REMS assessment report and postmarketing safety data, mifepristone will remain safe, and efficacy will be maintained if the in-person dispensing requirement is removed from the Mifepristone REMS Program.

Based on the REMS assessment data, FAERS data from the time period when the in-person dispensing requirement was not being enforced, our review of the literature, and information provided by advocacy groups, individuals, the Applicants, and the plaintiffs in the *Chelius v. Becerra* litigation, we conclude that mifepristone will remain safe and effective for medical abortion if the in-person dispensing requirement is removed, provided all the other requirements of the REMS are met, and pharmacy certification is added as described below.

Removing the in-person dispensing requirement will render the REMS less burdensome to healthcare providers and patients and provided all other requirements of the REMS are met, including the additional requirement for pharmacy certification, the REMS will continue to

ensure that the benefits of mifepristone for medical abortion outweigh the risks. Therefore, to reduce the burden imposed by the REMS, the Mifepristone REMS Program should be modified to remove the in-person dispensing requirement, which would allow, for example, dispensing of mifepristone by mail via certified prescribers or pharmacies, in addition to in-person dispensing in clinics, medical offices and hospitals as currently outlined in ETASU C.

New requirement to be added for pharmacy certification

The current distribution model requires the certified prescriber to dispense mifepristone directly to the patient in a clinic, medical office, or hospital. During the periods when the in-person dispensing requirement was not being enforced, both applicants used mail order pharmacies to receive and hold mifepristone on behalf of the certified healthcare providers who had purchased the product.[j,y,z] Pursuant to a prescription for mifepristone, the mail order pharmacy would ship the product to a named patient.

The Mifepristone REMS Program continues to require that mifepristone be prescribed only by certified prescribers. With the removal of the in-person dispensing requirement, however, the drug is no longer required to be dispensed only in a clinic, medical office or hospital. Under the REMS as modified, mifepristone can be dispensed through a pharmacy, provided the product is prescribed by a certified prescriber and all other requirements of the REMS are met. Given this modification to the dispensing requirements in the REMS, it is necessary to add a requirement for certification of pharmacies under ETASU B. Adding the pharmacy certification requirement incorporates pharmacies into the REMS, ensures that pharmacies are aware of and agree to follow applicable REMS requirements, and ensures that mifepristone is only dispensed pursuant to prescriptions that are written by certified prescribers. Without pharmacy certification, a pharmacy might dispense product that was not prescribed by a certified prescriber. Adding pharmacy certification ensures that ETASU A is met prior to dispensing the product to a patient; certified prescribers, in turn, have agreed to meet all the conditions of the REMS, including ensuring that the *Patient Agreement Form* (ETASU D) is completed. In addition, wholesalers and distributors can only ship to certified pharmacies. Based on our review of the safety data and our consideration of the distribution model implemented by the Applicants during the periods

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y ANDA 091178: September 23, 2021 response to the September 15, 2021 information request; October 11 and 16, 2021 responses to the June 30, 2021 and July 15, 2021 information requests; October 26, 2021 response to the October 22, 2021 information request; October 29, 2021 response to the October 27 information request.
z NDA 020687: September 20, 2021 response to the September 15, 2021 information request; October 26, 2021 response to the October 22 information request.

when the in-person dispensing requirement was not being enforced, as well as REMS assessment data and published literature, we conclude that provided all other requirements of the REMS are met, the REMS program, with the removal of the in-person dispensing requirement and the addition of a requirement for pharmacy certification, will continue to ensure the benefits of mifepristone for medical abortion outweigh the risks while minimizing the burden imposed by the REMS on healthcare providers and patients. As modified, the REMS would allow, for example, dispensing by mail order or specialty pharmacies, similar to the distribution model used by applicants during the periods when the in-person dispensing requirement was not being enforced.[aa]

The above recommendations were discussed with the (b) (6) ((b) (6) and senior leadership from CDER on November 2, 2021. The (b) (6) (b) (6) along with senior CDER leadership, concurred with removing the in-person dispensing requirement provided that all of the remaining REMS requirements are met, including but not limited to prescriber certification where prescribers need to attest to having certain qualifications, and maintaining the *Patient Agreement Form*. The (b) (6) (b) (6) and senior leadership from CDER were also in favor of adding pharmacy certification to assure the safe use of mifepristone.

5. Conclusions and Recommendations

Based on the results of REMS assessments; our review of safety data collected during the PHE as well as data from FAERS; our literature search; and information provided by advocacy groups, individuals, the Applicants, and the plaintiffs in the *Chelius v. Becerra* litigation, (b) (6) and (b) (6) have concluded that a REMS modification is necessary and should include the following changes:

- Removing the requirement under ETASU C that mifepristone be dispensed only in certain healthcare settings, specifically clinics, medical offices, and hospitals.
- Adding a requirement under ETASU B that pharmacies that dispense the drug be specially certified.

[aa] Our current conclusion that the REMS would allow dispensing by mail order or specialty pharmacies is based on data received from Applicants relating to the periods when the in-person dispensing requirement was not enforced and mail-order pharmacies were used to dispense the product, as well as our analysis of postmarketing safety data and available literature. At this time we do not have data (from the Applicants or from other sources) to assess the certification of retail pharmacies under the REMS. We have not yet determined the details of pharmacy certification requirements, including whether any limitations on the types of pharmacies that may dispense the product are necessary.

(b) (6) and (b) (6) recommend the Applicants be issued a REMS Modification Notification Letter that requests submission within 120 days from the date of the letter.

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7. Appendix A

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Schummers L et al, Contraception 2020; 102(4): 273	Abstract
Upadhyay UD et al.) Obstet & Gynecol 2015; 125: 175	Published prior to March 29, 2016-July 26, 2021 timeframe for current literature review. We note that the extensive literature review conducted as part of the 2016 review, which was consistent with the division's standard approach for reviewing an efficacy supplement

Reference ID: 4905882

	and encompassed 90 references, did not capture this publication. However, the authors' conclusion in this publication is consistent with our review of the safety data in 2016.
Kapp N et al. Best Pract Clin Obstet Gynaecol. 2020;63:37-44	Abstract. Also outside the scope of first trimester medical abortion.
Fuentes L et al. J Women's Health 2019; 28 (12): 1623, 1625 Bearak JM, Lancet Pub Health 2017 Nov;2(11): e493, e495-96 Cartwright A et al 20 J Med Internet Res 2018 20(5):e10235 Barr-Walker J, et al PLoS One 2019;14(4): e0209991 Grossman et al JAMA Network 2017;317(4):437, 437-438 Dobie S et al 31 Fam Plan Persp 1999; 31(5): 241-244 Shelton JD 8 Fam Plan Persp 1976; 8(6):260, 260-262 Norris AH et al Am J Pub Health 2020; 110 (8): 1228,1232 Upadhyay UD et al Am J Pub Health 2014; 104(9):1687, 1689	Focused on the logistics of accessing abortion care.
CDC MMWR Abortion Surveillance – United States, 2018 https://www.cdc.gov/mmwr/volumes/69/ss/ss6907a1.htm#T5_down	Contains primarily general statistics on abortion care by state.

References cited in appendix from *Chelius v. Becerra* Plaintiffs (September 29, 2021)
References included in the REMS review
None

Reference ID: 4905882

References excluded from the REMS review	Rationale for Exclusion
Jones RK et al Guttmacher Institute Abortion Incidence and Service Availability in the United States, 2017 (2019) Guttmacher Inst, Induced Abortion in the United States (2019)	Contains primarily general statistics on abortion care and logistics of accessing abortion care.
University of Minnesota Healthy Youth Dev. Prevention Rsch Ctr, 2019 Minnesota Adolescent Sexual Health Report 3 (2019)	Not related specifically to abortion care.
Jerman J et al Guttmacher Inst, Characteristics of U.S. Abortion Patients in 2014 and Changes since 2008 (2016)	Contains figures on patient characteristics from 2008-2014.
Roberts CM et al Women's Health Issues 2014; 24:e211, e215	Focused on cost of abortion.
CDC MMWR Abortion Surveillance 2018 https://www.cdc.gov/mmwr/volumes/69/ss/ss6907a1.htm#T7 down (last updated Nov. 7, 2020)	Contains primarily statistics on number of abortions in the US.
Jones RK Persp on Sexual & Reprod Health 2017; 49:17, 20	Focused on abortion incidence and service availability.
Fuentes L et al (as above) Bearak JM et al (as above) Cartwright A et al (as above) Johns NE et al. BMC Health Serv Res 2017; 17: 287, 294	Focused on logistics of accessing abortion care.

References cited in letter from Society of Family Planning (August 11, 2021)
References included in the REMS review
Grossman D. Obstet Gynecol 2019;133 (3): 477-483

Grossman D et al. Obstet Gynecol 2021; 137 (4): 613-622.	
Winikoff B et al. Obstet Gynecol 2012; 120: 1070-1076 reviewed in 2016 clinical memo	
Chen MJ et al. Obstet Gynecol 2015;126(1):12-21 reviewed in 2016 memo	
Chong et al. Contraception 2021;104(1): 43-48	
Aiken A et al. BJOG 2021; 128 (9): 1464 -1474	
Hyland 2018 et al. Aust New Zeal J Obstet Gynaecol 2018; 58 (3): 335-340	
References excluded from the REMS review	**Rationale for Exclusion**
Schummers L et al. BMJ Sex Reprod Heal 2021;47(e1)	Abstract
Kapp et al. 2020 (as above)	Abstract
Upadhyay et al. 2015 (as above)	(See rationale above)
Srinivasulu et al. Contraception 2021; 104(1):92-97	Survey on clinician perspectives on access to mifepristone.
Calloway D et al. Contraception 2021; 104(1): 24-28	Primarily addresses provider stigma around abortion care.
Rasmussen et al. Contraception; 104(1): 98-103	Opinion/commentary
Cleland et al. Obstet Gynecol 2013;121(1):166-171	Published prior to March 29, 2016 - July 26, 2021 timeframe for current literature review. We note that the extensive literature search conducted as part of the 2016 clinical review, which was consistent with the division's standard approach for reviewing an efficacy supplement and encompassed 90 references, did not capture this publication. However, the authors' conclusion in this publication is consistent with our review of the safety data in 2016.
National Academy of Sciences, Engineering, and Medicine. Safety and Quality of Abortion Care in the US 2018	General information about abortion care in the US. Did not provide safety data relevant to the elements of the REMS
Raymond EG. Obstet Gynecol 2012: 119(2): 215-219	Does not separate out medical and surgical abortion.

Bartlett LA et al. Obstet Gynecol 2004; 103(4): 729-737	Focused on surgical abortion.
Jones RK, Jerman J. Time to appointment and delays in accessing care among U.S. abortion patients, Guttmacher 2016	Focused on logistics of accessing abortion care.
Foster DG et al. Perspect Sex Reprod Health 2013; 45(4):210-218	Focused on second trimester abortion.
Ely G et al. Heal Soc Work 2019;44(1):13-21	Focused on logistics of accessing abortion care.
Munro S et al. Ann Fam Med 2020; 18(5):413-421.	Survey on physician perspectives on implementing medical abortion with mifepristone.

EXHIBIT 2

FDA Adverse Events Reporting System
(FAERS) Public Dashboard

FDA Adverse Events Reporting System (FAERS) Public Dashboard

The FAERS public dashboard is a new, user-friendly and interactive web-based tool that was created to give the public the ability to query the FDA FAERS database and improve transparency. The data presented in the FAERS public dashboard has several key limitations. The existence of adverse event reports for a drug or biologic in FAERS does not mean that the drug or biologic caused the adverse event. Importantly, the FAERS data is not an indicator of the safety profile of the drug or biologic. For more information, please refer to the question What points should I consider while viewing the dashboard content?

Frequently Asked Questions (FAQs)

Expand all | Collapse all

General Questions

− What is FAERS?

The FDA Adverse Event Reporting System (FAERS) is a database that contains adverse event reports, medication error reports and product quality complaints resulting in adverse events that were submitted to FDA. The database is designed to support the FDA's post-marketing safety surveillance program for drug and therapeutic biologic products. The informatic structure of the FAERS database adheres to the international safety reporting guidance issued by the International Conference on Harmonisation (ICH E2B). Adverse events and medication errors are coded using terms in the Medical Dictionary for Regulatory Activities (MedDRA) terminology.

− How does FDA use the information in FAERS?

FAERS is a useful tool for FDA for activities such as looking for new safety concerns that might be related to a marketed product, evaluating a manufacturer's compliance to reporting regulations and responding to outside requests for information. The reports in FAERS are evaluated by clinical reviewers, in the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER), to monitor the safety of products after they are approved by FDA.

If a potential safety concern is identified in FAERS, further evaluation is performed. Further evaluation might include conducting studies using other large databases, such as those available in the Sentinel System. Based on an evaluation of the potential safety concern, FDA may take regulatory action(s) to improve product safety and protect the public health, such as updating a product's labeling information, restricting the use of the drug, communicating new safety information to the public, or, in rare cases, removing a product from the market.

− Who sends reports to FAERS?

Healthcare professionals, consumers, and manufacturers submit reports to FAERS. FDA receives voluntary reports directly from healthcare professionals (such as physicians, pharmacists, nurses and others) and consumers (such as patients, family members, lawyers and others). Healthcare professionals and consumers may also report to the products' manufacturers. If a manufacturer receives a report from a healthcare professional or consumer, it is required to send the report to FDA as specified by regulations.

− How can I report an adverse event or medication error to FDA?

The MedWatch website provides information about voluntary and mandatory reporting.

− Can mandatory reporters submit adverse events electronically?

Yes, the FDA Adverse Events Reporting System (FAERS) Electronic Submissions website provides drug and therapeutic biological product manufacturers, distributors, packers, and other interested parties with information about FDA Adverse Event Reporting System (FAERS) electronic submissions and instructions on how to electronically submit post-marketing individual case safety reports (ICSRs), with and without attachments.

− Does FAERS data have limitations?

Yes, FAERS data does have limitations. First, there is no certainty that the reported event (adverse event or medication error) was due to the product. FDA does not require that a causal relationship between a product and event be proven, and reports do not always contain enough detail to properly evaluate an event. Furthermore, FDA does not receive reports for every adverse event or medication error that occurs with a product. Many factors can influence whether an event will be reported, such as the time a product has been marketed and publicity about an event. There are also duplicate reports where the same report was submitted by a consumer and by the sponsor. Therefore, FAERS data cannot be used to calculate the incidence of an adverse event or medication error in the U.S. population. For more information, please refer to the question What points should I consider while viewing the dashboard content?

− Is FAERS data available to the public?

FAERS data is available to the public in the following ways:

- FAERS dashboard: a highly interactive web-based tool that allows for the querying of FAERS data in a user friendly fashion.
- FAERS data files: provides raw data consisting of individual case safety reports extracted from the FAERS database. A simple search of FAERS data cannot be performed with these files by persons who are not familiar with the creation of relational databases.
- Individual case safety reports from the FAERS database can also be obtained by sending a Freedom of Information (FOI) request to FDA.

– How do I find or confirm my report is in FAERS?

To confirm that your report is in FAERS, please send a Freedom of Information (FOI) request to FDA.

– What are the benefits of the FAERS public dashboard?

This tool makes the data easier to query and produces user-friendly information and charts. For example, users can view a summary of adverse event reports received from 1968 to the present or for a specific timeframe. In addition, users can search for products or reactions of interest within a specific timeframe.

– Will there be a tutorial so I can learn how to use this database?

Yes, a recorded webinar is available which reviews the capabilities, and limitations, of the FAERS public dashboard.

Please note that a new webinar addressing the version 2.0 updates to the FAERS Public dashboard will be available soon.

– Is the FAERS public dashboard accessible on an Android™ or iPhone®?

Yes, but the user interface layout may not be very user friendly. FDA will continue to work on the dashboard to make the user interface Android and iPhone friendly.

– Can I download my search results from the dashboard?

Yes, you will be able to export a limited set of search data to an Excel® spreadsheet and then download it. FDA will still continue to provide the FAERS Latest Quarterly Data Files online.

– Where else can I find safety information?

- Potential Signals of Serious Risks/New Safety Information Identified from the FDA Adverse Event Reporting System (FAERS): quarterly reports on potential serious side effects identified by FAERS.
- Post-marketing Drug and Biologic Safety Evaluations: provides summary information about ongoing and completed post-marketing safety evaluations of adverse experience reports made to FDA for New Drug Applications (NDAs) and Biologic License Applications (BLAs) approved since September 27, 2007.
- Center for Drug Evaluation and Research (CDER): Drug Safety and Availability
- Post-market Drug Safety Information for Patients and Providers
- MedWatch: The FDA Safety Information and Adverse Event Reporting Program

– How are versions of a case in FAERS handled?

Each unique submission of a case received is assigned a version number (for example, Case #1234567, version 1). The initial version received will be version 1. If a follow up is received on a previously submitted case, then that version of the case will be version 2, and so on. The latest version of a case represents the most current information about that case.

– How frequently is the data in the FAERS public dashboard updated?

The data is updated quarterly. Dates for upcoming dashboard updates are shown below:

Quarter	Estimated data update
Q1 – 2019 (January – March)	*Updated on 8-May-2019*
Q2 – 2019 (April – June)	*Updated on 1-Aug-2019*
Q3 – 2019 (July – September)	*Updated on 7-Nov-2019*
Q4 – 2019 (October – December)	*Updated on 5-Feb-2019*
Q1 – 2020 (January – March)	*Updated on 30-Apr-2020*
Q2 – 2020 (April – June)	*Updated on 4-Aug-2020*
Q3 – 2020 (July – September)	*Updated on 17-Nov-2020*
Q4 – 2020 (October – December)	*Updated on 29-Jan-2021*
Q1 – 2021 (January – March)	*Updated on 10-May-2021*
Q2 – 2021 (April – June)	*Updated on 3-Aug-2021*
Q3 – 2021 (July – September)	*Updated on 4-Nov-2021*
Q4 – 2021 (October – December)	*Updated on 15-Feb-2022*
Q1 – 2022 (January – March)	*Updated on 2-May-2022*
Q2 – 2022 (April – June)	*Updated on 1-Aug-2022*
Q3 – 2022 (July – September)	*Updated on 4-Nov-2022*
Q4 – 2022 (October – December)	*Updated on 30-Jan-2023*
Q1 – 2023 (January – March)	*Updated on 27-Jan-2023*
Q2 – 2023 (April – June)	*Updated on 1-Aug-2023*
Q3 – 2023 (July – September)	*Updated on 2-Nov-2023*
Q4 – 2023 (October – December)	*Updated on 23-Jan-2024*
Q1 – 2024 (January – March)	*Updated on 22-Apr-2024*
Q2 – 2024 (April – June)	*Updated on 30-Jul-2024*
Q3 – 2024 (July – September)	*Updated on 30-Oct-2024*

Q4 – 2024 (October – December)	*Updated on 28-Jan-2025*
Q1 – 2025 (January – March)	*Updated on 28-Apr-2025*
Q2 – 2025 (April – June)	30-July-2025

– What points should I consider while viewing the dashboard content?

When you view the website output of reported reactions (side effects or adverse drug reactions) for a drug product, it is important to consider the following points:

- **Data Quality:** There are many instances of duplicative reports and some reports do not contain all the necessary information. Duplicate reporting occurs when the same report is submitted by the consumer and the sponsor. The information in FAERS evolves daily and the number of individual cases may increase or decrease. It is therefore possible that the information on this website may change over time.
- **Existence of a report does not establish causation:** For any given report, there is no certainty that a suspected drug caused the reaction. While consumers and healthcare professionals are encouraged to report adverse events, the reaction may have been related to the underlying disease being treated, or caused by some other drug being taken concurrently, or occurred for other reasons. The information in these reports reflects only the reporter's observations and opinions.
- **Information in reports has not been verified:** Submission of a report does not mean that the information included in it has been medically confirmed nor is it necessarily a conclusion from the reporter that the drug caused or contributed to the event.
- **Rates of occurrence cannot be established with reports:** The number of suspected reactions in FAERS should not be used to determine the likelihood of a side effect occurring. The FDA does not receive reports for every adverse event or medication error that occurs with a product. Many factors can influence whether an event will be reported, such as the time a product has been marketed and publicity about an event. Therefore, information in these reports cannot be used to estimate the incidence (occurrence rates) of the reactions reported.
- **Patients should talk to their doctor** before stopping or changing how they take their medications.
- **Patient Outcomes received in FAERS**: These data describe the outcome of the patient as defined in U.S. reporting regulations (21 CFR 310.305, 314.80, 314.98, 600.80). Serious means that one or more of the following outcomes were documented in the report: death, hospitalization, life-threatening, disability, congenital anomaly, and/or other serious outcome. Documenting one or more of these outcomes in a report does not necessarily mean that the suspect product(s) named in the report was the cause of the outcomes.

Importantly, the FAERS data by themselves are not an indicator of the safety profile of the drug.

Back to top

Data Questions

– How do I know if a side effect I saw on the dashboard is related to the drug I was taking?

The best sources of information for the known side effects of a drug are the FDA approved product information (also known as full prescribing information or US package insert) and your health care provider. This dashboard tells you what was reported to the FDA, but it is difficult to know what caused a particular event in a particular patient from the information on the dashboard. Even if a symptom is a known side effect for a drug, it can be difficult to know if the symptom that a patient had was caused by a particular drug, since there may be other possible causes as well. For example, some medications cause headaches, but many people have headaches even when they aren't on any medications.

– If an adverse event wasn't caused by a drug, what could have caused it?

Although some adverse events can be caused by a drug, there are also other possible explanations for symptoms that appear while a patient is taking a drug. For example, the adverse event could be related to a disease that a patient already has, something in the environment, diet, or sleep habits, to name a few, could cause symptoms that could be misinterpreted as adverse events caused by a drug.

– Is every adverse event reported with a drug on the dashboard caused by the drug?

Although it is difficult to generalize, it is unlikely that every adverse event reported for a given drug was caused by that drug.

– Are drugs with fewer side effects reported to the dashboard safer than those that have a higher number of side effects reported?

The FAERS dashboard should not be used to determine the safety profile of one drug compared to another. Even identical drug products can have widely differing levels of adverse event reporting due to the voluntary nature of the reporting system.

– How should reports of death be interpreted?

The same caution that applies to all of the FAERS reports, should be applied to death reports. The existence of a death report in the FAERS dashboard does not mean that the drug caused the person to die. Fatal outcome could be from the natural progression of the disease being treated.

– Does the FAERS Dashboard have all the side effects that have occurred with a drug?

No. The FAERS database contains only a small fraction of the side effects that occur with a drug. This is due to a variety of reasons. Most importantly, there is no requirement for healthcare professionals and consumers to report side effects to either the FDA or to the manufacturer. Even for side effects that have been reported to the manufacturer, only certain categories of adverse events are required to be submitted to the FDA. Lastly, there are a variety of factors that can cause more or less reporting to both the FDA and manufacturers, including whether a particular side effect is known for a drug, how long a drug has been on the market and even whether there have been recent news reports about possible side effects for a given drug or a group of drugs.

– What is the difference between an adverse event, a side effect, and an adverse drug reaction?

An adverse event (AE) is any symptom that occurs while taking a drug, which may or may not have been caused by the drug. This is different from an adverse drug reaction (ADR), where there is specific evidence that the AE is related to the drug. A side effect is the same as an ADR. As a result, ADR is always an AE, but an AE may or may not be an ADR.

– Should I discontinue a prescription drug I'm taking if I think that it's causing an adverse event?

You should always check with your healthcare provider before discontinuing any medication that you have been prescribed.

– I looked up a drug that I am taking on the FAERS dashboard and the list of adverse events includes deaths. What should I do?

You should check with your healthcare provider if you have any concerns about a medication that you are taking. You and your healthcare provider should decide if the potential benefits of you taking a particular drug outweigh its potential risks as well as the risks of an illness being left untreated.

– Where can I find the safety profile of the drug?

Please consult with your health care provider to discuss the safety profile and the overall benefit-safety balance of the drug.

– After the data refresh for Q4 2021, why do I now see reduced counts in the Home page for previous time periods (Q3 2021 and older)?

The **Home** page displays the count of reports received each year and quarter by the FDA. This includes both initial and follow-ups reports submitted in FAERS.
In Q4 2021, the FAERS system was modernized and the data was migrated to a new database. The new database handles deletion of report submissions slightly differently compared to the previous system. Whenever a case is deleted, the previous system deleted only the latest follow-up report for the case and left the older reports in the case untouched. As a result, the counts displayed in the **Home** page included older reports for deleted cases. However, in the new FAERS database currently in use, all reports (initial and follow-ups) for a case are deleted upon the deletion of a case. Because of this, the counts of reports displayed in the **Home** page are now reduced compared to previous iterations of the FAERS Public Dashboard.

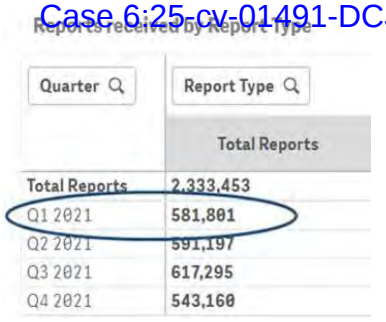
As an example, the comparison below highlights the difference in counts of reports for Q1 2021 before and after the data refresh for Q4 2021.

Q1 2021 report count before the data refresh for Q4 2021:

Reports received by Report Type

Quarter	Report Type	Total Reports
Total Reports		1,801,429
Q1 2021		587,876
Q2 2021		593,598
Q3 2021		619,955

Q1 2021 report count after the data refresh for Q4 2021:



Back to top

Technical Questions

− Which internet browsers can I use to access the dashboard?

You can use any of the following internet browsers to access and view the dashboard:
Microsoft Internet Explorer 11, Microsoft Edge, Google Chrome, Mozilla Firefox, Apple Safari.

− What is the recommended screen resolution for viewing the dashboard?

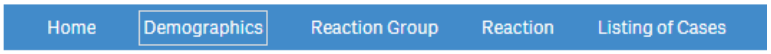
For the best dashboard viewing experience, the recommended screen resolution for your desktop or laptop is 1920x1080.

− How do I navigate through different sheets of the dashboard?

You may use the navigation bar on the top of the dashboard to navigate through different sheets. Depending on the sheet you are currently viewing, you may see different options to select in the navigation bar.

When viewing the “Home” or “Search” sheets, you will see the options shown below in the navigation bar.

When viewing any other page in the dashboard after searching for a product, you will see the options shown below.

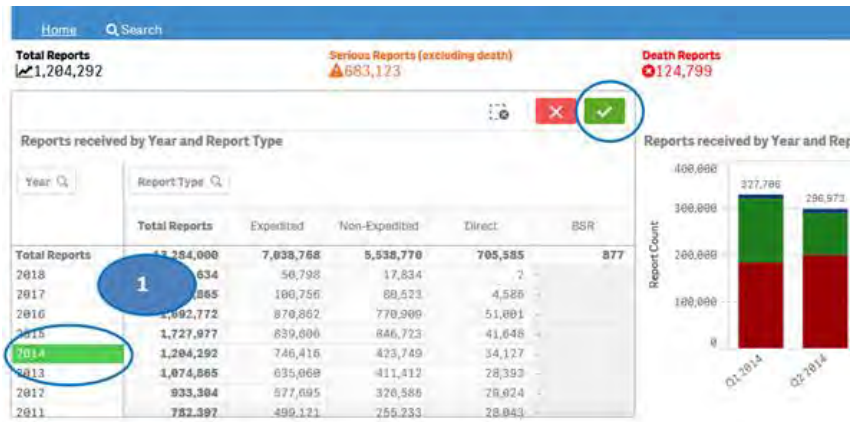


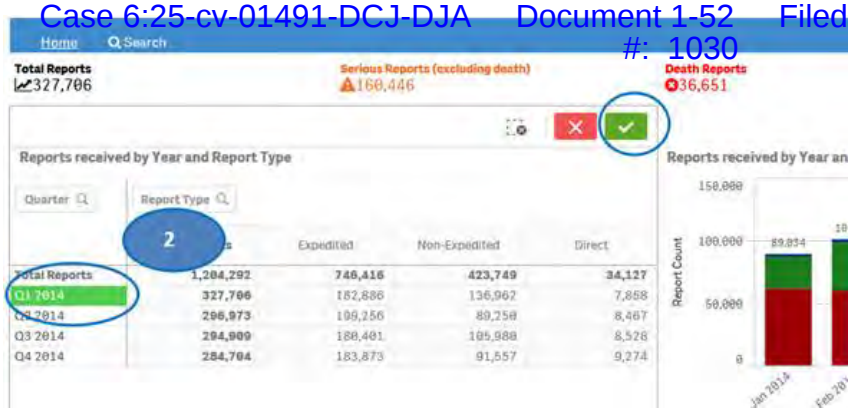
− How can I view report statistics for quarters and months of a specific year?

The “Home” sheet displays report statistics for all the years by default. But you may view report statistics for quarters and months of any specific year. You can view statistics for quarters of only one year at time. You can view statistics for months of only one quarter at a time.

1. Click on any year in the table or chart and confirm selection to view statistics for the year by quarters.
2. Then select any quarter by clicking on it to view statistics for the months of the selected quarter.
3. Clear the selected quarter to go back to view statistics by quarters.
4. Clear the year selection to go back to view statistics for all year.

Note: If a year has just one quarter of data, selecting the year will directly display months for the year without displaying quarters.





− How do I search for cases for a product or products?

After accepting the disclaimer, click on the “Search” option and then:

1. Type a product value in the search bar.
2. Click or double-click on a desired value from the list of values to select it.
3. The selected product will be displayed under the list “Selected Products”.
4. To clear the search text, click on the ‘X’ button in the right corner of the search bar.
5. If you want to add more products to your search, repeat the steps above for the products you are interested in. You may select up to five products for your search.
6. If you want to deselect a product you have already selected, click or double-click on the product you want to deselect from the list “Selected Products”.
7. Once you have selected all the products you want to search for, click on the “Go” button.

Please note that you can select no more than five products at a time for your search.

– Can I search for generic products as well as specific trade names?

es. You can search for a generic product or a specific trade name by simply typing the name in the search bar. The search box pop-p includes icons to indicate whether a suggested product is a trade name or a generic product based on FDA's internal product ctionary.

- P indicates that the suggested value is a product name or trade name.
- G indicates that the suggested value is a generic product.

– How can I change my product search?

f you have already done a product search, the navigation bar will display a search box where you can type in and select new products or your search.

Back to top

– Does FAERS include over-the-counter (OTC) or just prescription drugs?

FAERS includes both OTC and prescription drugs.

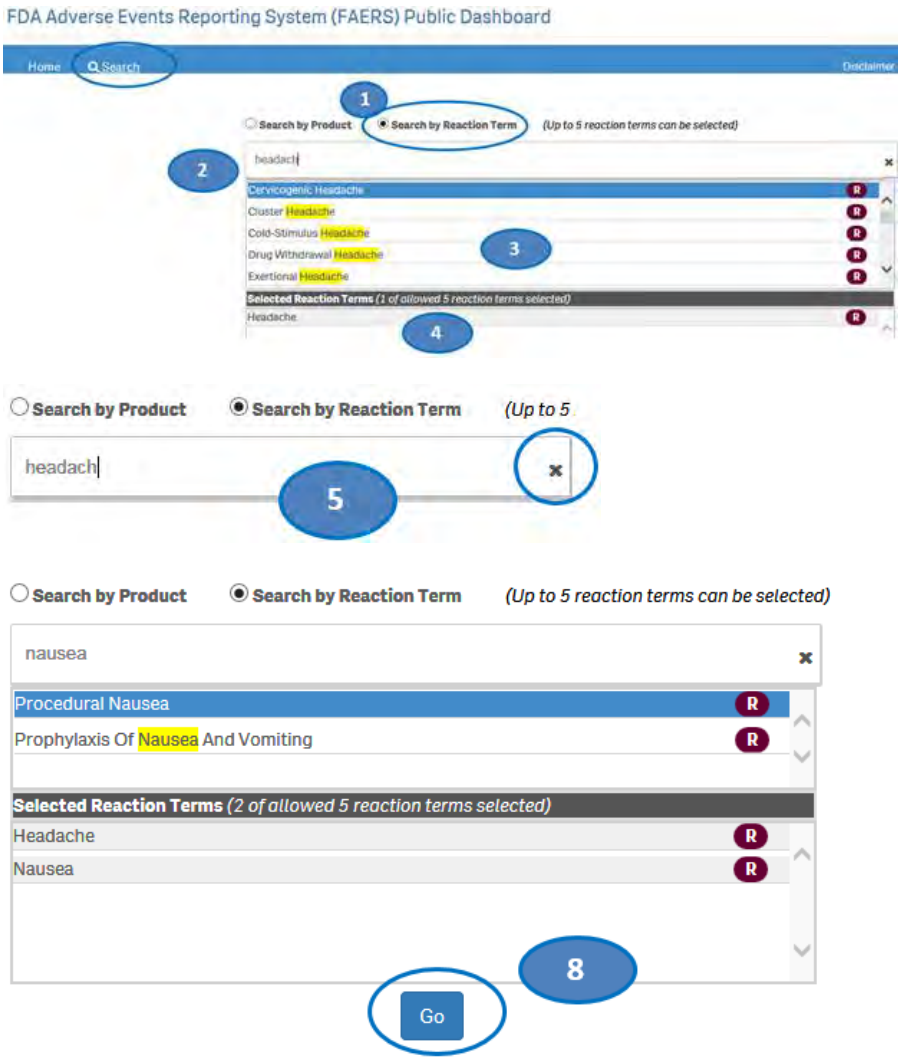
– How can I search for cases for specific side effects/reactions?

From the "Home" sheet, click on the "Search" option and then:

1. Select option "Search by Reaction Term".
2. Type a reaction term value in the search bar.
3. Click or double-click on a desired value from the list of values to select it.
4. The selected reaction term will be displayed under the list "Selected Reactions".
5. To clear the search text, click on the 'X' button in the right corner of the search bar.
6. If you want to add more reactions to your search, repeat the steps above for the reactions you are interested in. You may select up to five reactions for your search.

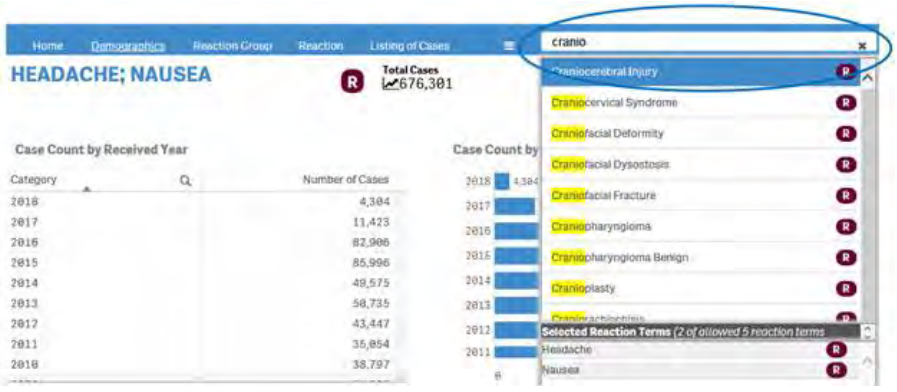
7. If you want to deselect a reaction you have already selected, click or double-click on the reaction you want to deselect from the list “Selected Reactions”.
8. Once you have selected all the reactions you want to search for, click on the “Go” button.

Please note that you can select no more than five reaction terms at a time for your search.



− How can I change my reaction search?

If you have already done a reaction search, the navigation bar will display a search box where you can type in and select new reactions for your search.



− What can I search for using the search box in the navigation bar?

Depending on your initial search, you can use the search box in the navigation to search for either products or reactions terms.

If your initial search in the “Search” sheet was based on product(s), you can only search for products in the search box of the navigation bar.

If your initial search in the "Search" sheet was based on reaction term(s), you can only search for reaction terms in the search box of the navigation bar.

How many products or reactions can I search for at a time?

You can select up to five products or reactions at a time for a search.

Note: This restriction is applicable for products and reactions only. Multiple value selections can be made for all other data elements such as sex, country, and outcomes.

Does the "Search" sheet allow selecting products and reactions for the same search?

No, the search sheet allows you to select either products or reactions for your search but not both. For example, if you select specific products using the "Search by Product" option and then choose the "Search by Reaction Term" option, the products you have selected will be removed from the search.

You may, however, filter for products and reactions after your initial search in subsequent sheets.

How can I view the distribution of report or case counts for different parameters?

To view distribution of counts for different parameters, click on the drop-down menu on the top right corner of a sheet and select the desired option.

Can I view charts and tables in full screen mode? How do I exit from full screen mode?

When you hover over any chart or table, a symbol is displayed on the right top corner of the chart or table. Clicking on this icon will enable you to view the chart or table in full screen mode. To exit the full screen mode, click the X on the top right corner of the chart or table.

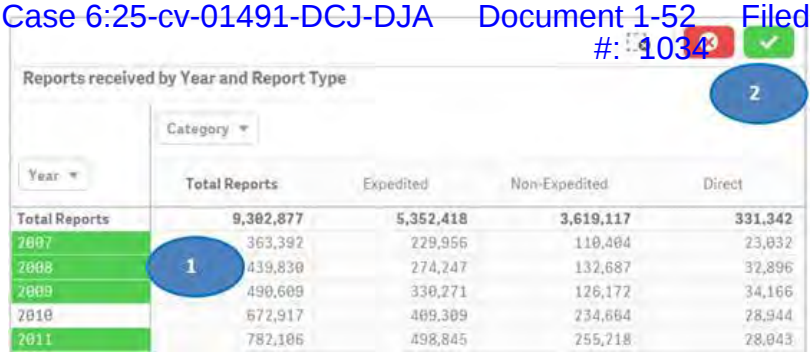
Can I filter data in charts and tables?

Yes, the dashboard provides extensive filtering capabilities on both charts and tables.

Note: When you apply filters on a table or chart within the "Home" sheet, the filters will be applied only on charts and tables in this sheet. Conversely, when you apply filters on tables or charts in any other sheet, after searching for a product, the filters will be applied on all sheets except for the "Home" sheet.

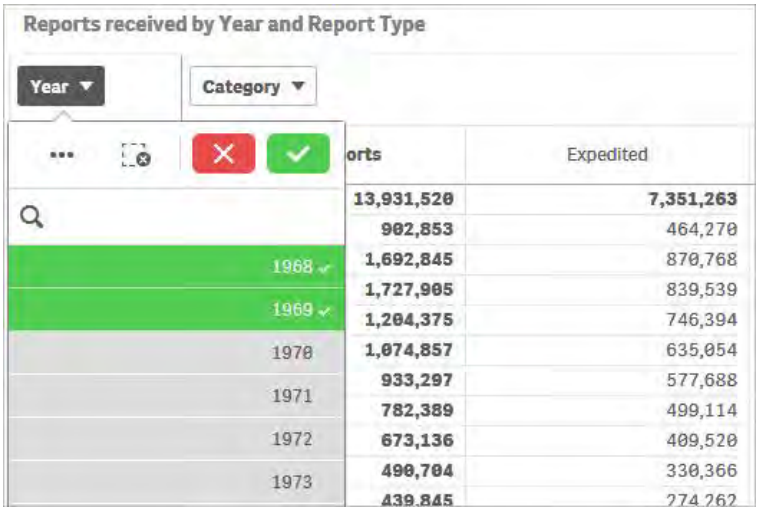
To filter data in a table, for example, filtering by year, there are two options:
Option 1:

1. Click on one or multiple columns or rows. You may also click and drag multiple rows or columns to select them for filtering data.
2. Click on the icon to confirm your selection.



Option 2:

You may also use drop-downs (also known as filter panes) displayed on top of the rows or columns to choose your values for filtering. Please see screenshot below which shows how to select specific years for filtering.



To filter data in a chart, for example, filtering by year, there are two options:

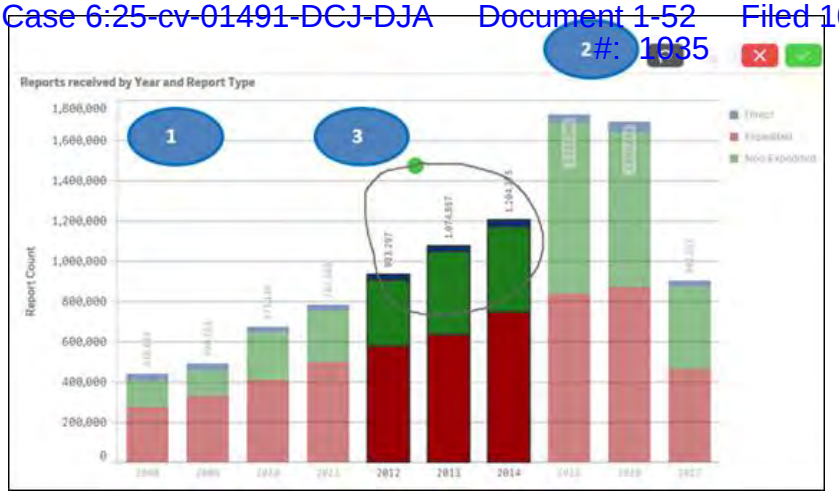
Option 1:

1. Click on one or multiple bars in the chart or items in the chart legend. You may also click and drag multiple bars to select them for filtering data.
2. Click on the ✓ button to confirm your selection.

Option 2:

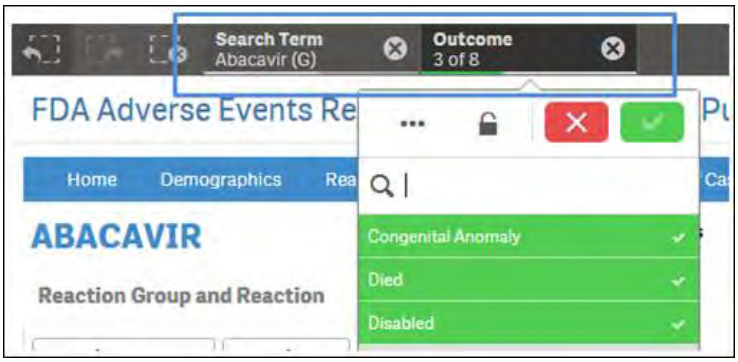
You may also use “lasso selection tool” to select multiple values from the chart. To use this feature:

1. Click anywhere on the chart.
2. Click on the lasso icon.
3. Click and drag to draw on the chart and select the bars you want to use for filtering.



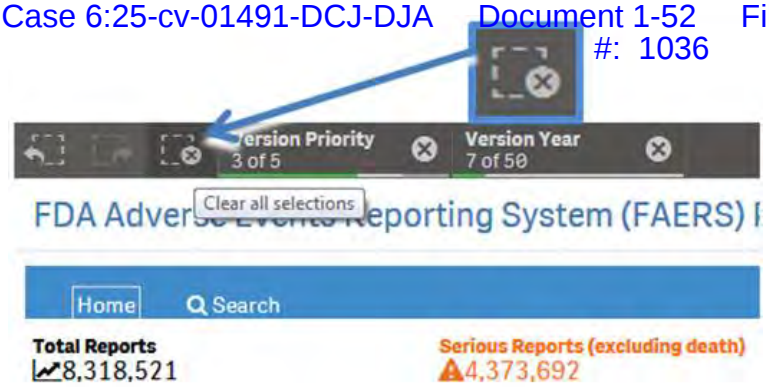
You may also select values from a chart's legend for filtering by clicking on the values.

Note that the applied filters show up on the top selection bar.



– How do I reset selected search criteria and remove all filters?

On the top left side of every sheet, you can see the icon shown below, with a dotted lined square with an "X" on it. Click the icon to clear any product you have selected for searching and all selected values used for filtering.



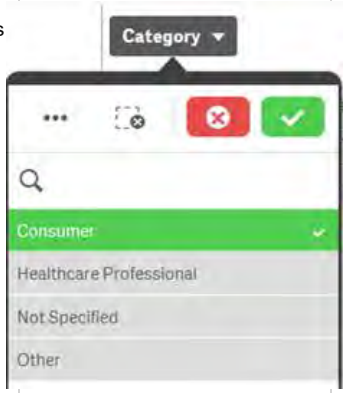
– Can I extract or download dashboard data?

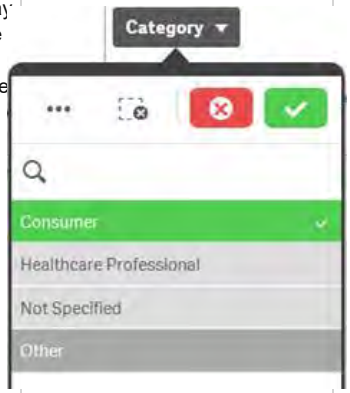
Yes, you may export or download dashboard data. Right-click on any table or chart in the dashboard and click on the “Export” option. You may choose from the following three options for exporting and downloading data:

1. Export as an image: This option will export a snapshot of the table or chart that you are viewing to an image file.
2. Export to PDF: This option will export a snapshot of the table or chart that you are viewing to a PDF file.
3. Export data: This option will export the underlying data of the table or chart that you are viewing to a Microsoft Excel (.xlsx) file. This option is explained in more detail in the final question of the FAQs below.

Back to top

– When using filter panes (or drop-downs) for filtering, I have noticed that different colors are used to highlight different values. What do these colors indicate?

Action	Color Code	Description	Screenshot
Selected	Green, with a check mark as a selection indicator	When you select one or more values in a filter pane and the values turn green, they are in the selected state. In the example screenshot, the value “Consumer” has been selected.	
Possible	White	In the screenshot of the “Category” filter pane for “Reporter Region”, the values “Domestic” and “Foreign” are white (possible), because selecting these values will return data. You could refine your data set by selecting one or more of these possible values.	

Action	Color Code	Description	Screenshot
Alternative	Light gray	Selecting a light gray value will add to the previously selected value to broaden the filtering.	
Excluded	Dark gray	Dark gray value indicates that there is no data for the specific value based on other filters that have already been applied to the data. Caution: Selecting a dark gray value: • May clear some or all other existing filters and apply that value as the new filter. • May cause the selected product to be removed. If that happens, restart your search using the Search for Product option in the navigation bar.	

– Can I use the dashboard without accepting the disclaimer?

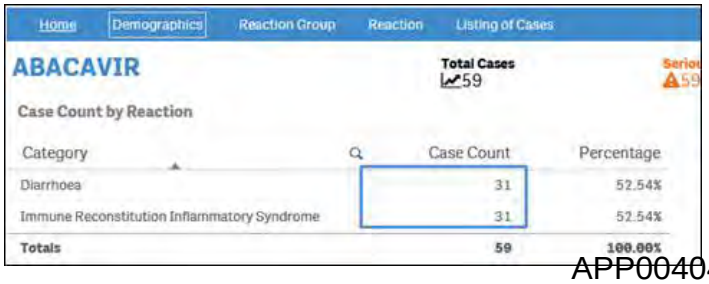
No. You will not be able to view any data in the dashboard without accepting the disclaimer.

– How recent is the data in the dashboard?

Data in the FAERS Public Dashboard is as of March 31, 2025. Data is updated quarterly.

– Why does the sum of case counts for individual reactions not add up to the overall case count for the product?

Each case might have more than one reaction term. Therefore, the sum of the case counts for individual reactions may be same or more than the total count of distinct cases.



– Why does the sum of individual outcome counts not add up to the overall count for the product?

Each case might have more than one outcome. Therefore, the sum of counts for individual outcomes may not match the total count of distinct cases.

– How do I scroll in the “Listing of Cases” table?

The “Listing of Cases” table allows you to scroll vertically or horizontally using vertical and horizontal scroll bars respectively. To view the scroll bars, hover over the listing of cases table.

- Scroll up or down in the Listing of Cases table using the vertical scroll bar on the right side of the table. This will allow you to see all the rows in the table.
- Scroll to the left or right in the Listing of Cases table using the horizontal scroll bar on the bottom of the table. This will allow you to see all the columns in the table.

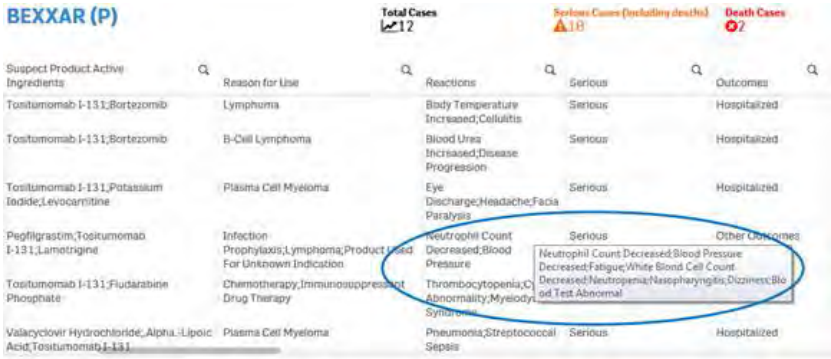
– Can I rearrange columns in the “Listing of Cases” table?

Yes, you may rearrange columns by dragging and dropping column headers anywhere in the table. To move a particular column:

1. Click and hold on the column header.
2. Drag it next to a column you want to move it to and release the click.

– Some of the cells seem to be showing only partial data. How can I see the entire content of such cells?

Due to space constraints, some cells display only partial data. To view the entire content of any cell, simply hover over the cell with your mouse. The entire content of the cell appears in a pop-up.



– How do I filter and sort data in the “Listing of Cases” table?

You can filter and sort data in the table using any column or any value in a cell. To filter using a value in cell, simply click on the cell.

The table is refreshed with the filtered data. To filter using a column, click on the 🔍 icon next to the column header, and then select from the list of values for that column.

To sort data using a specific column, simply click on the column header. Click once on the column header to view data in ascending order. Click again on the column heading to sort the values in descending order.

– How do I download data from the “Listing of Cases” table?

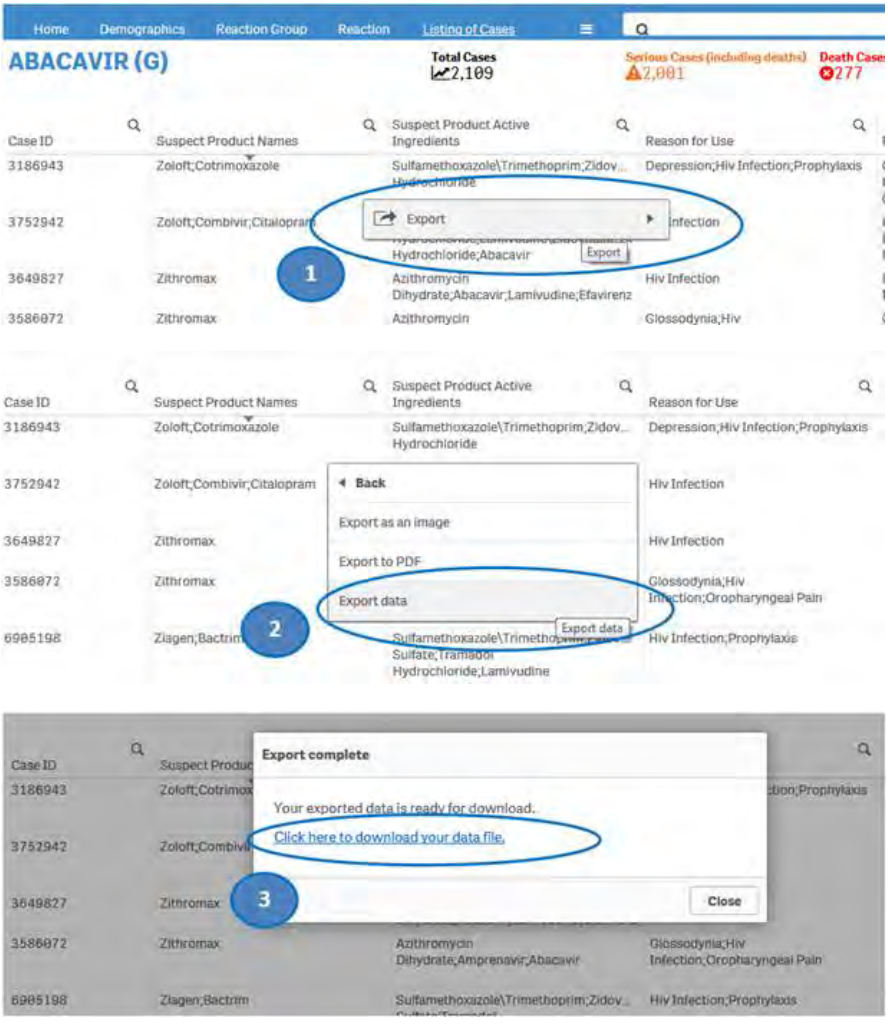
You can download data from the “Listing of Cases” table to a Microsoft Excel (.xlsx) file by using the “Export data” option.

Note: The “Listing of Cases” table provides a limited set of columns for case data. If you require a more comprehensive data set for download, you may download FAERS (FDA Adverse Events Reporting System) Quarterly Data files.

The data displayed in the FAERS Public Dashboard may not be identical to the data in the FAERS Quarterly Data files due to several reasons. Please refer to the Data Questions section for more information.

To download data from the “Listing of Cases” table:

1. Right-click anywhere on the “Listing of Cases” table and click on “Export”.
2. Select “Export data” option.
3. Then click on “Click here to download your data file” to save the file to your machine.



Back to top

EXHIBIT

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Admini tration ffort to Protect Reproducti e ealt
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(Jan. , 2023)

An official website of the United States government

U.S. Department of Health and Human Services
Enhancing the health and well-being of all Americans

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FOR IMMEDIATE RELEASE
January 19, 2023

Contact: HHS Press Office
202-690-6343
media@hhs.gov

HHS Releases Report Detailing Biden-Harris Administration Efforts to Protect Reproductive Health Care Since Dobbs

Sunday Marks 50th Anniversary of Supreme Court's Roe v. Wade Decision

Today, the U.S. Department of Health and Human Services (HHS) released a report entitled: "Marking the 50th Anniversary of Roe: Biden-Harris Administration Efforts to Protect Reproductive Health Care," which outlines the actions HHS has taken in the face of the health crisis precipitated by the *Dobbs* decision, which overturned *Roe v. Wade*.

"On the 50th anniversary of the *Roe v. Wade* decision, abortion, contraception, and other forms of reproductive health care are under attack in our nation like never before because the Supreme Court undermined nearly half a century of precedent protecting women's access to this critical care," said HHS Secretary Xavier Becerra. "As a result, our daughters have fewer rights than their mothers and grandmothers, and women seeking care are being put in dangerous situations with heartbreaking results."

"The Biden-Harris Administration continues to fight shoulder-to-shoulder with women and families who face this frightening new reality in states across the nation. This anniversary reminds us of what America's women lost as a result of the *Dobbs* decision, and of the importance of HHS's work to protect and expand women's access to reproductive health care. Our work won't stop until all women have access to this critical care."

Since *Dobbs,* HHS has worked to protect and expand access to reproductive care amidst unprecedented efforts by Republican officials at the national and state level to restrict access to abortion and contraception. They have taken action using the tools available to them under the Department's jurisdiction in light of the *Dobbs* decision. HHS actions have been centered on six core priorities:

1. **Protecting Access to Abortion Services**

2. **Safeguarding Access to Birth Control**
3. **Protecting Patient Privacy**
4. **Promoting Access to Accurate Information**
5. **Ensuring Non-discrimination in Healthcare Delivery**
6. **Evidence-Based Decision Making at FDA**

A few key actions HHS has taken include:

- Reaffirming the Department's commitment to protecting the right to abortion care in emergency settings under EMTALA.
- Issuing guidance <https://rejouer.perma.cc/replay web page/w/id 55f3852527e2/mp_/https://www.hhs.gov/about/news/2022/07/28/hhs-dol-treasury-issue-guidance-regarding-birth-control-coverage.html> to clarify protections for birth control coverage under the Affordable Care Act.
- Protecting medical privacy by empowering patients to protect their medical information on smart phones and Apps.

The full report can be read at https://www.hhs.gov/sites/default/files/roe-report.pdf - PDF <https://rejouer.perma.cc/replay-web-page/w/id-55f3852527e2/mp_/https://www.hhs.gov/sites/default/files/roe-report.pdf>.

This week, Secretary Becerra will meet with advocates and providers in Wisconsin, a state where abortion care is no longer being provided, and Minnesota, a state where abortion remains legal and legislators recently introduced a bill to codify the right to abortion into state law. During these visits, he will reiterate the Biden-Harris Administration's steadfast commitment to protecting access to reproductive health care, including abortion and contraception.

###

Note: All HHS press releases, fact sheets and other news materials are available at https://www.hhs.gov/news </replay-web-page/w/id-55f3852527e2/mp_/https://www.hhs.gov/news>.
Like HHS on Facebook </replay-web-page/w/id-55f3852527e2/mp_/https://www.hhs.gov/disclaimer.html>, follow HHS on Twitter @HHSgov <https://rejouer.perma.cc/replay-web-page/w/id-55f3852527e2/mp_/https://twitter.com/#!/hhsgov> </replay-web-page/w/id-55f3852527e2/mp_/https://www.hhs.gov/disclaimer.html>, and sign up for HHS Email Updates <https://rejouer.perma.cc/replay-web-page/w/id-55f3852527e2/mp /https://cloud.connect.hhs.gov/subscriptioncenter>.
Last revised: January 19, 2023

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Statement by Secretary Xavier Becerra on the Passing of Former Pan American Health Organization (PAHO) Director, Dr. Carissa F. Etienne </replay-web-page/w/id-55f3852527e2/mp_/https://www.hhs.gov/about/news/2023/12/01/statement-by-secretary-xavier-becerra-passing-former-pan-american-health-organization-director-dr-carissa-f-etienne.html>

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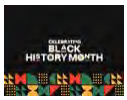

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Media Inquiries

For general media inquiries, please contact media@hhs.gov.

Content created by Assistant Secretary for Public Affairs (ASPA)
Content last reviewed January 19, 2023

EXHIBIT

W ite ou e,
FAC S e iden arri Admini tration
Record on Protecting Acce to Medication Abortion
(Apr. 2, 2023)

APRIL 12, 2023

FACTSHEET: The Biden-Harris Administration's Record on Protecting Access to Medication Abortion

Protecting access to reproductive health care has been a priority since the beginning of the Biden-Harris Administration, made even more urgent by the Supreme Court's decision to overturn Roe v. Wade. The President and Vice President are focused on ensuring access to mifepristone, which the FDA first approved as safe and effective to end early pregnancy more than twenty years ago and which accounts for more than half of abortions in the United States.

Despite this decades-long safety record, a single court in Texas has taken the dangerous step of attempting to override FDA's approval of medication abortion—which is used not only for abortion but also for helping women manage miscarriages. If this decision stands, it will put women's health at risk and undermine FDA's ability to ensure patients have access to safe and effective medications when they need them.

This lawsuit is part of broader efforts to ban abortion nationwide and to prevent women from making their own decisions about their own bodies without government interference.

The Administration is fighting this ruling in the courts, and stands by FDA's scientific and evidence-based judgment that mifepristone is safe and effective. Shortly after the ruling last Friday, the Justice Department filed a notice of appeal to the Fifth Circuit and sought a stay of the injunction pending appeal. A wide range of stakeholders, including FDA scholars, leading medical organizations, and pharmaceutical companies, have expressed their support for maintaining access to this FDA-approved medication.

In addition to defending in court FDA's ability to approve safe and effective medications, the Biden-Harris Administration has taken the following steps to protect access to medication abortion:

- Elevating Medication Abortion in the Administration's Response to the Dobbs Decision. On the day of the Supreme Court's decision to overturn *Roe v. Wade* in June 2022, the President identified preserving access to medication abortion as one of two key priorities to guide the Administration's immediate response to the ruling. President Biden directed the Secretary of the Department of Health and Human Services (HHS) to ensure that mifepristone is as widely accessible as possible in light of the FDA's determination that the drug is safe and effective. He also emphasized the need to protect access to medication abortion in the face of attacks and to stand with medical experts who have stressed that restrictions on medication abortion are not based in science. On the same day, the Attorney General made clear that states may not ban mifepristone, a drug used in medication abortion, based on disagreement with the FDA's expert judgment about its safety and efficacy.

- Issuing an Executive Order to Protect Access to Abortion, including Medication Abortion. In an Executive Order on Protecting Access to Reproductive Healthcare Services issued in July 2022, President Biden reiterated the importance of medication abortion and directed the Secretary of HHS to identify potential actions to protect and expand access to abortion care, including medication abortion. In response, HHS developed an action plan to protect and strengthen access to reproductive care and has made significant progress in executing this plan and protecting access to care nationwide.

- Addressing Barriers to Accessing Care. In his second Executive Order on Securing Access to Reproductive and Other Healthcare Services issued in August 2022, President Biden addressed the challenges that women have faced in accessing prescription medication at pharmacies in the wake of *Dobbs*, including medication abortion, which is also used to manage miscarriages. These included reports of women of reproductive age being denied prescription medication at pharmacies—including medication that is used to treat stomach ulcers, lupus, arthritis, and cancer—due to concerns that these medications, some of which can be used in medication abortion, could be used to terminate a pregnancy. To help ensure access to medication, HHS issued guidance to roughly 60,000 U.S. retail pharmacies to emphasize their obligations under federal civil rights laws to ensure access to comprehensive reproductive health care services.

- Directing Further Efforts to Ensure Safe Access to Medication Abortion. On what would have been the 50th anniversary of *Roe v. Wade* in January 2023, President Biden issued a Presidential Memorandum on Further Efforts to Protect Access to Reproductive Healthcare Services to further protect access to medication abortion. The Presidential Memorandum directed the Attorney General, the Secretary of the Department of Homeland Security, and the Secretary of HHS to consider new actions to protect the safety and security of patients, providers, and pharmacies who wish to legally access or provide mifepristone.

This Presidential Memorandum was issued in the face of attacks by state officials to prevent women from accessing mifepristone and discourage pharmacies from becoming certified to dispense the medication. These attacks, and the Presidential Memorandum, followed independent, evidence-based action taken by FDA to allow mifepristone to continue to be prescribed by telehealth and sent by mail as well as to enable interested pharmacies to become certified.

- Engaging Medical Experts and Reproductive Rights Leaders to Underscore the Need for Medication Abortion. In February 2023, Vice President Harris convened a roundtable of leading medical experts and reproductive rights advocates to discuss how a court decision to invalidate the approval of mifepristone would affect patients and providers. Participants represented Physicians for Reproductive Health, American Medical Women's Association, the Society of Family Planning, the American Academy of Family Physicians, Planned Parenthood of Metropolitan DC, the National Women's Law Center, NARAL Pro-Choice America, the Center for Reproductive Rights, the American College of Obstetricians and Gynecologists, the ACLU, and Sister Song.

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EXHIBIT

S, Secretary Report,
ealt Care nder Attac An Action Plan to Protect
and Strengt en Reproducti e Care
(Aug. 2022)

Secretary's Report

HEALTH CARE UNDER ATTACK

An Action Plan to Protect and Strengthen Reproductive Care

A Report Required by Executive Order 14076

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Version date: August 2022*

* The posted version of the report includes a minor correction, made in November 2022, to avoid confusion.

MESSAGE FROM SECRETARY

For nearly 50 years, women in America lived in a country that guaranteed them the freedom, privacy, and autonomy to control their own bodies. Women could make decisions on their health care in consultation with their physicians, faith leaders, partners, families or whoever they trusted, without interference from a politician or the government.

On June 24, 2022, the Supreme Court of the United States overturned *Roe v. Wade*, a longstanding precedent, undermining women's privacy, autonomy, health and rights. At the Department of Health and Human Services (HHS), we have been preparing for such a decision for some time.

Earlier this year, on the 49th anniversary of *Roe v. Wade*, we launched a Reproductive Healthcare Access Task Force at HHS to plan for every action necessary to protect women's access to reproductive health care in case the unimaginable became a reality. In the time since the Supreme Court ruled in *Dobbs v. Jackson Women's Health,* we have taken several actions to protect Americans' reproductive rights and care:

Protecting Emergency Medical Care: HHS issued guidance[1] and a letter from Secretary Becerra[2] to reaffirm that the Emergency Medical Treatment and Active Labor Act (EMTALA, also known as the Emergency Medical Treatment and Labor Act) protects providers when offering legally-mandated, life- or health-saving abortion services as stabilizing care for emergency medical conditions.[3]

Safeguarding Information on Health and Rights for Patients and Providers: HHS launched the ReproductiveRights.gov public awareness website, [4] which includes accurate information about reproductive health, including a Know-Your-Rights patient fact sheet to help patients and providers.

Protecting Patients and Providers from Discrimination:

- HHS issued a proposed rule that would strengthen the regulations interpreting the nondiscrimination provision of the Affordable Care Act (ACA) and would reinforce that discrimination on the basis of sex includes discrimination on the basis of pregnancy or related conditions.[5]

- HHS issued guidance to roughly 60,000 U.S. retail pharmacies, clarifying their obligations under federal civil rights laws.[6]

Protecting Patient Privacy: HHS issued guidance that clarifies to patients and providers the extent to which federal law and regulations protect individuals' private medical information when seeking abortion and other forms of reproductive health care, as well as when using apps on smartphones.[7]

Supporting Quality Reproductive Health Care: HHS announced nearly $3 million in new funding to bolster training and technical assistance for the nationwide network of Title X family planning providers.[8]

Protecting Access to Birth Control:

- With the Departments of the Treasury and Labor, we convened a meeting with health insurers and sent them a letter, calling on the industry to commit to meeting their obligations to provide contraceptives as required by the ACA.[9]

- Later, in response to this conversation, we issued guidance to clarify protections for birth control coverage under the ACA.[10] Under the ACA, most private health plans are required to provide birth control and family planning counseling at no additional cost.

This report builds on these efforts and initiatives and outlines an action plan in response to the President's call for us to act. Further, it demonstrates the importance and continued commitment of the Administration in responding to this national crisis.

This is a critical moment in history and how we respond will speak to how we view the rights, dignity, and well-being of women everywhere. Therefore, until the day that the freedom and the autonomy to control their own bodies is afforded to all women in this country once again, we will use every tool at our disposal to protect the reproductive health of women in this country.

Xavier Becerra

Executive Summary

On June 24, 2022, the Supreme Court of the United States upended decades of precedent and well-established reproductive and privacy rights when it overturned the constitutional right to safe and legal abortion care recognized by *Roe v. Wade* and *Planned Parenthood v. Casey*.

On July 8, 2022, President Biden issued Executive Order 14076, "Executive Order on Protecting Access to Reproductive Healthcare Services," which among other things, requires the Secretary of Health and Human Services (HHS) to submit a report to the President identifying a plan and supporting actions to:

- Protect and expand access to the full range of reproductive health care, including abortion care;
- Increase outreach and education about access to reproductive health care services, including by launching a public awareness initiative; and
- Ensure all patients receive the full protections for emergency medical care afforded under the law.[11]

On August 3, 2022, President Biden issued Executive Order 14079, "Securing Access to Reproductive and Other Healthcare Services," which applauded the work already in progress by HHS and directed it to:

- Consider additional actions to advance access to reproductive health care services, including through Medicaid for patients traveling out of state for medical care;
- Consider all appropriate actions to ensure health care providers that receive federal financial assistance comply with federal non-discrimination law; and
- Evaluate the adequacy of current interagency data collection and analysis on the effect of access to reproductive healthcare on maternal health outcomes and take actions to improve these efforts.[12]

This report responds to these Executive Orders and outlines actions to protect and expand access to abortion care and other reproductive health care nationwide. It also includes an overview of the historical and legal context relevant to the Executive Orders and current and potential HHS actions to: (a) protect and expand access to abortion care and the full range of reproductive health care services; (b) bolster outreach and education about access to reproductive health care, including medication abortion and contraception; and (c) ensure women, pregnant individuals, and those experiencing pregnancy loss receive the full protections available under federal law with regards to emergency medical care.

In response to the Supreme Court's *Dobbs v. Jackson Women's Health* decision, Secretary Becerra directed HHS to take immediate action to help people across the country as they face this harsh new reality of restricted health care and rights.[13] As a result, HHS took swift, concrete actions to protect access to reproductive health care, consistent with the Administration's priorities.

In the weeks and months to come, access to reproductive health care will continue to face new attacks, in addition to ongoing challenges. Because of the *Dobbs* decision, access to reproductive health care services now depends on where an individual lives to an even greater extent than it did before. The United

States of America has an expanding patchwork of laws, wherein some states criminalize health care providers and others for providing or facilitating medical care—sometimes without meaningful exceptions for the life or health of the woman, or when the pregnancy is a result of rape or incest. Some states and localities have expressed their intention to have prosecutors enforce restrictions against women, health care providers, and others. Further, health care providers in many jurisdictions are facing potential criminal and civil liability as well as loss of licensure for providing necessary abortion related services.

Additional efforts are underway that imperil other basic health care and rights. There have been numerous reports of women denied health- and life-saving emergency care, as providers fearful of legal reprisal delay necessary treatment for patients until their conditions worsen to dangerous levels. There are also reports of women of reproductive age being denied prescription medication at pharmacies—including medication that is used to treat stomach ulcers, lupus, arthritis, and cancer—due to concerns that these medications, some of which can be used in medication abortions, could be used to terminate a pregnancy. Bans and limits are being considered on access to birth control care, including emergency contraception.

This new reality will only worsen health outcomes for women and families, especially individuals who are already underserved in our health care system, including women of color, working families, people with disabilities, and LGBTQI+ patients. The Supreme Court's *Dobbs* decision also renders the United States an outlier globally, putting our nation on a short list of countries seeking to restrict, rather than expand, access to sexual and reproductive health care.[14]

Now, more than ever, the federal government needs to play a critical role helping to ensure access to reproductive health care, including by creating safeguards for providers and patients. HHS will continue to use its authority to protect access to care, including abortion care, and enforce federal law when women's rights to care are violated.

Introduction

On June 24, 2022, the Supreme Court of the United States eliminated the constitutional right to an abortion in its ruling on *Dobbs v. Jackson Women's Health*, reversing a nearly 50-year precedent established by *Roe v. Wade* and subsequently reaffirmed in *Planned Parenthood v. Casey*—and with it, decades of accepted law. At the time of the *Dobbs* ruling, thirteen states had laws in place to ban abortion under varying circumstances in the event that *Roe v. Wade* and *Planned Parenthood v. Casey* were overturned. Several other states are considering laws to ban or further restrict abortion access in the near future.

The Supreme Court's *Dobbs* ruling and state actions to ban health care have already had dire consequences for women across the country. These restrictions will exacerbate preexisting inequities and worsen maternal health outcomes and fuel a national public health crisis with negative effects on how women access and receive care. These impacts will be felt most acutely by underserved communities, including those with low incomes and people of color. The decision is also an assault on patient privacy and bodily autonomy, with broader implications for the freedoms millions of Americans hold dear. Further, for those states and localities that intend to have prosecutors enforce restrictions against women and others who facilitate their access to health care, this may exacerbate existing disparities in the criminal justice system broadly.

It is well established that both medication and surgical abortions are safe and effective.

There have been several studies examining the impact of abortion on the health and well-being of women. For instance, the National Academies of Science, Engineering, and Medicine (NASEM) conducted a comprehensive review of the literature on the physical and mental health implications of abortion and found consistent, high-quality evidence that, contrary to certain misconceptions, abortion does not increase the risk of breast cancer, secondary infertility, pregnancy-related hypertensive disorders, preterm birth, depression, anxiety, posttraumatic stress disorder, or other mental health harms. Given strong evidence from numerous studies showing that lower socioeconomic status is associated with shorter life expectancy and various forms of morbidity including worse mental health,[15,16,17,18,19] lack of access to abortion may lead to compounding adverse health effects in the future.

This report makes recommendations on actions to help protect access to abortion care, as well as broader reproductive health care services, in the wake of the *Dobbs* decision.

SECTION 1. Access to Medication Abortion and Contraception

Abortion Care

Medication Abortion Background:

The use of medication abortion is becoming increasingly common and may help preserve access for women seeking abortions in certain circumstances who may otherwise not have access. The regulatory history of mifepristone, the FDA-approved product for medication abortion, spans more than two decades. On September 28, 2000, FDA approved Mifeprex (mifepristone, 200 mg), in a regimen with another drug (misoprostol), as safe and effective for the medical termination of early pregnancy through seven weeks gestation; and that approval was extended through ten weeks gestation in 2016.[20] Misoprostol is also sometimes prescribed by providers to help women experiencing miscarriages.

Enforcement Discretion on the REMS—COVID-19

The Mifepristone Risk Evaluation and Mitigation Strategy (REMS) Program currently requires, among other things, that the product be dispensed in-person by a certified prescriber in certain types of health care settings, as well as the use of a Patient Agreement Form.[21]

In April 2021, FDA communicated that, provided all other requirements of the Mifepristone REMS Program are met, the Agency was exercising its enforcement discretion to not pursue violations of the in-person dispensing requirement of the Mifepristone REMS Program during the COVID-19 public health emergency (PHE), including any in-person requirements that may be related to the Patient Agreement Form. The COVID-19 PHE is ongoing, and thus FDA intends to continue to exercise its enforcement discretion in this manner. As a result, pharmacies are dispensing mifepristone to patients by mail on behalf of certified health care prescribers who have purchased the product.

FDA has also undertaken a full review of the Mifepristone REMS Program and has determined that the in-person dispensing requirement is no longer necessary to assure the safe use of mifepristone for medical termination of early pregnancy, provided all the other requirements of the REMS continue to be met and that dispensing pharmacies are certified. **HHS will continue its work to protect access to FDA-regulated products for abortion that have been found to be safe and effective.**

Initiation of the REMS Modification Process

On December 16, 2021, FDA sent REMS modification notification letters to the applicants for Mifeprex and the approved generic version of Mifeprex, Mifepristone Tablets 200 mg, subject to the standard process for this type of REMS modification.[22] In response to these letters, the applicants prepared proposals to modify the REMS and submitted them to FDA. FDA is currently reviewing these REMS modifications. If the REMS modification submissions are approved, the REMS modifications will become effective. Should the submissions be approved consistent with the December 2021 letters to the applicants, people seeking medication abortion will continue to have access to Mifeprex and the approved generic version without in-person dispensing via mail-order pharmacy once the COVID-19 PHE is over.

FDA will continue the REMS modification process and review the applicants' proposed changes to the REMS related to removing the in-person dispensing requirement.

Federal Preemption—Protecting Access to Medication Abortion

The Attorney General of the United States made clear that states may not ban mifepristone based on disagreement with FDA's expert judgment about its safety and efficacy.[23] **HHS is working with the U.S. Department of Justice (DOJ) to help ensure access to care and preserve FDA's role in determining what is safe and effective for patients.**

Coverage of Abortion Services

The Hyde Amendment

The Hyde Amendment permits use of federal funds for abortions only in limited circumstances: when the pregnancy is the result of rape or incest, or when the woman suffers from a physical disorder, physical injury, or physical illness, including a life-endangering physical condition caused by or arising from the pregnancy itself that would place the woman in danger of death unless an abortion is performed. The Hyde Amendment applies to federal funds in programs and activities across HHS, including Medicaid, Medicare, the Children's Health Insurance Program, and others.[24,25]

In the wake of the *Dobbs* decision, the Centers for Medicare and Medicaid Services (CMS) continues to evaluate the impact of Hyde restrictions on coverage and further steps to expand care. **To that end, the Centers for Medicare & Medicaid Services (CMS) continues to evaluate the effect of *Dobbs* and will work to ensure states provide reproductive health care in federally funded programs, consistent with applicable Hyde Amendment restrictions.**

The Hyde Amendment disproportionately impacts access to abortion for low-income communities, people of color, and people with disabilities nationwide for whom Medicaid is the primary source of coverage for health care.[26, 27]

CMS will work with states to advance access to reproductive health care, including to the extent permitted by federal law, through Medicaid for patients traveling across state lines for medical care consistent with President Biden's Executive Order 14079. It took a first step on this action in releasing a letter to states, inviting them to work with HHS on Medicaid waivers to increase access to reproductive health care within the legal limits of the Medicaid Act.

Federal Protections for Family Planning and Birth Control Care

Reproductive Health Care Coverage—Private Market and Medicaid

Private Market

The Affordable Care Act (ACA) helps make prevention services affordable and accessible for all Americans by requiring most employer health plans and other health insurance plans to provide coverage to their enrollees for certain recommended preventive services at no additional cost. A recent HHS report

estimated that more than 58 million women were benefiting from these provisions.[28] The recommended preventive services include preventive care and screenings provided for in comprehensive guidelines supported by the Health Resources and Services Administration (HRSA). The Women's Preventive Services Initiative reviews and recommends updates to the guidelines, including contraception and contraceptive counseling. The guidelines were last updated in December of 2021, effective for plan years starting on or after December 30, 2022, and are reviewed on an annual basis.[29]

Following President Biden's July 2022 Executive Order on ensuring access to reproductive health care, HHS, alongside the Departments of Labor and of the Treasury (the Departments), released guidance to clarify protections for birth control coverage under the ACA.[30] Under the ACA, most private health plans are required to provide coverage of birth control and family planning counseling at no additional cost. This guidance followed action in June, when the three Departments sent a letter to health insurers and employer health plan organizations,[31] and the Departments convened a meeting with them, calling on the industry to commit to meeting their obligations to provide coverage for contraceptive services at no additional cost as required by the ACA. **HHS will enforce the law to ensure access to birth control coverage under the ACA and continue to work to ensure that patients understand their coverage rights.**

Medicaid

Medicaid plays a critical role in helping to ensure access to reproductive health care for the populations it serves, including women's preventive care, family planning, and pregnancy-related care such as prenatal care, childbirth, and postpartum care. Nearly all women use some form of family planning during their reproductive years, and Medicaid is the largest source of public funding for family planning services nationally.[32] The mandatory Medicaid family planning benefit provides coverage for services and supplies to prevent or delay pregnancy and may include education and counseling in the method of contraception desired or currently in use by the individual, a medical visit to change the method of contraception, and infertility treatment. States receive an enhanced federal matching rate of 90 percent for expenditures for family planning services and supplies. **CMS will continue to work with states to expand access to reproductive health care.**

Federal Family Planning Programs – Title X, Community Health Centers and More

The Office of the Assistant Secretary for Health runs the Title X program, which supports high-quality, family planning services, and preventive care including breast and cervical cancer screening, contraceptive counseling and care, sexually transmitted infection testing and treatment, and HIV screening. In October 2021, HHS issued a final rule to strengthen the nation's family planning program with nationally recognized standards of care. Subsequently, HHS awarded more than $270 million to support family planning service delivery, and more than $16 million to support telehealth enhancement and expansion. A critical part of this was funding released in Fall 2021 to help clinics in dire need as a result of the Texas abortion ban, SB 8. This funding went to support clinics in eight states. **HHS is considering other grants to help with training and capacity for clinics on sexual and reproductive health and will make family planning care a priority in its programs and services, as well as considering options to make family planning a specific condition for certain grants.**

As a result of state abortion bans, abortion providers are closing their doors and patients are at risk of losing access to providers they trust and the care they need. On June 29, 2022, HHS further issued guidance to clinics, providers, others on how Title X projects can support pregnant clients and use funds to respond to changing reproductive health care needs. **HHS is evaluating the opportunity to provide**

grants to clinics to support patient navigation and ongoing clinic stability in underserved areas that may face closure from revenue losses and state bans. Further, HHS will continue to work to make more funding available under the Title X program to help clinics with capacity limitations and support increased needs in providing Title X services to patients who travel from states where clinics have closed due to bans on abortion. HHS has also made clear to Congress that more funding is needed for the Title X program given the capacity issues in both states with bans and those without restrictions on reproductive health care.

In addition to helping clinics navigate the post-*Dobbs* reality, **HHS is also working to support more training and resources to help providers build capacity and expertise as the need for family planning care and patient information continues to grow. HRSA plans an initiative for the fall of 2022 to increase capacity for recipients of the Ryan White HIV/AIDS Program** to implement evidence-informed interventions and promising strategies around reproductive health care needs for people with HIV. This will include preventive screenings, education (including pre-conception counseling), family planning, and other reproductive health care needs for people with HIV, as well as post-natal care. CDC serves as a source of clinical guidance for health care providers and provides evidence-based guidance to reduce medical barriers to contraception access and use.[33] **CDC anticipates issuing an updated Contraceptive Guidance for Health Care Providers and has conducted the initial steps for this update**—including soliciting public comments and conducting systematic reviews.

HRSA runs our nation's health centers program. These centers provide primary and preventive health services to underserved communities, including family planning services. Services include patient-centered counseling, contraceptive services (including the full range of FDA-approved methods), pregnancy testing and counseling, assistance for patients who want to conceive, basic infertility services and screening for sexually transmitted infections. It is critical that these providers stay up to date on reproductive health care and are able to continue providing services that meet the necessary standard of care. **HRSA is in the process of updating its technical assistance guide and HHS will update and expand technical assistance guidance for Title X and community health center providers.**

Section 2: Access to Care Under the Law

Nondiscriminatory Access to Healthcare

Since the *Dobbs* decision, there have been an uptick in cases around the country where people—especially women of reproductive age—have been denied care, including medical care that is not directly related to reproductive health. Such incidents have happened in pharmacies when persons with disabilities seek their prescribed medications, some have impacted women experiencing miscarriages, and others have been the product of confusion from the decision and resulting denials of care.

The Office for Civil Rights (OCR) enforces a range of federal civil rights laws, including Section 1557 of the ACA (Section 1557),[34] which prohibits discrimination based on sex in health programs and activities. Sex discrimination includes discrimination based on current pregnancy, past pregnancy, and related medical conditions.

Section 1557 and Section 504 of the Rehabilitation Act of 1973 (Section 504) prohibits discrimination on the basis of disability by recipients of federal funding, and Title II of the Americans with Disabilities Act prohibits disability discrimination by state and local government entities. Under these laws, a covered entity cannot deny, exclude, or fail to provide an equal opportunity to benefit from a program, service, or activity, including reproductive health care services to people with disabilities. These laws prohibit discrimination in a covered entity's provision of reproductive health care services, and individuals experiencing discrimination in the provision of such care can file complaints with HHS OCR.[35] OCR is actively monitoring cases around the country and will act against entities not following their obligations under federal law. To that end, the Administration for Community Living (ACL) funds Protection and Advocacy Systems in each state that also can provide legal assistance to individuals with disabilities who face barriers in accessing reproductive health care services.[36]

Pharmacies that receive federal financial assistance are covered entities under Section 1557 and other federal civil rights laws, including Section 504. On July 13, 2022, OCR released guidance to pharmacies on their obligations under federal civil rights laws to ensure nondiscriminatory access to pharmacy services.[37] The guidance reminds covered pharmacies that they may not discriminate on the grounds prohibited by Section 1557 and Section 504, including with regard to supplying medications; making determinations regarding the suitability of a prescribed medication for a patient; or advising patients about medications and how to take them.

On August 3, 2022, President Biden signed Executive Order 14079 on "Securing Access to Reproductive and Other Healthcare Services," which directed OCR to consider all appropriate actions to advance the prompt understanding of and compliance with nondiscrimination law in obtaining medical care. This includes providing technical assistance to providers, convening providers to increase awareness of the law, and working to promote compliance. **OCR will take further action in response to this Executive Order to promote compliance, including vigorous enforcement of federal civil rights laws. As part of this important work, OCR will continue to provide technical assistance to providers on their obligations under federal civil rights law and will convene providers to help ensure providers understand their obligations under federal civil rights laws.**

On August 4, 2022, OCR published a notice of proposed rulemaking (NPRM) on Section 1557 of the Affordable Care Act.[38] The proposed rule, among other things, implements the statutory prohibition on

discrimination on the basis of sex in federal health programs and activities. The NPRM recognizes discrimination on the basis of pregnancy or related conditions as a form of prohibited sex discrimination and seeks comment on whether the Final Rule should include a stand-alone provision to this effect and what impact, if any, the *Dobbs* decision has on the implementation of Section 1557 and the implementing regulations.

Access to Emergency Medical Care

The Emergency Medical Treatment and Labor Act (EMTALA) requires that all patients who present at an emergency department of a hospital that receives Medicare funds and who request examination or treatment shall receive an appropriate medical screening examination, stabilizing treatment, and transfer if necessary, irrespective of any directly conflicting state laws or mandates. CMS released guidance on September 17, 2021, and again on July 11, 2022, emphasizing that under EMTALA, a health care provider has a legal duty to provide stabilizing medical treatment to a patient who presents to the emergency department and is found to have an emergency medical condition, and that requirement preempts any directly conflicting state law or mandate that might otherwise prohibit such treatment. [39] **HHS will continue to make information available to help patients and providers understand this important right and provide technical assistance and information to providers on their obligations under EMTALA.**[40]

As indicated in CMS guidance, the determination of an emergency medical condition is the responsibility of the examining physician or other qualified medical personnel. Emergency medical conditions involving pregnant patients may include but are not limited to ectopic pregnancy, complications of pregnancy loss, or emergent hypertensive disorders, such as severe preeclampsia. Any state laws or mandates that employ a more restrictive definition of an emergency medical condition that directly conflicts with the EMTALA definition are preempted by the EMTALA statute to the extent of this conflict.

The course of treatment necessary to stabilize such emergency medical conditions is also under the purview of the physician or other qualified medical personnel. Stabilizing treatment could include medical and/or surgical interventions (e.g., abortion, removal of one or both fallopian tubes, anti-hypertensive therapy, methotrexate therapy, etc.), irrespective of any directly conflicting state laws or mandates.

Thus, if a physician believes that a pregnant patient presenting at an emergency department, including certain labor and delivery departments, is experiencing an emergency medical condition as defined by EMTALA, and that abortion is the stabilizing treatment necessary to resolve the emergency medical condition, the physician must ensure that the patient receives that treatment. And when a state law directly conflicts with EMTALA because it prohibits abortion and does not include an exception for the life and health of the pregnant woman—or draws the exception more narrowly than EMTALA's emergency medical condition definition—that state law is preempted in the area of this direct conflict.

The enforcement of EMTALA is generally a complaint-driven process. **HHS will continue to enforce EMTALA and investigate complaints where consistent with law.**

Investigating

CMS investigations of a hospital's policies, procedures and processes, or the actions of medical personnel, are initiated by a complaint. Complaints can be filed in each state. CMS may also open an investigation based on public reports.

Enforcement

If the results of a complaint investigation indicate that a hospital violated one or more of the provisions of EMTALA, a hospital may be subject to termination of its Medicare provider agreement and/or the imposition of civil monetary penalties. Civil monetary penalties and exclusion from Medicare and Medicaid participation may be imposed against individual physicians for EMTALA violations. Furthermore, where a state purports to prohibit providers from offering the emergency care that EMTALA requires, HHS will not hesitate to refer the matter to the DOJ to take appropriate legal action. On August 2, 2022, the United States sued the State of Idaho over a law that imposes a ban on abortion.[41] Under the Idaho law, a prosecutor can indict, arrest and prosecute a physician merely by showing that an abortion has been performed, without regard to the circumstances. A physician who provides an abortion in Idaho can ultimately avoid criminal liability only by establishing as an affirmative defense that "the abortion was necessary to prevent the death of the pregnant woman" or that, before performing the abortion, the pregnant patient (or, in some circumstances, their parent or guardian) reported an "act of rape or incest" against the patient to a specified agency and provided a copy of the report to the physician. The Idaho law provides no defense for an abortion necessary to protect the health of the pregnant patient.

Idaho's criminal prohibition of all abortions, subject only to the statute's two limited affirmative defenses, directly conflicts with EMTALA and stands as an obstacle to the accomplishment of EMTALA's federal objectives of providing stabilizing care and treatment to anyone who needs it. On August 24, 2022, the United States, represented in this matter by HHS alongside DOJ, was awarded a preliminary injunction prohibiting enforcement of the Idaho law to the extent of its conflict with EMTALA. **HHS will continue to enforce the law as appropriate.**

Section 3: Protecting Patient Privacy

Recent reports indicate that state Attorneys General and other state actors may seek to use patient data to track women seeking reproductive health care, violating patient trust and privacy and creating dangerous and untenable situations for patients who are already facing limited options. Further, there have been reports about the risks posed by smart phones and mobile applications that allow patient data related to reproductive health to be shared, such as period trackers and geolocation data. These data may be used against patients and may also lead patients to feel stigma when accessing care or to not seek care at all.

The complexity of protecting the privacy of patients' reproductive health data is compounded by the dynamic nature of electronic health information and the ways it is encoded within health information technology systems. The Health Insurance Portability and Accountability Act of 1996 (HIPAA) plays an important role in patient privacy. Information relating to a patient's sexual and reproductive health can be directly accessed or indirectly inferred based on a wide range of data points that can be included within a patient's longitudinal care record. For example, a medication list could be used to infer medical or surgical abortion care. It is essential to protect the entirety of a patient's health information.

HIPAA Compliance

OCR issued guidance on June 29, 2022, to help protect patients seeking reproductive health care, as well as their health care providers.[42] The guidance addresses how the HIPAA Privacy Rule protects individuals' private medical information ("protected health information," or PHI) relating to abortion and other sexual and reproductive health care—making it clear that HIPAA does not require providers to disclose private medical information to third parties. **HHS will continue to rigorously enforce the HIPAA Privacy, Security, and Breach Notification Rules to help protect patients seeking reproductive health care.**

OCR also issued guidance outlining best practices for consumers that addresses the extent to which private medical information is protected on personal cell phones and tablets.[43] This guidance explains that, in most cases, the HIPAA Privacy, Security, and Breach Notification Rules do not protect the privacy or security of individuals' health information when they access or store the information on personal cell phones or tablets. This guidance provides tips about steps an individual can take to decrease how their cell phone or tablet collects and shares their health and other personal information without the individual's knowledge. **HHS will continue to issue guidance, technical assistance, and support to help protect the privacy of individuals' PHI related to abortion and other sexual and reproductive health care and will provide further guidance and policies to safeguard patient privacy.**

The Office of the National Coordinator for Health IT (ONC) certification and information blocking regulations already provide for protection of patient privacy and choice when it comes to sharing electronic health information. **HHS will continue to publish guidance reinforcing health care providers' awareness of the ways in which information blocking regulations support their ability to provide care while protecting patient privacy.**

Protecting patient privacy is a critical priority for HHS, which has already begun this important work. **HHS will also host public meetings with providers and others in the health care system, including health**

information technology developers and other stakeholders, to encourage awareness of how patients can obtain their electronic health information and make informed choices about whether to share it with others (including the use of mobile health applications).

Section 4: Improving Awareness, Education and Access to Accurate Information

This section describes actions HHS has taken or will take to provide education and outreach to individuals on how to access reproductive health care services and about their rights relating to privacy, as well as outreach to key partners on the Administration's actions in response to the *Dobbs* decision.

Federal Resources and Information—ReproductiveRights.gov

HHS has launched ReproductiveRights.gov, a website that serves as a central location for information on federal reproductive rights, including rights associated with accessing abortion, birth control, and other preventive services. This site provides accurate information in an accessible format to consumers to help them understand their rights to emergency care, birth control, medication, abortion services, and other preventive health services in one location. It also provides information for individuals who do not have health insurance, including information on how to locate Title X Family Planning Clinics, health centers, and Ryan White HIV/AIDS Programs. Additionally, the public can find information regarding filing a complaint with HHS OCR if a person's civil rights or health information privacy rights are violated. This website will continue to add timely, relevant information on a range of reproductive health issues to reflect the shifting environment, and efforts are underway to ensure that materials are accessible to individuals with limited English proficiency.

Reproductiverights.gov is also cross-linked with the DOJ's Reproductive Rights website, which provides information about federal legal protections for accessing reproductive health services.[44] DOJ's website provides helpful information for clinics and individuals seeking access to reproductive health services, such as the Freedom to Access Clinic Entrances (FACE) and how to report property damage, violence or threats of violence directed at providers.[45]

HHS will continue to add timely, relevant information on a range of reproductive health issues to the website.

Outreach Efforts

HHS launched a campaign to ensure the public has information on how to access birth control. Specifically, this campaign aims to provide patients and consumers with information regarding the requirement for most health insurance plans to cover the full range of FDA-approved contraceptives including emergency contraceptives and intrauterine devices with no cost to the consumer. Additionally, information will be provided to notify the public of the ability to access, depending on income, no-cost or low-cost contraceptive services, as well as cervical cancer screenings, sexually transmitted infection (including HIV) testing, and referrals for abortion and other patient care.

OCR plans to convene with health care providers to discuss federal civil rights and health privacy obligations. This will facilitate OCR's efforts to provide informative and timely guidance to covered entities and is in furtherance of President Biden's Executive Order 14079. Through these convenings OCR will provide support in complying with the law and also help inform areas where additional policy changes or technical assistance may be helpful to advance reproductive health care.

The HHS Reproductive Access Task Force also met with advocacy organizations, providers, civil rights groups, medical experts, and faith-based partners to better understand and respond to needs following *Dobbs*. These efforts helped inform HHS's early action in response to the *Dobbs* decision. **Further, HHS will leverage external relationships in communities across the country to improve education and understanding about women's preventive health services, including birth control coverage and family planning care, at Title X clinics, community health centers, and other HHS programs and services nationwide using its existing network of providers to expand information and access to coverage for patients.**

Countering Inaccurate Information

The Office of the Surgeon General has addressed the challenges of inaccurate health information with the release of the Surgeon General's Advisory on Health Misinformation in July of 2021.[46] This advisory outlined the harms of inaccurate health information and the ways individuals, health professionals, technology platforms, and many others can combat it. In November of 2021, the Office of the Surgeon General released a Community Toolkit for Addressing Health Misinformation to help educate the public on ways to identify and appropriately engage with others about inaccurate health information.[47] Thousands of individuals, community leaders, educators, and health workers have used the toolkit for teaching and training. These efforts will continue to create a safer information environment to inform health decisions, including those on reproductive health. **HHS will work with providers and patients nationwide to counter inaccurate information.**

Section 5: Improving Data and Research

Restrictions on abortions will likely have significant impacts on maternal health outcomes. This section briefly reviews data sources that are available to monitor maternal health outcomes and track access to reproductive health services. The Department is making a number of investments to improve maternal health data infrastructure. Some of this work is improving electronic health records data and linking mothers with their children to support longitudinal studies on maternal health.[48,49] On August 3, 2022, as part of Executive Order 14079 on Securing Access to Reproductive and Other Healthcare Services, HHS was directed to evaluate the adequacy of research, data collection, and data analysis and interpretation efforts at the National Institutes of Health (NIH), the CDC, and other relevant HHS components in accurately measuring the effect of access to reproductive health care on maternal health outcomes and other health outcomes.

The Department is taking additional steps to increase its monitoring and data collection to better understand the impact on health disparities and equity as well as determine areas with needs for increased federal resources and support to protect access to health care and patient privacy. **HHS is actively exploring approaches to improve its ability to track and understand the implications of lack of access to abortion through improved comprehensive and timely data.**

Tracking Maternal Mortality and Morbidity Data

Measures of maternal mortality and severe maternal morbidity are reported on an annual basis including the CDC's maternal mortality rate and pregnancy-related mortality ratio, and severe maternal morbidity rates measured by the Agency for Healthcare Research and Quality (AHRQ). **HHS will continue these reporting systems to better understand the impact of abortion bans on maternal mortality and morbidity.**

Tracking Abortion Data

The CDC collects data that states may voluntarily report on legal abortions, which includes information on the number and type of abortions and on basic characteristics of the women who receive them.[50] Given the voluntary nature of this data collection, these data are not complete. The CDC also runs the Pregnancy Mortality Surveillance System.[51] This system monitors the impact of abortion deaths from legal abortions, illegal abortions, or abortion arising from miscarriages or pregnancy related complications. These data are also available in the Abortion Surveillance Report.[52]

Family Planning Data

Self-reported information directly from women about access to and use of services such as family planning and contraception is another relevant data resource. **Early reporting suggests that there have been changes in the types of contraceptive methods some women are seeking since the *Dobbs* decision was announced with as much as 21 percent of women reporting that they changed their contraception method in the preceding month.**[53] The CDC's Pregnancy Risk Assessment Monitoring System collects state-level population-based data on maternal attitudes and experiences before, during, and shortly after pregnancy, as well as pregnancy intention and contraceptive use.[54] The CDC also conducts the National Survey of Family Growth, which collects information about fertility, contraceptive-use, pregnancy-

intention, adoption-intention, and pregnancy, among other related topics which will help measure the impact of the *Dobbs* decision on health care decisions in family planning care.

CDC's Behavioral Risk Factor Surveillance System includes questions in the Family Planning Module to understand contraceptive use. Data collected in 2017 and 2019 from 45 jurisdictions were used to estimate the proportion of women aged 18 to 49 years who were at risk for unintended pregnancy and had ongoing or potential need for contraceptive services.[55] The CDC's Youth Risk Behavioral Surveillance System has also monitored health-related behaviors and experiences among high school students, including sexual health behaviors, unintended pregnancy, and sexually transmitted diseases.[56] These data become imperative as we examine national impacts.

Conclusion

HHS will continue to work to strengthen and expand access to reproductive health care services. As part of this work, the Secretary has directed every part of HHS to evaluate its work and act accordingly. Specifically, the Department is taking all possible steps to increase access to medication abortion and contraception; ensure access to health care under the law; protect patient privacy related to reproductive health; increase awareness, education, and access to accurate information; and expand the collection of accurate data and research in this sphere. HHS will also continue to work across the federal government to provide its expertise and partner with federal partners on its work.

Abortion is health care, and access to it and comprehensive reproductive health services can make a huge difference in a person's life—from the autonomy to make decisions about one's own body to improved health outcomes. This report lays out our current work and actions to address the proliferation of bans and restrictions on reproductive health care nationwide. We will continue this important work until every woman has equal, access to health care, privacy, and reproductive rights.

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[20] At the time of initial approval, the application was approved under part 314, subpart H (21 C.F.R. part 314, subpart H), which provides for approval with restrictions that are needed to assure the safe use of the drug product. Subsequently, once the Food and Drug Administration Amendments Act of 2007 (FDAAA) was passed, through which the Risk Evaluation and Mitigation Strategy (REMS) authority was created, Mifeprex was identified as one of the products that was deemed to have an approved REMS in effect because Mifeprex had in effect elements to assure safe use.
[21] A REMS is a drug safety program the FDA can require for particular medications with safety concerns to ensure that the benefits outweigh the risks. REMS are designed, for instance, to reinforce safe medication use by preventing, monitoring, or managing a specific risk for a particular drug. For more information, *see* Food & Drug Admin., Risk Evaluation and Mitigation Strategies | REMS (last updated Dec. 17, 2021).
[22] When FDA determines that a REMS must be modified, FDA will notify the applicant of the determination and describe the required change and the type of submission that is needed. For the REMS modifications here, the applicants were required to submit supplemental applications proposing revisions consistent with the FDA

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EXHIBIT

Aid Acce ,

et Abortion Pill Online in ouisiana

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You can buy an abortion pill online and get it by mail in Louisiana. The FDA has approved abortion pills by mail. Aid Acces works with U.S. based abortion providers in so called shield law states (this means that the states will protect the providers against legal action). Therefor Aid Access can provide abortion services to all 50 U.S. states including Louisiana.

Aid Access will help you order abortion pills and have them delivered to your home in New Orleans, Baton Rouge, Shreveport, Metairie, Lafayette, or anywhere else in Louisiana.

Louisiana abortion pill online orders:

- Louisiana abortion pill online orders costs $150 USD
- Reliable abortion pill shipping to Louisiana in 1-5 days
- Tracking numbers provided when the pills are mailed
- Help desk support available in 16 languages

An infographic explaining how to get an abortion pill in Louisiana from Aid Access.

How to order abortion pills in Louisiana

You can get a prescription from Aid Access and have abortion pills delivered to your home in Louisiana. **Order abortion pills by mail here.** These are the steps to get abortion pills delivered to your home by mail:

1 Start your online consultation for abortion pills in Louisiana

Once you begin your online consultation for abortion pills in Louisiana, you will be asked some questions about your health and pregnancy to ensure you are eligible. All information you share with us is private and protected.

2 Our U.S. based doctors approve your online abortion pill order

Your consultation will immediately be reviewed by our medical team. Our help desk will email you the next steps, ask you to send a donation of $150 USD, and then approve your online abortion pill order within 24 hours.

3 Receive abortion pills by mail in LA in 1-5 days

The abortion pills will be shipped by mail to your home in LA within 24 hours of your your order being approved. You will receive a tracking number so you can follow your package as it moves through the mail.

Start now: Get the abortion pill online here

More ways to get Louisiana abortion pill access

If Aid Access is not able to meet your reproductive health needs, there are multiple ways people get Louisiana abortion pill access. To learn about other online telehealth services that are available to you, visit the Plan C Guide to Abortion Pills: **How to Order an Abortion Pill Online in Louisiana**

Louisiana abortion clinic guides from Plan C Pills

If you determine that abortion pills will not meet your reproductive health needs, you can find information about local abortion support resources near you in the **Louisiana Abortion Clinic Guide** from Plan C Pills.

Additional guides to abortion clinics near Louisiana from Plan C Pills:

- **Abortion clinics near Baton Rouge, LA**
- **Abortion clinics near New Orleans, LA**
- **Abortion clinics near Shreveport, LA**
- **Abortion clinics near Metairie, LA**
- **Abortion clinics near Lafayette, LA**

[Abortion clinics near Lake Charles, LA]

Abortion laws in the State of Louisiana

For the most up to date information about abortion laws in Louisiana, visit **Guttmacher Institute**, **Center for Reproductive Rights**, or **AbortionFinder.org**.

How much does the abortion pill cost in Louisiana?

The abortion pill service costs $150 USD when shipping the pills to Louisiana. If you cannot afford this, please tell us you need help after you fill in **the form**.

Begin here: Order abortion pills online from Aid Access

Which Louisiana cities does Aid Access provide online abortion pill service?

Aid access provides online abortion pill order access throughout Louisiana including these cities and everywhere in-between:

Order the abortion pill in Kenner, Louisiana

Get abortion pills in Bossier City, Louisiana

Buy an abortion pill in Monroe, Louisiana

Buy abortion pills in Alexandria, Louisiana

Start your consultation now: Order abortion pills online

EXHIBIT

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A ter Historic Indictment Doctors Will eep Mailin Abortion Pills Over State ines

PR (Mar. , 2025)

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SHOTS - HEALTH NEWS

After historic indictment, doctors will keep mailing abortion pills over state lines

MARCH 19, 2025 · 5:00 AM ET

HEARD ON MORNING EDITION

By Rosemary Westwood

wwno

4-Minute Listen PLAYLIST TRANSCRIPT

At the Massachusetts Medication Abortion Access Project (MAP), physicians use telehealth to prescribe and mail pills to people who live in states that ban or restrict abortion.

Elissa Nadworny/NPR

Editor's Note: Previous audio and web versions of this story incorrectly said that Maine Family Planning staff and the clinic's medical director, Dr. Kohar Der Simonian, mail abortion medication to patients in states where abortion is banned. Maine Family Planning mails abortion pills to patients within Maine but does not ship them across state lines. However, it does provide abortion procedures and

abortion pills to people who travel to Maine from other states. The web and audio versions of this story have been revised to correct the error and have otherwise been edited for concision and clarity.

When the news broke on Jan. 31 that a New York physician had been indicted for shipping abortion medications to a woman in Louisiana, it stoked fear across the network of doctors and medical clinics who engage in similar work.

"It's scary, it's frustrating," said Dr. Angel Foster, the co-founder of the Massachusetts Medication Abortion Access Project, a clinic near Boston that mails mifepristone and misoprostol pills to patients in states with abortion bans. But, Foster added, "it's not entirely surprising."

Ever since the Supreme Court overturned *Roe v. Wade* in 2022, abortion providers like her had been expecting prosecution or another kind of legal challenge from states with abortion bans, she said.

KFF Health News

This story was produced in partnership with KFF Health News.

"It was unclear when those tests would come, and would it be against an individual provider or a practice or organization?" she said. "Would it be a criminal indictment, or would it be a civil lawsuit or [attack on] licensure? All of that was kind of unknown, and we're starting to see some of this play out."

The indictment also sparked worry among abortion providers like Dr. Kohar Der Simonian, the medical director for Maine Family Planning. The clinic doesn't mail pills into states with bans, but it does treat patients who travel from those states to Maine for abortion care.

"It just hit home that this is real, like this could happen to anybody, at any time now, which is scary," said Der Simonian.

Der Simonian and Foster both know the indicted doctor, Margaret Carpenter.

PUBLIC HEALTH

Some red states report zero abortions. Doctors and researchers say it's not true

"I feel for her. I very much support her," Foster said. "I feel very sad for her that she has to go through all of this."

On Jan. 31, Carpenter became the first U.S. doctor criminally charged for providing abortion pills across state lines — a medical practice that grew after the U.S. Supreme Court's *Dobbs* decision on June 24, 2022, which overturned *Roe v. Wade*.

Since Dobbs, 12 states have enacted near-total abortion bans, and an additional eight states have outlawed the procedure after a certain point in pregnancy, but before a fetus is viable.

Carpenter was indicted alongside a Louisiana mother who allegedly received the mailed package and gave the pills prescribed by Carpenter to her minor daughter.

NATIONAL

Inside a medical practice sending abortion pills to states where they're banned

The teen wanted to keep the pregnancy and called 911 after taking the pills, according to an NPR interview with Tony Clayton, the Louisiana local district attorney prosecuting the case. When police responded, they learned of the medication, which included the prescriber's name, Margaret Carpenter, Clayton said.

On Feb. 11, Louisiana's Republican governor, Jeff Landry, signed an extradition warrant for Carpenter. He later posted a video arguing she "must face extradition to Louisiana, where she can stand trial and justice will be served."

New York's Democratic governor, Kathy Hochul, countered by releasing her own video, confirming she was refusing to extradite Carpenter. The charges carry a possible 5-year prison sentence.

"Louisiana has changed their laws, but that has no bearing on the laws here in the state of New York," Hochul said.

Eight states — New York, Maine, California, Colorado, Massachusetts, Rhode Island, Vermont, and Washington have passed laws since 2022 to protect doctors who mail abortion pills out of state, and thereby block or "shield" them from extradition in such cases. But this is the first criminal test of these relatively new "shield laws."

SHOTS - HEALTH NEWS

Despite bans in some states, more than a million abortions were provided in 2023

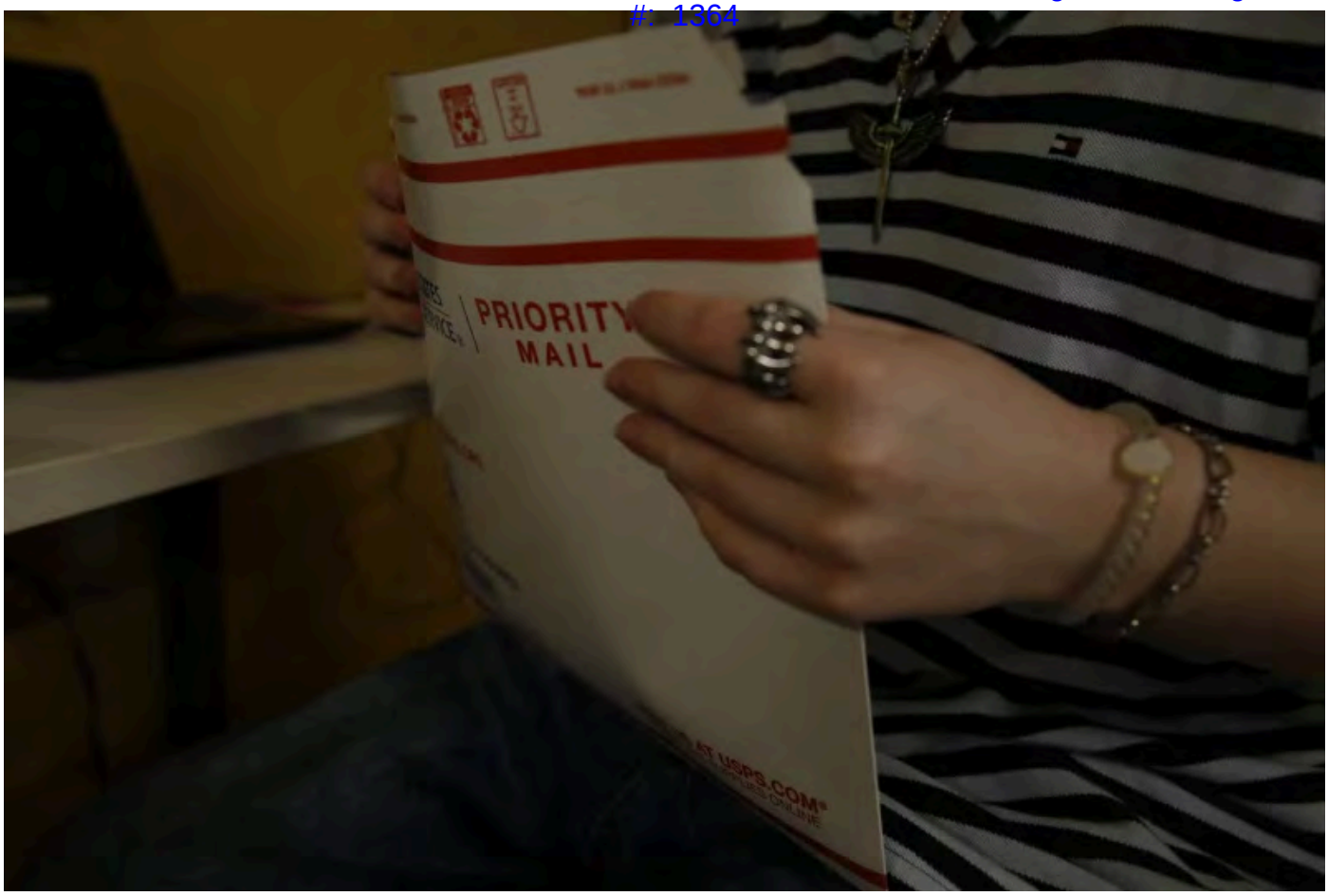
The telemedicine practice of consulting with remote patients and prescribing them medication abortion via the mail has been growing in recent years — and is now playing a critical role in keeping abortion somewhat accessible in states with strict abortion laws, according to research from the Society of Family Planning, a group that supports abortion access.

Doctors who prescribe the pills across state lines describe facing a new reality where the criminal risk is no longer hypothetical. The doctors say that if they stop, tens of thousands of patients would no longer be able to end early pregnancies safely at home, under the care of a U.S. physician. But the doctors could end up in the crosshairs of a legal clash over the interstate practice of medicine when two states disagree on whether people have a right to end a pregnancy.

Doctors are on alert, but remain defiant

Maine Family Planning, a network of clinics across 19 locations, offers abortions, birth control, gender-affirming care and other services. One patient recently drove over 17 hours from South Carolina, a state with a six-week abortion ban, Der Simonian said.

For Der Simonian, that case illustrates how desperate some of the practice's patients are for abortion access. It's why she supported Maine's 2024 shield law, she said.



Last year, MAP was mailing abortion medications to nearly 500 patients a month. Since January, they're averaging 3,000 prescriptions a month, according to the clinic's co-founder Angel Foster. Nearly all of the clinic's patients — 95% — live in states with bans on abortion or on telemedicine abortions.

Elissa Nadworny/NPR

Maine Family Planning has discussed whether to start mailing abortion medication to patients in states with bans, but it has decided against it for now, according to Kat Mavengere, a spokesperson for Maine Family Planning.

Reflecting on the indictment of Carpenter, Der Simonian said it underscored the stakes for herself — and her clinic — of providing any abortion care to out-of-state patients. Shield laws were written to protect against the possibility that a state with an abortion ban charges and tries to extradite a doctor who performed a legal, in-person procedure on someone who had traveled there from another state, according to a review of shield laws by the Center on Reproductive Health, Law, and Policy at the UCLA School of Law.

"It is a fearful time to do this line of work in the United States right now," Der Simonian said. "There will be a next case." And even though Maine's shield law protects abortion providers, she said, "you just don't know what's going to happen."

Data shows that in states with total or six-week abortion bans, an average of 7,700 people a month were prescribed and took mifepristone and misoprostol to end their pregnancies by out of state doctors practicing in states with shield laws. The data is part of a #WeCount survey estimating the volume and types of abortions

in the U.S. covering the second quarter of 2024, conducted by the Society of Family Planning.

SHOTS - HEALTH NEWS

Standard pregnancy care is now dangerously disrupted in Louisiana, report reveals

Among Louisiana residents over the same time period, nearly 60% of abortions were via telemedicine, giving Louisiana the highest rate of telemedicine abortions among states that passed strict bans after *Dobbs*, according to the #WeCount survey.

Organizations like the Massachusetts Medication Abortion Access Project (MAP) are responding to the demand for remote care. The MAP was launched after the *Dobbs* ruling, with the mission of writing prescriptions for patients in other states.

During 2024, the MAP says they were mailing abortion medications to nearly 500 patients a month. In the new year, the monthly average has grown to 3,000 prescriptions a month, said Foster, the co-founder.

The majority of the MAP's patients — 80% — live in Texas or states in the Southeast, a region blanketed with near-total abortion restrictions, Foster said.

But the recent indictment from Louisiana will not change the MAP's plans, Foster said. The MAP currently has four staff doctors and is hiring one more.

"I think there will be some providers who will step out of the space, and some new providers will step in. But it has not changed our practice," Foster said. "It has not changed our intention to continue to practice."

POLICY-ISH

Women sharing personal stories about abortion bans have become a political force

The MAP's organizational structure was designed to spread potential liability, Foster said.

"The person who orders the pills is different than the person who prescribes the pills, is different from the person who ships the pills, is different from the person who does the payments," she explained.

In 22 states, Democratic leaders helped establish shield laws or similarly protective executive orders, according to the UCLA School of Law review of shield laws.

The review found that in 8 states, the shield law applies to in-person and telemedicine abortions. In the other 14 states, the protections don't explicitly extend to abortion via telemedicine.

Most of the shield laws also apply to civil lawsuits against doctors. A month before Louisiana indicted Carpenter, the Texas attorney general, Ken Paxton, filed a civil suit against her. A Texas judge ruled against Carpenter on Feb. 13, imposing penalties of more than $100,000.

By definition, state shield laws can't protect doctors when they leave the state. If they move or even travel elsewhere, they lose the first state's protection and risk arrest in the destination state, and maybe extradition to a third state.

Physicians doing this type of work accept there are parts of the U.S. that they should no longer go, said Julie F. Kay, a human rights lawyer who helps doctors set up telemedicine practices.

"There's really a commitment not to visit those banned and restricted states," said Kay, who worked with Carpenter to help start the Abortion Coalition for Telemedicine.

"We didn't have anybody going to the Super Bowl or Mardi Gras or anything like that," Kay said of the doctors who practice abortion telemedicine across state lines.

She said she has talked to other interested doctors who decided against doing it "because they have an elderly parent in Florida, or a college student somewhere, or family in the South." Any visits, even for a relative's illness or death, would be too risky.

"I don't use the word 'hero' lightly or toss it around, but it's a pretty heroic level of providing care," Kay said.

Governors clash over doctor's fate

Margaret Carpenter's case remains unresolved. New York's rebuff of Louisiana's extradition request shows the state's shield law is working as designed, according to David Cohen and Rachel Rebouché, law professors with expertise in abortion laws.

Louisiana officials, for their part, have pushed back in social media posts and media interviews.

"It is not any different than if she had sent fentanyl here. It's really not," Louisiana Attorney General Liz Murrill told Fox 8 News in New Orleans. "She sent drugs that are illegal to send into our state."

POLICY-ISH

Women sharing personal stories about abortion bans have become a political force

Louisiana's next step would be challenging New York in federal courts, according to legal experts across the political spectrum.

NPR asked Tony Clayton, the Louisiana prosecutor who charged Carpenter, whether Louisiana has plans to do that. Clayton declined to answer.

Case highlights fraught new legal frontier

A major problem with the new shield laws is that they challenge the basic fabric of U.S. law, which relies on reciprocity between states, including in criminal cases, according to Thomas Jipping, a senior legal fellow with The Heritage Foundation, which supports a national abortion ban.

"This actually tries to undermine another state's ability to enforce its own laws, and that's a very grave challenge to this tradition in our country," Jipping said. "It's unclear what legal issues, or potentially constitutional issues, it may raise."

But other legal scholars disagree with Jipping's interpretation. The U.S. Constitution requires extradition only for those who commit crimes in one state and then flee to another state, said Cohen, a law professor at Drexel University's Kline School of Law.

Telemedicine abortion providers aren't located in states with abortion bans and have not fled from those states — therefore they aren't required to be extradited back to those states, Cohen said. If Louisiana tries to take its case to federal court, he said, "they're going to lose because the Constitution is clear on this."

"The shield laws certainly do undermine the notion of interstate cooperation, and comity, and respect for the policy choices of each state," Cohen said, "but that has long been a part of American law and history."

When different states make different policy choices, sometimes they're willing to give up those policy choices to cooperate with another state, and sometimes they're not, he said.

The conflicting legal theories will be put to the test if this case goes to federal court, other legal scholars said.

"It probably puts New York and Louisiana in real conflict, potentially a conflict that the Supreme Court is going to have to decide," said Rebouché, dean of the Temple University Beasley School of Law.

Rebouché, Cohen and law professor Greer Donley worked together to draft a proposal for how state shield laws might work. Connecticut passed the first law — though it did not include protections specifically for telemedicine. It was signed by the state's governor in May 2022, a month before the Supreme Court overturned *Roe v. Wade*, in anticipation of potential future clashes between states over abortion rights.

In some shield-law states, there's a call to add more protections in response to Carpenter's indictment.

New York state officials already have. On Feb. 3, Hochul signed a new law that allows physicians to name their clinic as the prescriber — instead of using their own names on abortion medications they mail out of state. The intent is to

make it more difficult to indict individual doctors. Der Simonian is pushing for a similar law in Maine.

Dr. Samantha Glass, a family medicine physician in New York, has written such prescriptions in a previous job, and plans to find a clinic where she could offer that again. Once a month, she travels to a clinic in Kansas to perform in person abortion procedures.

Carpenter's indictment could cause some doctors to stop sending pills to states with bans, Glass said. But she believes abortion should be as accessible as any other health care.

"Someone has to do it. So why wouldn't it be me?" Glass said. "I just think access to this care is such a life-saving thing for so many people that I just couldn't turn my back on it."

This story comes from NPR's health reporting partnership with WWNO *and* KFF Health News.

dr. margaret carpenter medication ab telemedicine lousiana abortion ban

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ouisiana DA arns there s trove o evidence a ainst doctor ho alle edl mailed abortion pills to teen ho as plannin ender reveal part : report

e or Po t (Feb. 5, 2025)

NEW YORK POST

US NEWS

Louisiana DA warns there's trove of evidence against NY doctor who allegedly mailed abortion pills to teen — who was planning gender reveal party: report

By Katherine Donlevy

Published Feb. 15, 2025, 12:24 p.m. ET

Louisiana prosecutors threatened to have enough clear evidence to extradite a New York doctor who allegedly prescribed abortion pills to an out-of-state teenager — as it was revealed the girl was planning a gender reveal party at the time of the so-called crime, according to a report.

West Baton Rouge District Attorney Tony Clayton warned that he would eventually catch Dr. Margaret Carpenter despite Gov. Kathy Hochul's staunch defense of the New Paltz-based doctor and refusal to send her to Louisana to face charges.

"There's a warrant for her arrest in all 50 states. The issue is, do you live like an Afghan terrorist? You hide in a cave ducking the authorities?" Clayton told NOLA.com in an interview published Friday.

Dr. Margaret Carpenter is wanted by Louisiana prosecutors for allegedly mailing abortion pills to a pregnant teen.

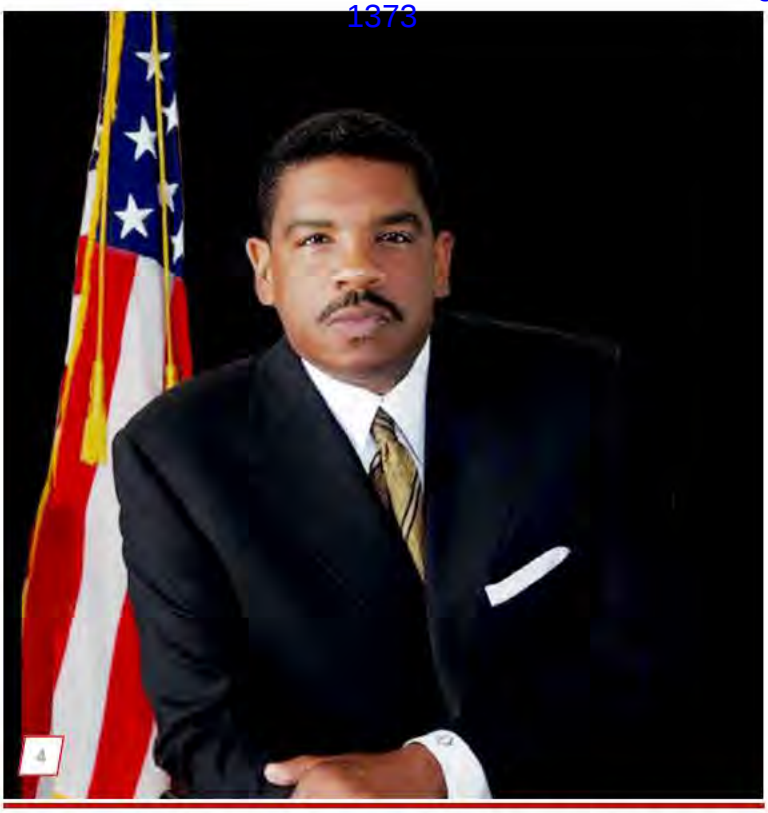
Instagram/godocgoorg

"She has to go to New Jersey, Philadelphia to visit relatives. If she goes on a cruise, if she does anything" outside of New York, we're going to effectuate the warrant."

Clayton has repeatedly claimed that Carpenter violated Lousiana's anti-abortion laws when she mailed a "cocktail of pills" to the teen's mother last year, who allegedly pretended they were for herself before she forced them on her 17-year-old daughter.

Prosecutors claim the guise would have been avoided if Carpenter had asked the family to present more than a questionnaire. The request was fulfilled without a direct consultation, Clayton alleged.

"She should have Zoomed this young lady. FaceTimed this young lady. Spoken to the mother," Clayton told the outlet. "If she had spoken to the mother, she would have seen the mother was not pregnant … For 150 bucks, she put that poison in the mail."



District Attorney Tony Clayton claims the teen was planning a gender reveal party and wanted to keep her baby.

Tony Clayton, District Attorney

The mother paid by credit card for the shipment of medication, Clayton said, then told the 17-year-old that she had to take the pills "or else."

The girl, who has not been identified, accepted the ultimatum despite initially pleading to keep the baby.

"She told the mother she wanted to have the baby. She even planned the gender reveal party. She wanted the child. She was 17 at the time," said Clayton.

The teen's mother has been charged with criminal abortion by means of abortion-inducing drugs, a felony that carries a possible one- to five-year prison sentence.

Carpenter allegedly mailed a "cocktail of pills" without a direct consultation with the patient.
AP

Carpenter and her company, Nightingale Medical, PC, also face the same charge — but have evaded arrest thanks to Hochul's refusal to comply with Lousiana's extradition orders submitted Thursday.

"I want to make sure everyone in the state knows: Keep your hands off this doctor," Hochul said upon receiving the paperwork.

"I'm respecting the laws of New York. Am I supposed to make those subservient to laws of another state?"

New York Attorney General Letitia James also piled on, calling the indictment a "cowardly attempt out of Louisiana to weaponize the law against out-of-state providers," adding that the indictment is "unjust and un-American."

Gov. Kathy Hochul has refused to comply with Louisiana's extradition order for Carpenter.

Erik Pendzich/Shutterstock

Clayton, however, remains unwavering and warned that he could rely on a 1987 Supreme Court decision that granted federal authorities the power to enforce extraditions of fugitives, in a case out of Puerto Rico.

The ruling came up in 2023 in relation to a pledge by Florida Gov. Ron DeSantis that he wouldn't assist in President Trump's extradition from Florida to face hush-money charges in New York. Trump went on his own, NOLA.com reported.

"I'm terming it a forced abortion, which makes it even more egregious," Clayton told the outlet.

"Ignorance of the law is no excuse. If Dr. Carpenter did not know the mother was using this pill to induce abortion involving a child, that's on her. She should not have shipped the pills."

FILED UNDER ABORTION, KATHY HOCHUL, LOUISIANA, NEW YORK, WOMEN'S RIGHTS, 2/15/25

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ABORTION POLICY CRIMINAL JUSTICE GOVT + POLITICS HEALTH CARE

Louisiana mother pleads not guilty following abortion pill indictment

BY: **LORENA O'NEIL** - MARCH 11, 2025 4:59 PM

A Louisiana district attorney is prosecuting a New York doctor and West Baton Rouge Parish mother who allegedly provided abortion pills to her minor daughter. (Phil Walter/Getty Images)

A mother from Port Allen caught up in a landmark abortion pills case pleaded not guilty Tuesday to felony criminal charges for allegedly providing her minor daughter with medication to end her pregnancy.

The woman was indicted Jan. 31 for allegedly giving her teen daughter pills she had obtained through the mail. Dr. Margaret Carpenter, the New York physician who allegedly prescribed and sent the pills to Louisiana, was also indicted on felony charges. It's the first criminal case of its kind in the country since the U.S. Supreme Court overturned *Roe v. Wade* in 2022.

The Illuminator is not identifying the mother in order to protect her daughter's privacy. The case involves a 2022 Louisiana law that makes it a crime to knowingly cause an abortion with medication. It carries penalties of one to five years in prison and a fine ranging from $5,000-$50,000.

The mother was taken into custody the same day as her indictment and posted bond that evening. West Baton Rouge District Attorney Tony Clayton is prosecuting this case with Louisiana Attorney General Liz Murrill.

"I'm charging the mother because she ordered the pill, and she paid for the pill with her credit card and she gave the pill to a minor," Clayton told the Illuminator. "That's illegal in the state of Louisiana."

Brusly attorney Victor Woods is representing the mother, his office confirmed Tuesday. He is not currently accepting interview requests.

Clayton and Murrill allege the Port Allen mother gave her pregnant teen daughter an ultimatum to take the medication or move out of the house.

"The child took the pill and was home by herself," Clayton said, adding that she later started bleeding, called 911 and was taken to a hospital in an ambulance.

A police officer who responded to the call initially thought the teen was experiencing a miscarriage but "found out" she had taken abortion pills provided from an out-of-state clinic, the district attorney said.

Murrill has repeatedly claimed the crime is "about coercion" and "forcing somebody to have an abortion who didn't want one." However, no charges of coerced abortion have been brought against the teen's mother or Carpenter, the doctor.

The case has received national attention because Louisiana officials have sought to extradite Carpenter, testing New York's shield laws protecting providers who prescribe abortion medication to patients out of state.

Democratic Gov. Kathy Hochul of New York said she will "never" extradite Carpenter after Republican Louisiana Gov. Jeff Landry filed paperwork requesting it. Murrill, also a GOP member, warned Carpenter to "be careful" with her travel plans, suggesting other states might cooperate with Louisiana's extradition request.

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LORENA O'NEIL

Lorena O'Neil is a freelance reporter based in New Orleans. She covers reproductive health, gender, culture and politics.

MORE FROM AUTHOR

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May 23, 2025

Case of a brain-dead pregnant woman kept on life support is 'gut-wrenching,' advocates say

BY **GRACE PANETTA, THE 19TH** AND **BARBARA RODRIGUEZ, THE 19TH**

May 18, 2025

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STATES NEWSROOM

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EXHIBIT

o ernor at y oc ul (o at y oc ul),
(May 3, 2025, 4 2 PM)

Governor Kathy Hochul
@GovKathyHochul

The anti-choice zealots can file as many cases as they want.

In New York, we protect our providers.

Let me be clear: we will never comply with Louisiana's extradition request. Not now, not ever.

TIMES UNION

HUDSON VALLEY // NEWS

Louisiana investigating second abortion case against New Paltz doctor

Dr. Margaret Daley Carpenter is accused of mailing abortion pills to a Louisiana woman who used them while 20 weeks pregnant

By **Maria M. Silva**, *Staff Writer*
May 13, 2025

4:28 PM · May 13, 2025 · **58** Views

145 28 84 3

EXHIBIT 2

Rosalie Mar e ic Declaration

UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF LOUISIANA
LAFAYETTE DIVISION

THE STATE OF LOUISIANA, by and through its Attorney General, LIZ MURRILL, and ROSALIE MARKEZICH,

PLAINTIFFS,

v.

U.S. FOOD AND DRUG ADMINISTRATION; MARTIN A. MAKARY, M.D., M.P.H., in his official capacity as Commissioner of Food and Drugs, U.S. Food and Drug Administration; GEORGE FRANCIS TIDMARSH, M.D., PH.D., in his official capacity as Director, Center for Drug Evaluation and Research, U.S. Food and Drug Administration; U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; and ROBERT F. KENNEDY, JR., in his official capacity as Secretary, U.S. Department of Health and Human Services,

DEFENDANTS.

Civ. No. 6:25-cv-01491

Judge: _____

Mag. Judge: _____

DECLARATION OF ROSALIE MARKEZICH

I, Rosalie Markezich, a citizen of the United States of America and a resident of the State of Louisiana, declare under penalty of perjury under 28 U.S.C. § 1746 that the following is true and correct to the best of my knowledge.

1. I am over eighteen years old and make this declaration on personal knowledge.
2. I was born in Mandeville, Louisiana, in 2001 and—with the exception of the year 2017—have lived in Louisiana since that time.
3. Around October 2023, my then-boyfriend and I had unprotected sex. Afraid he got me pregnant, he procured and I took Plan B (also known as the "morning-after pill"). I didn't think I was ready to have a child at that moment because of my financial situation. And my boyfriend and I had only been dating for two months.
4. I found out I was pregnant on October 13, 2023. I had missed my period, so I took a pregnancy test. Deep down, I knew it would be positive. And deep down, I was hoping it would be positive. And when I saw the positive pregnancy test, I just smiled. I was overjoyed that Plan B had not worked.
5. I wanted to keep my child and feared my boyfriend's reaction, so I debated whether to tell him that I was pregnant. Ultimately, I decided he had the right to know.
6. When I first told my boyfriend that I was pregnant, he was excited and wanted to live together. He said raising our child together would be "legendary." But he soon changed his mind. He said his sister knew how to get chemical abortion drugs, and he wanted me to take them.
7. Using my personal email address and mailing address, my boyfriend filled out an online form and ordered the drugs (mifepristone and misoprostol) from an online provider that his sister has used multiple times before.

8. He sent me $150 through the Venmo banking app to pay for the drugs he ordered. I forwarded the payment directly to the prescriber, Remy Coeytaux, MD PC, the next day. This was the only touch point I had with a doctor before receiving the drugs.

9. The drugs were sent from a provider located in California and delivered to my home address in Louisiana a few days later via the United States Postal Service. The tracking number was 9400109105156542182650.

10. I did not want to take the drugs. When I saw my boyfriend the next weekend, I pretended that I had already taken the drugs, but he did not believe me.

11. We took a drive to discuss the matter further. My boyfriend said that his life would be ruined if I kept the baby. I stood my ground. I repeated that I wanted to keep the baby and would raise the baby with my mother in Michigan. But he did not like that plan either. He did not want a child, let alone a child he would have to support in another state. I told him that if I aborted this child, I would never be the same. I pleaded with him: "Don't make me do this."

12. He became angry. He abruptly pulled the car into a hospital parking lot and started shouting at me. My boyfriend had anger issues and a criminal record, so I was terrified and started crying. I also have suffered prior domestic abuse, so I knew the signs of an unpredictable man and that I needed to be careful about my next move. My roommates did not know that I was with him. Should anything happen to me, no one would know where I was. So to pacify him, I told him I would take the drugs. I planned to throw up the drugs as soon as I could.

13. My boyfriend took me to his house and watched me take both drugs at the same time. I had hoped that taking them simultaneously might stop them from working. He started to drive me home, but I had a panic attack during the drive because I feared for my baby's safety and that I would not be able to throw up the drugs in time. I shook violently and my arms locked up. So he turned around and took me back to his house, where his parents also lived.

14. I went to the bathroom to throw up the drugs, but I was unsuccessful. Ten minutes later, I started bleeding. I lay in the bathroom for approximately an hour, bleeding and crying for the loss of my child. I could not look at my boyfriend. To avoid him, I went to the garage and lay there on a blood-soaked towel for the rest of the night.

15. In the morning, my boyfriend was still mad. After his mother brought me a stuffed animal and I refused it, he threw the stuffed animal across the room. I climbed into bed and stared into space for the rest of the weekend. I continued to bleed heavily for about a week.

16. I did not want to have an abortion.

17. I was a daycare teacher and worked with one-year-old children. When I returned to work on Monday, it was so hard being there knowing that I would never hold the hand of my own child. I mourned the child I thought I was going to have. I eventually switched jobs so I could work with older children at a Christian school.

18. The trauma of my chemical abortion still haunts me. I often re-live the experience of feeling forced to abort and lose my baby, causing me to become anxious, depressed, and afraid. Because of this ongoing trauma, I am seeing a psychiatrist who has prescribed me medication to help relieve these effects. My trauma also hurt my relationships with my friends and roommates, who could not understand why I needed so much time and space to heal. I am still healing.

19. Had the FDA required an in-person visit with a doctor before dispensing the drugs, my boyfriend would never been able to obtain the drugs that he made me take. I also would have told the doctor that I did not want to take them. And I would have told the doctor that I wanted to keep my baby. I do not believe a doctor would have prescribed me the drugs if I told her I did not want them.

20. I searched for post-abortion support online and came across a pro-life webpage. I was eventually connected with a counselor who helped me heal by pointing me to

God. I am grateful for her support and prayerful encouragement. With her help, I started to glue my heart back together.

21. I attempted to hold a baby supply drive on the anniversary of my due date, but I was unable to pool enough resources in time. I would still love to do so in the future to honor my baby.

22. In 2024, I testified under the pseudonym "Samantha" in support of Senator Thomas Pressly's SB 276. And I am sharing my story now because I want to be the helper I wish I had.

23. No woman should have to experience what I went through.

Executed this 17 day of July, 2025.

By Rosalie Markezich
Rosalie Markezich

EXHIBIT 106

The Associated Press,
Texas Has a New Abortion Pill Law. But At Least One Provider Plans to Keep Shipping Them There,
Newsday (Sept. 18, 2025)

Advertisement

NEWS / NATION/WORLD

Texas has a new abortion pill law. But at least one provider plans to keep shipping them there

Dr. Angel Foster, co-founder of Massachusetts Medication Abortion Access Project, points out on a map of the United States on May 13, 2025, in Somerville, Mass., to show where her organization provides care. Credit: AP/Charles Krupa

By The Associated Press
September 18, 2025 11:41 am

SHARE

Republican Texas Gov. Greg Abbott has signed a first-of-its-kind law that lets anyone sue prescribers and others responsible for getting abortion pills into the state.

Supporters are heralding the law, which Abbott signed Wednesday, as a way to enforce an existing ban. Abortion-rights advocates are bashing the law, saying it has the potential to turn abortion opponents, aggrieved former lovers and others into bounty hunters.

But it doesn't mean that organizations will stop sending pills into Texas.

Advertisement

Angel Foster, who runs Massachusetts-based The MAP, which prescribes the regimen of pills to women in every state, said her organization will keep sending pills to women in Texas, as it has about 10,000 times in the past two years.

“We really don’t change things unless we’re legally required to,” she said.

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Rebecca Nall, the founder of I Need an A, which runs a website with abortion access information, suggested other providers also won't change.

“We’re confident people in Texas (and every state) will still be able to get abortion pills by mail,” she said in an email.

Pills are at the heart of a new generation of abortion lawsuits

The majority of abortions in the U.S. employ pills, usually a combination of the drugs misoprostol and mifepristone.

Since the U.S. Supreme Court overturned Roe v. Wade in 2022 and allowed states to enforce abortion bans, the method has moved to the center of the latest legal and political battles.

At least eight Democratic-controlled states have adopted shield laws that seek to protect medical professionals in their borders who prescribe the pills via telehealth and send them to patients in states where abortion or telehealth pill prescriptions are banned.

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Those prescriptions are a key reason that the number of abortions has not fallen despite 12 states enforcing bans on abortion at all stages of pregnancy, with limited exceptions, and four more barring it after about six weeks of gestation.

The Texas law allows $100,000 claims against prescribers and others

The Texas law, which is to take effect in three months, builds on an approach the state used when it implemented an earlier abortion ban: leaving enforcement to private people filing lawsuits rather than the government.

Under this measure, anyone could file a claim for $100,000 against people who cause the pills to be sent to Texas.

If a pregnant woman, the man who impregnated her or other close relatives sue successfully, they could be entitled to collect the entire $100,000. Others who sue would be in line for $10,000 — with the other $90,000 going to charity.

The law also answers a provision of shield laws that allows protected prescribers to sue those who sue them. The Texas law says that would not apply for the civil suits that originate there.

Advertisement

One provider says her group won't be deterred

The Abortion Coalition for Telemedicine, which provides legal and other support for abortion pill prescribers, is telling members that the shield laws should protect them from civil suits from Texas, said McKensey Smith, the group's deputy director.

Texas, the nation’s second most populous state, accounts for about one-third of the pills The MAP prescribes.

Foster said that she expects other prescribers to keep sending the pills to Texas, too.

She still anticipates the law will have an impact: Women seeking abortion in Texas could stop telling others that they are planning to seek pills from out-of-state providers lest those confidants use the information to launch lawsuits.

"One of the effects will be to isolate abortion patients in Texas," Foster said.

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Pill access is facing other court challenges

Mary Ziegler, a law professor at the University of California, Davis, said she expects that people sued under the Texas law will make their own court claims, arguing that it is not enforceable.

"The drug manufacturers and the providers are all willing to take the risk that the shield laws will protect them," she said.

She said the result could be individual court decisions on whether the Texas law applies in certain circumstances rather than one sweeping ruling.

Those suits won't be the first legal test around abortion pills, though.

Last month, Texas and Florida asked a court if they could join a lawsuit filed by the attorneys general of Idaho, Kansas and Missouri that seeks to have some federal approvals for mifepristone rolled back — and possibly blocking telehealth prescriptions for it.

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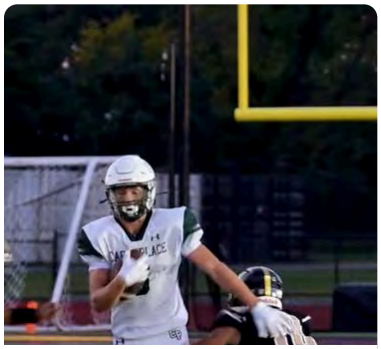
And a New York doctor accused of shipping pills out of state faces two legal actions: criminal charges in Louisiana and a civil judgment in Texas. New York officials are refusing to extradite her or to enforce the judgment.

Newsday TV SHORTS



Carle Place athlete told he can't play both football and soccer

02:17

'The most rewarding hobby I've ever had'

03:33

What's up on LI: Greenp Maritime Festival, Grea Cow Harbor Day and Ompahfest

01:02

EXHIBIT 110

Letter from Robert F. Kennedy, Jr., Secretary of Health and Human Services, to Attorneys General (Sept. 19, 2025)

DEPARTMENT OF HEALTH & HUMAN SERVICES
Office of the Secretary
Washington, D.C. 20201

September 19, 2025

Dear Attorneys General:

Thank you for your letter of July 31, 2025, regarding the review of mifepristone by the Food and Drug Administration (FDA), an agency of the U.S. Department of Health and Human Services (HHS). We write to provide an update on this review.

As you noted, the FDA first approved Mifeprex (mifepristone) in September 2000 for medical termination of pregnancy (abortion) through seven weeks gestation. In 2016, the FDA extended this window to ten weeks gestation, and relaxed certain other requirements under the drug's Risk Evaluation and Mitigation Strategy (REMS). Most recently, in 2023, the FDA modified the REMS program again by removing the in-person dispensing requirement.

Since its original approval, the FDA has received reports of serious adverse events in patients who took mifepristone. As with all approved drugs, when the FDA receives new information regarding adverse events, the agency reviews the new information and, as appropriate, takes necessary action. The FDA continuously reviews reports of adverse events to determine, among other things, whether they are known risks or whether they are signals of emerging safety concerns.

Under the Food and Drug Administration Amendments Act, the Secretary is authorized to require a REMS when "necessary to ensure that the benefits of the drug outweigh the risks of the drug." 21 U.S.C. § 355-1(a). For drugs that are "inherent[ly] toxic[] or potential[ly] harmful[]," the Secretary "may require that the [REMS] include such elements as are necessary to assure safe use of the drug." *Id.* § 355-1(f)(1). The Secretary is also authorized to require modifications to an existing REMS when he, among other things, "determines that 1 or more goals or elements should be added, modified, or removed from the [current REMS] to … ensure the benefits of the drug outweigh the risks of the drug." *Id.* § 355-1(g)(4)(B).

HHS is committed to studying the adverse consequences reported in relation to mifepristone to ensure the REMS are sufficient to protect women from unstated risks. Therefore, through the FDA, HHS will conduct a study of the safety of the current REMS, in order to determine whether modifications are necessary. HHS's decision to do so is informed by the lack of adequate consideration underlying the prior REMS approvals, and by recent studies raising concerns about the safety of mifepristone as currently administered.

To that end, HHS—through the FDA—is conducting its own review of the evidence, including real-world outcomes and evidence, relating to the safety and efficacy of the drug. Given the 2016 FDA decision to eliminate the REMS requirement for certified prescribers to report non-fatal serious adverse events to the mifepristone sponsors, this review will contribute to the understanding of the drug's safety profile.

Recent studies—such as the study by the Ethics and Public Policy Center (EPPC), which you highlighted in your letter—indicate potential dangers that may attend offering mifepristone without sufficient medical support or supervision. FDA's own data collected between 2000 to 2012 indicated 2,740 adverse events, including 416 events involving blood loss requiring transfusions. Since then, safeguards for women regarding the administration of mifepristone have been significantly reduced.

The concerns you have raised in your letter merit close examination. This Administration will ensure that women's health is properly protected by thoroughly investigating the circumstances under which mifepristone can be safely dispensed.

* * *

HHS and FDA remain committed to protecting the health and safety of pregnant women. This review will help ensure that the FDA's decisions are grounded in Gold Standard Science and rigorous, transparent, and objective evidence.

Thank you again for your continued engagement in this matter. We will keep you informed as the FDA's review of mifepristone progresses.

Sincerely,

/s/

Robert F. Kennedy, Jr.
Secretary

/s/

Martin A. Makary, MD, MPH
Commissioner of Food and Drugs

UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF LOUISIANA
LAFAYETTE DIVISION

THE STATE OF LOUISIANA, by and through its Attorney General, LIZ MURRILL, and ROSALIE MARKEZICH, *Plaintiffs*, v. U.S. FOOD AND DRUG ADMINISTRATION, *et al.*, *Defendants.*	Case No.: 6:25-cv-01491-DCJ-DJA Judge David C. Joseph Magistrate Judge David J. Ayo

PLAINTIFFS STATE OF LOUISIANA AND ROSALIE MARKEZICH'S MOTION FOR PRELIMINARY RELIEF UNDER 5 U.S.C. § 705

Plaintiffs State of Louisiana and Rosalie Markezich respectfully move under 5 U.S.C. § 705 for an order staying or postponing the effective date of the 2023 Risk Evaluation and Mitigation Strategy that the U.S. Food & Drug Administration (FDA) issued to allow mifepristone to be dispensed remotely (the 2023 REMS). Plaintiffs also move in the alternative under 5 U.S.C. § 705 for a preliminary injunction under Rule 65 of the Federal Rules of Civil Procedure ordering FDA to suspend or withdraw the 2023 REMS while this case proceeds.

The 2023 REMS is unlawful for at least the following reasons:

First, as five Fifth Circuit judges already have indicated, the 2023 REMS is arbitrary and capricious and an abuse of discretion in violation of the Administrative Procedure Act, 5 U.S.C. § 706(2)(A). *All. for Hippocratic Med. v. FDA*, No. 23-10362, 2023 WL 2913725, at *17–18 (5th Cir. Apr. 12, 2023) (*Alliance I*); *All. for Hippocratic Med. v. FDA*, 78 F.4th 210, 249–51 (5th Cir. 2023) (*Alliance II*), *rev'd and remanded on other grounds*, 602 U.S. 367 (2024) (*Alliance*). That is because FDA permanently removed the in-person dispensing requirement and made other changes based on sources that the agency conceded did not support its decision.

Second, the 2023 REMS is "otherwise not in accordance with law." 5 U.S.C. § 706(2)(A). Under 18 U.S.C. § 1462, Congress prohibits the use of "any express company or other common carrier or interactive computer service" for "any drug, medicine, article, or thing designed, adapted, or intended for producing abortion." Because a federal agency cannot permit what federal law expressly prohibits, FDA lacked authority to permanently remove the in-person dispensing requirement.

For these reasons, and as set forth fully in Plaintiffs' Complaint and supporting Memorandum of Law, interim relief is necessary and appropriate to mitigate irreparable injuries caused by the 2023 REMS. Interim relief will serve the public interest and will not harm Defendants.

This Motion is made on the grounds specified in this Motion, the accompanying Memorandum of Law, the exhibits attached to this Motion, the Complaint, and the Complaint's accompanying exhibits, as well as on such other and further oral or documentary evidence as may be presented to the Court at or before a hearing on this Motion.[1] An exhibit list and a proposed order are attached.

CONCLUSION

Under 5 U.S.C. § 705, the Court should enter an order against Defendants, including their employees, agents, successors, and all persons in active concert or participation with them, in which the Court:

1. Stays or postpones the effective date of the 2023 REMS while this case proceeds, and ensures that the "[t]he in-person dispensing requirement[ ], and FDA's obligation to enforce [it], will continue to apply," *Alliance II*, 78 F.4th at 254, or

2. Issues a preliminary injunction ordering Defendants to withdraw or suspend the 2023 REMS and to restore the in-person dispensing requirement while this case proceeds.

[1] Because the injunctive relief requested would serve the public interest, Plaintiffs ask the Court to exercise its discretion to not require a security or bond under Fed. R. Civ. P. 65(c). *See City of Atlanta v. Metro. Atlanta Rapid Transit Auth.*, 636 F.2d 1084, 1094 (5th Cir. 1981).

Respectfully submitted this 17th day of December, 2025.

s/ Michael T. Johnson
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*pro hac vice forthcoming

CERTIFICATE OF CONFERENCE

I hereby certify that, pursuant to Local Rule 7.4.1, counsel conferred in good faith regarding the relief sought in this Motion. Defendants oppose Plaintiffs' Motion.

s/ Caitlin Huettemann
Caitlin Huettemann

EXHIBIT 2

#WeCount Report Summary Slides with National and 51 State-Level Findings April 2022 to June 2025 (Dec. 9, 2025)

#WeCount in context: the landscape of research efforts to count abortions

		#WeCount	Guttmacher Monthly Abortion Provision Study	CDC Abortion Surveillance
Timing	Reporting cadence every…	6 months	1 month	1 year (last 2022)
	Data interval	Monthly	Monthly	Annual
Type	Telehealth abortions to states where permitted	**Yes**	**Yes**	**Some**
	Abortions provided under shield laws to states with any legal abortion	**Yes**	**Yes**	No
	Abortions provided under shield laws to states with bans	**Yes**	No	No
	Abortions provided outside the formal healthcare system	No	No	No
Additional variables	Reports telehealth breakdown	**Yes**	No	No
	Abortion characteristics beyond counts	No	**Yes**	**Yes**

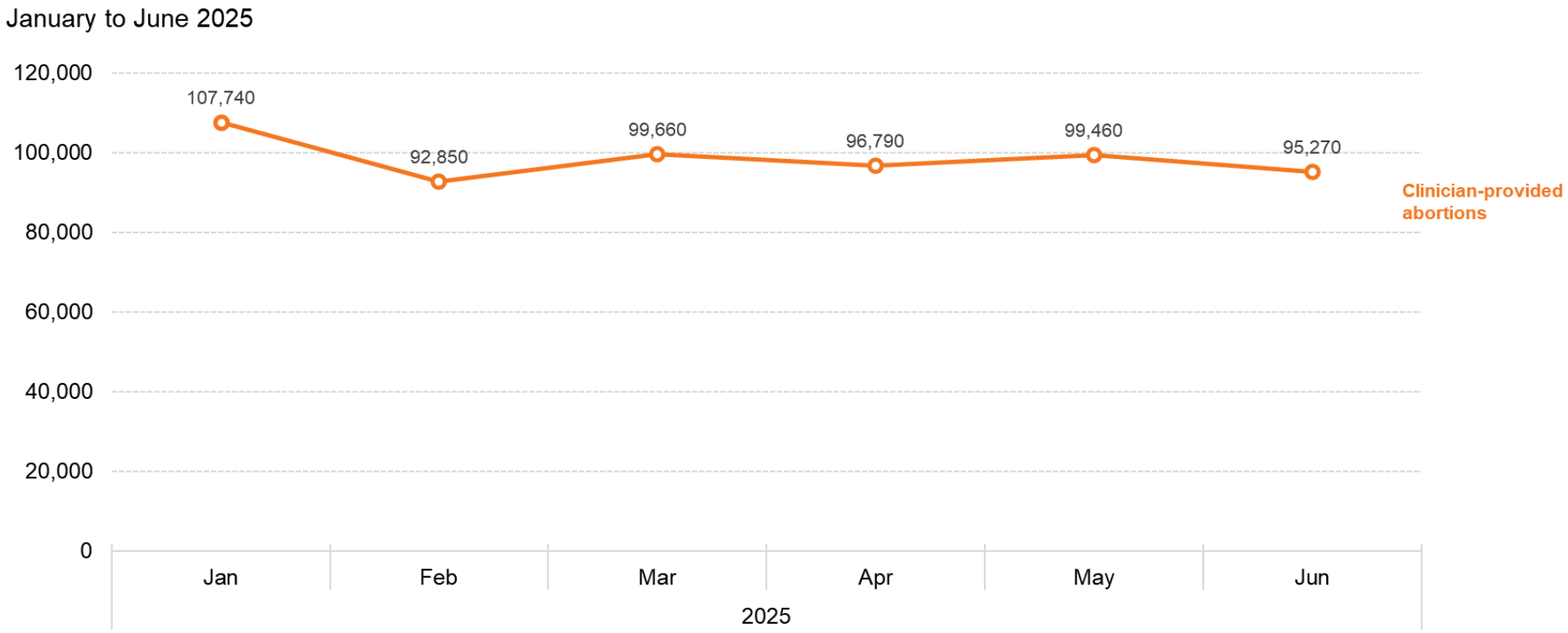
Source: Society of Family Planning, December 2025

States reflected across efforts to count abortions

Source: Society of Family Planning, December 2025

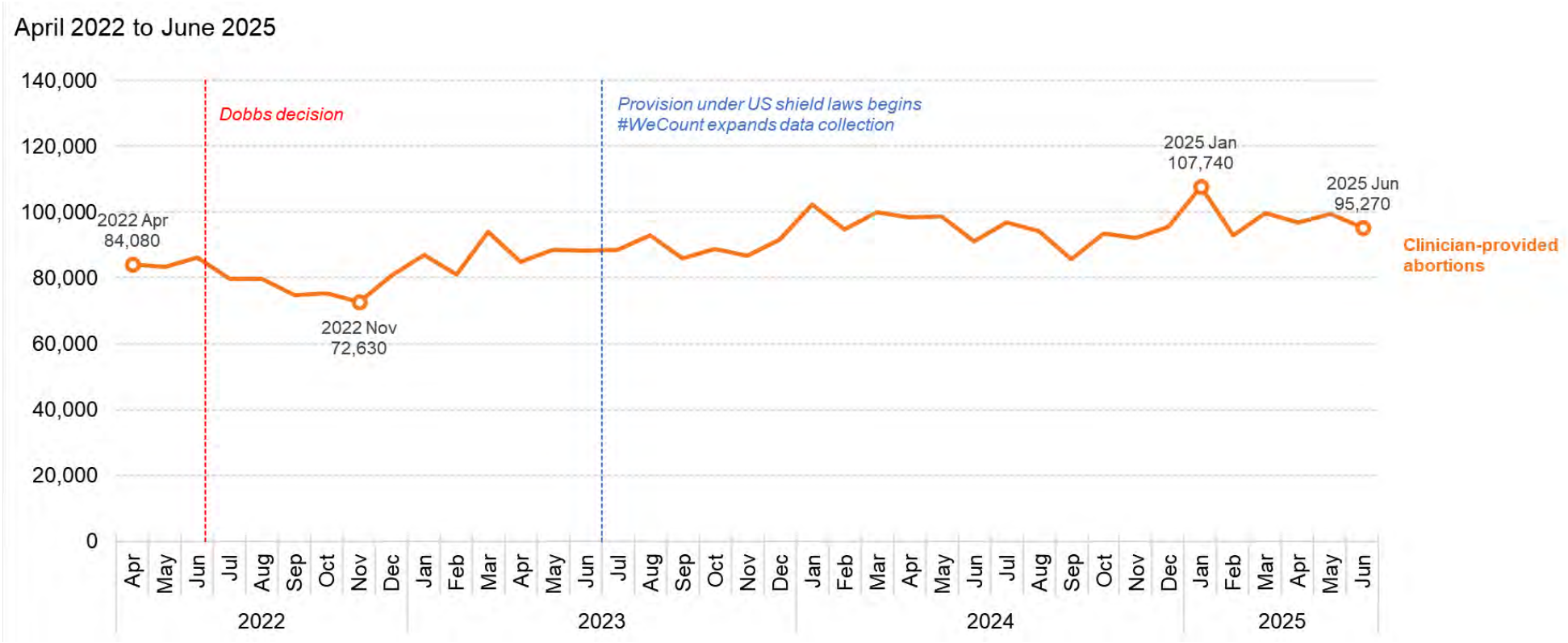
National findings

US abortions totaled 591,770 in the first six months of 2025



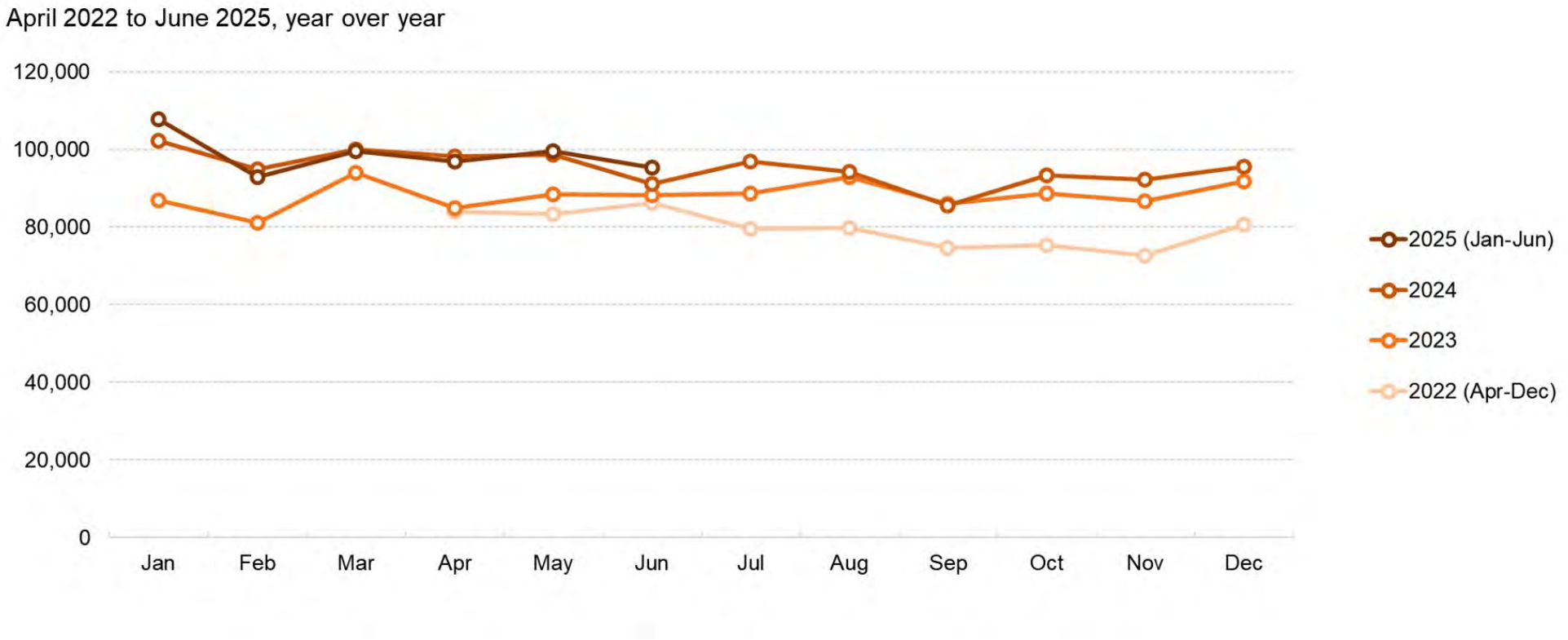
Source: Society of Family Planning, December 2025

Abortions in the US have increased since *Dobbs*



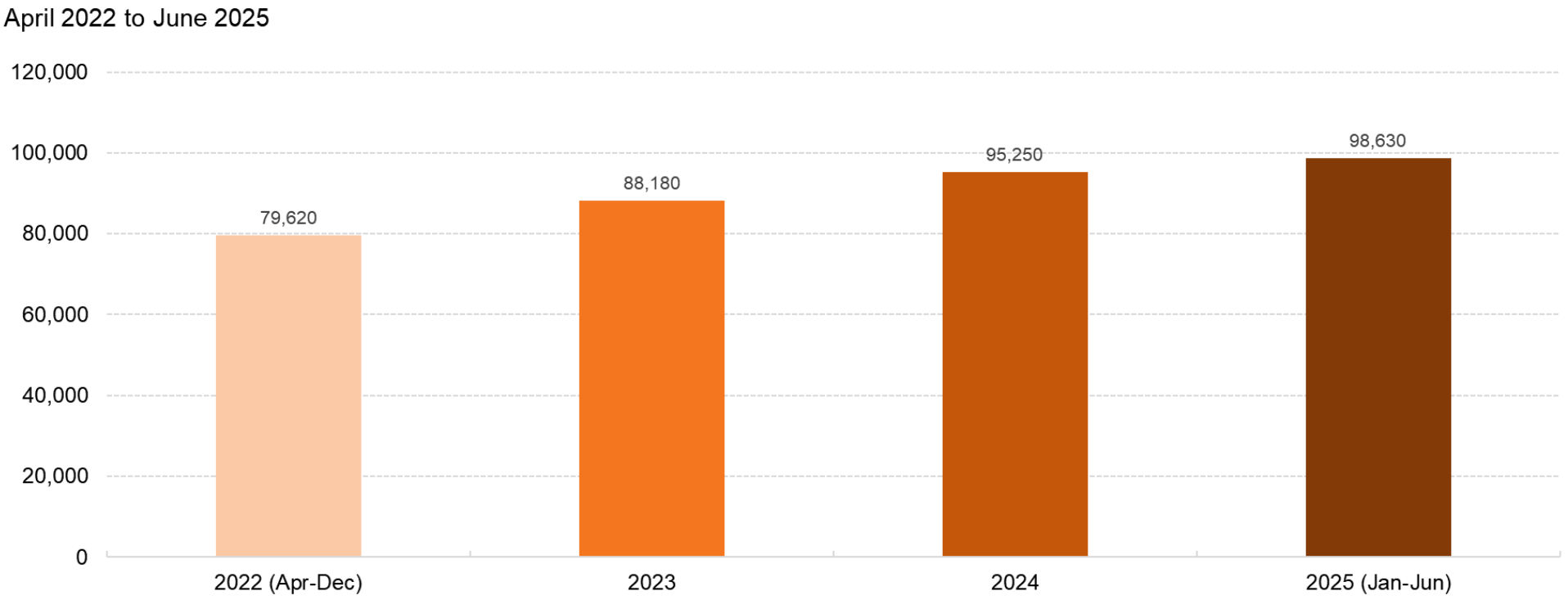
Source: Society of Family Planning, December 2025

Abortion volume fluctuates from month to month, and has increased year-over-year



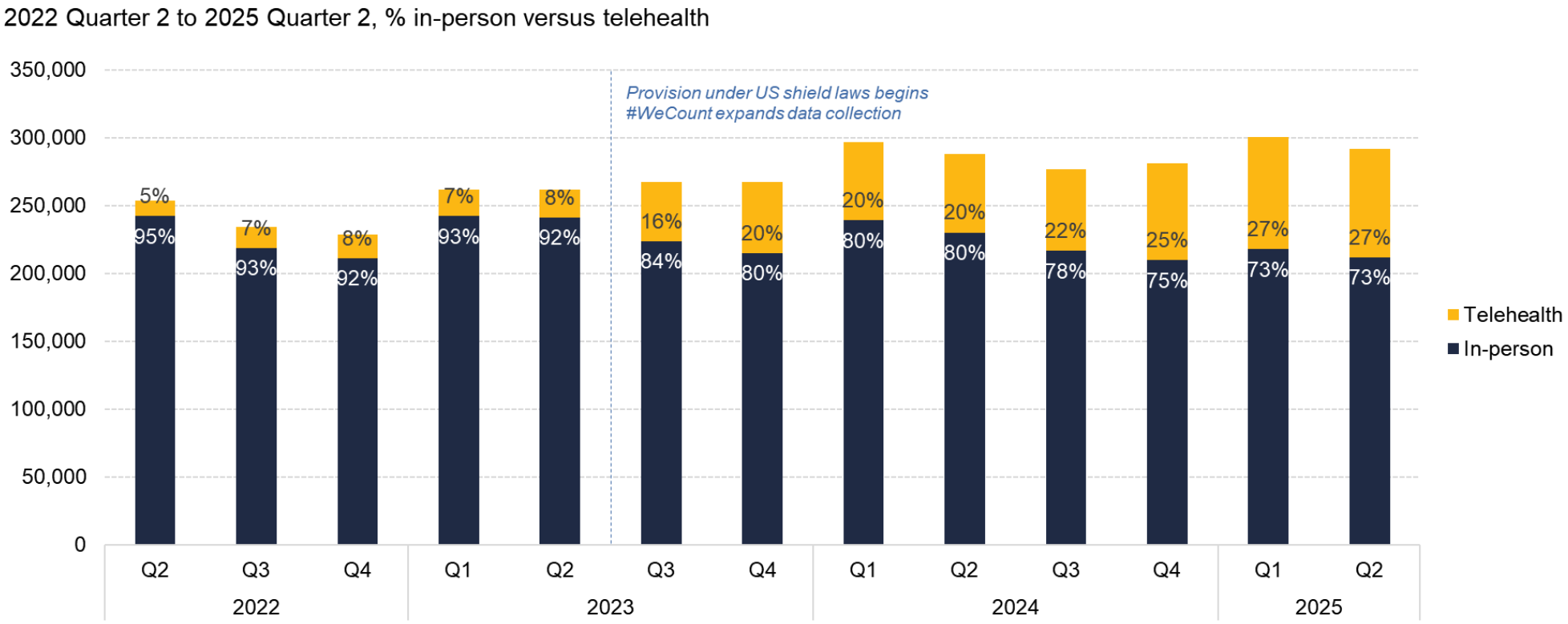
Source: Society of Family Planning, December 2025

Monthly average number of abortions increased each year



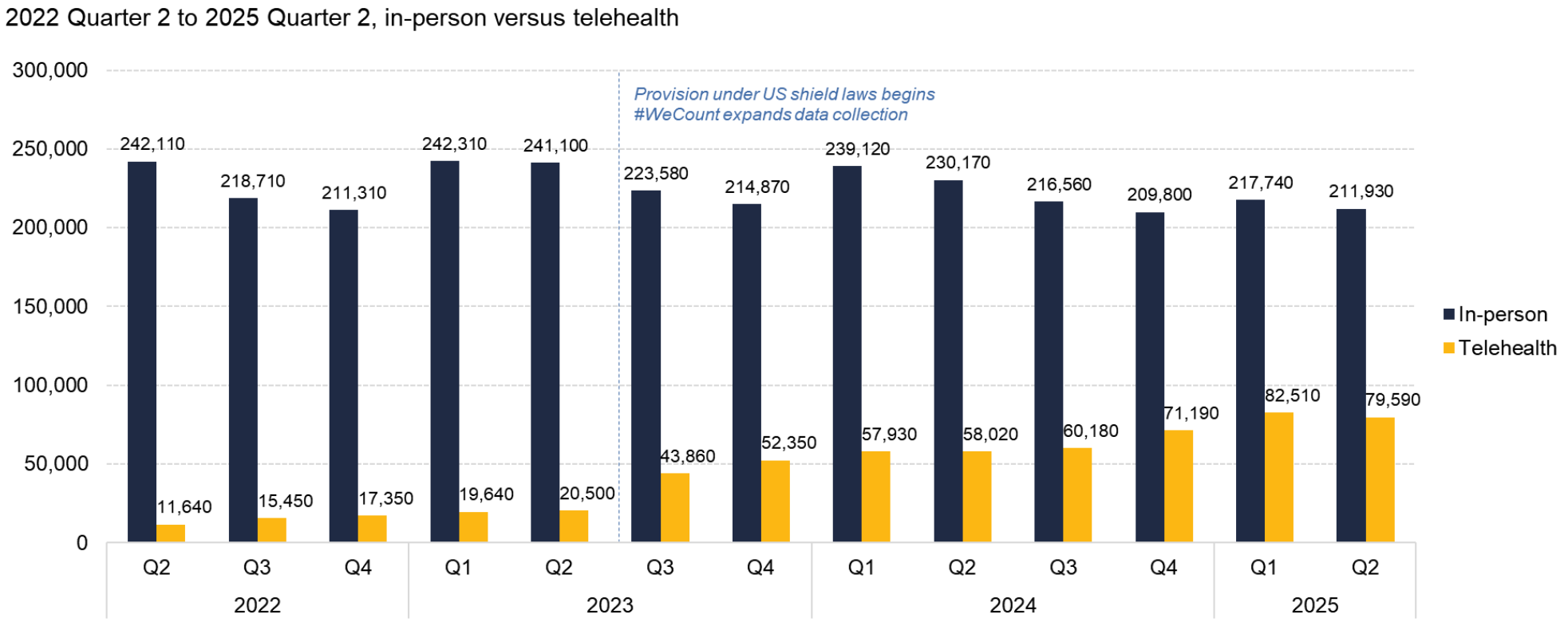
Source: Society of Family Planning, December 2025

In the first six months of 2025, 27% of abortions were provided via telehealth



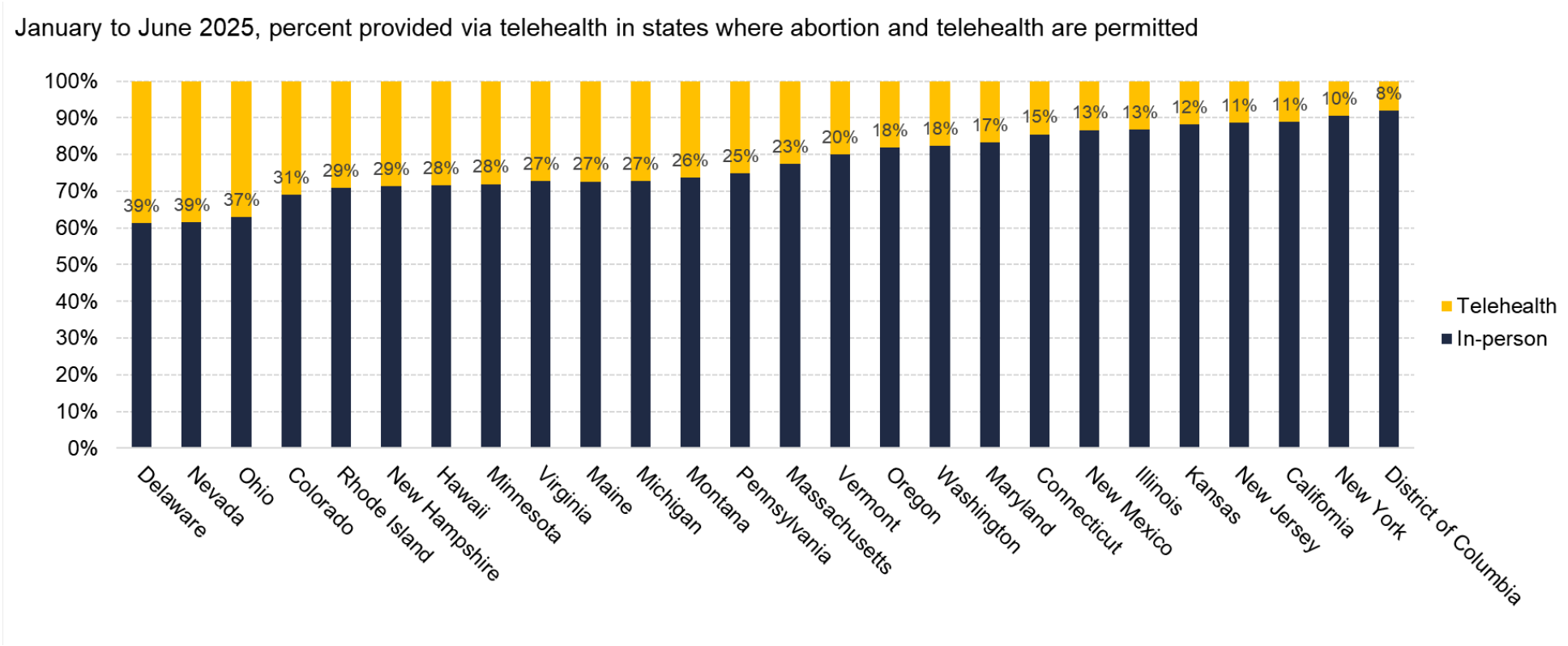
Source: Society of Family Planning, December 2025

In-person abortion care declined slightly, while telehealth grew



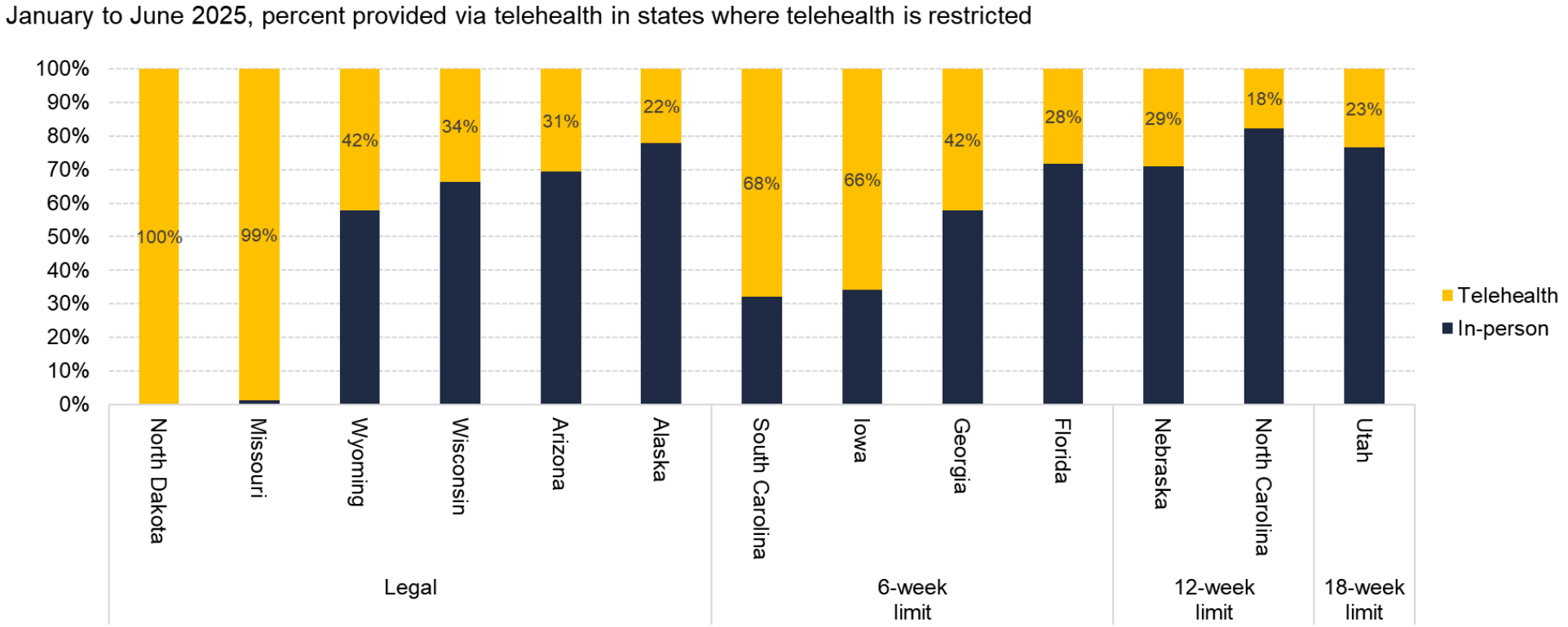
Source: Society of Family Planning, December 2025

Where abortion and telehealth are permitted, the share of abortions provided via telehealth varied widely



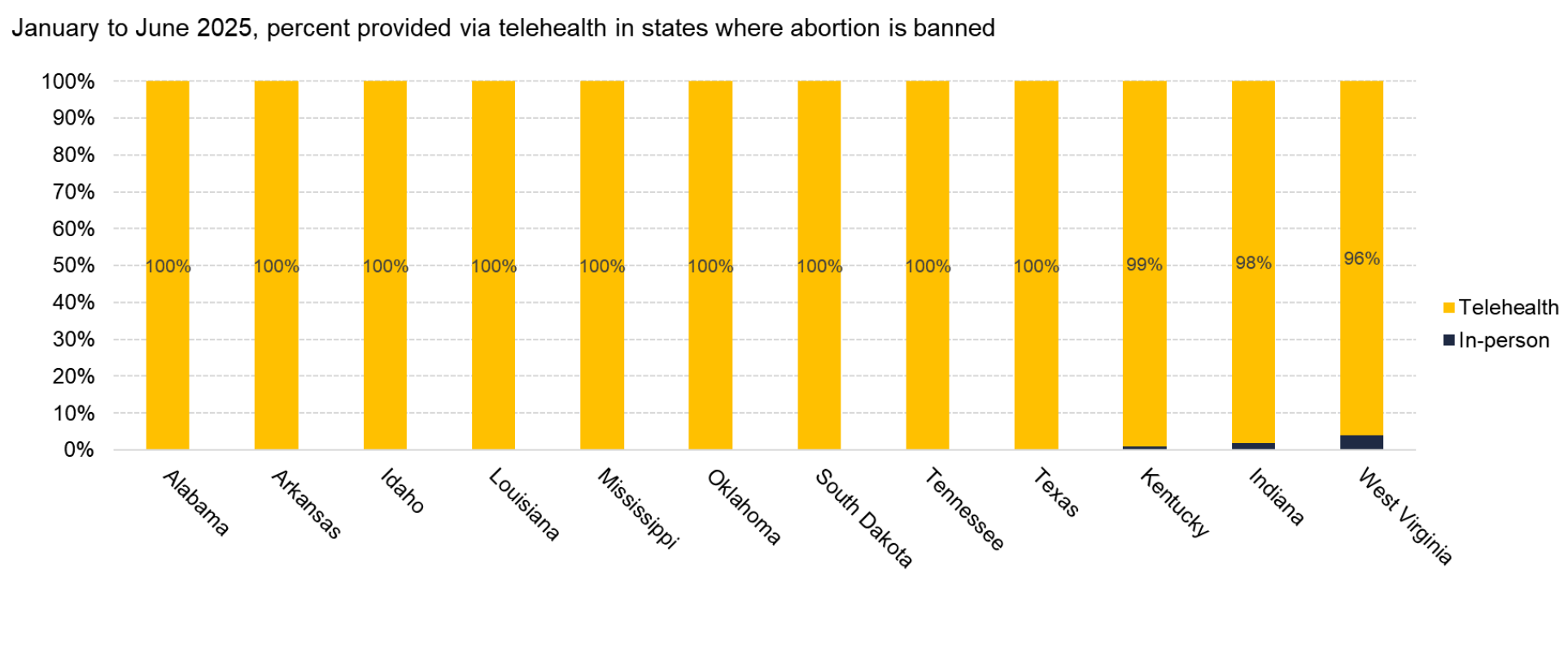
Source: Society of Family Planning, December 2025

Where telehealth abortion is restricted, the share of abortions provided via telehealth under shield laws varied widely



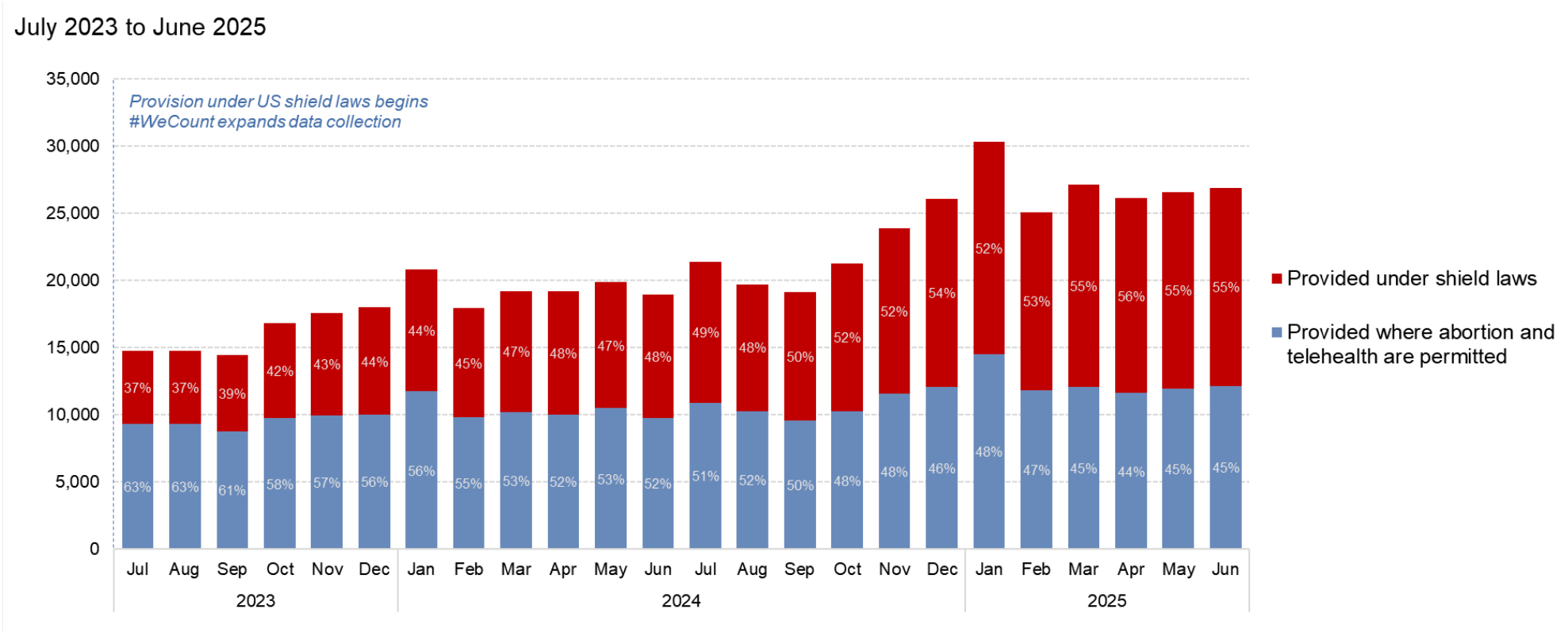
Source: Society of Family Planning, December 2025

Where abortion is banned, nearly all abortions were provided via telehealth under shield laws



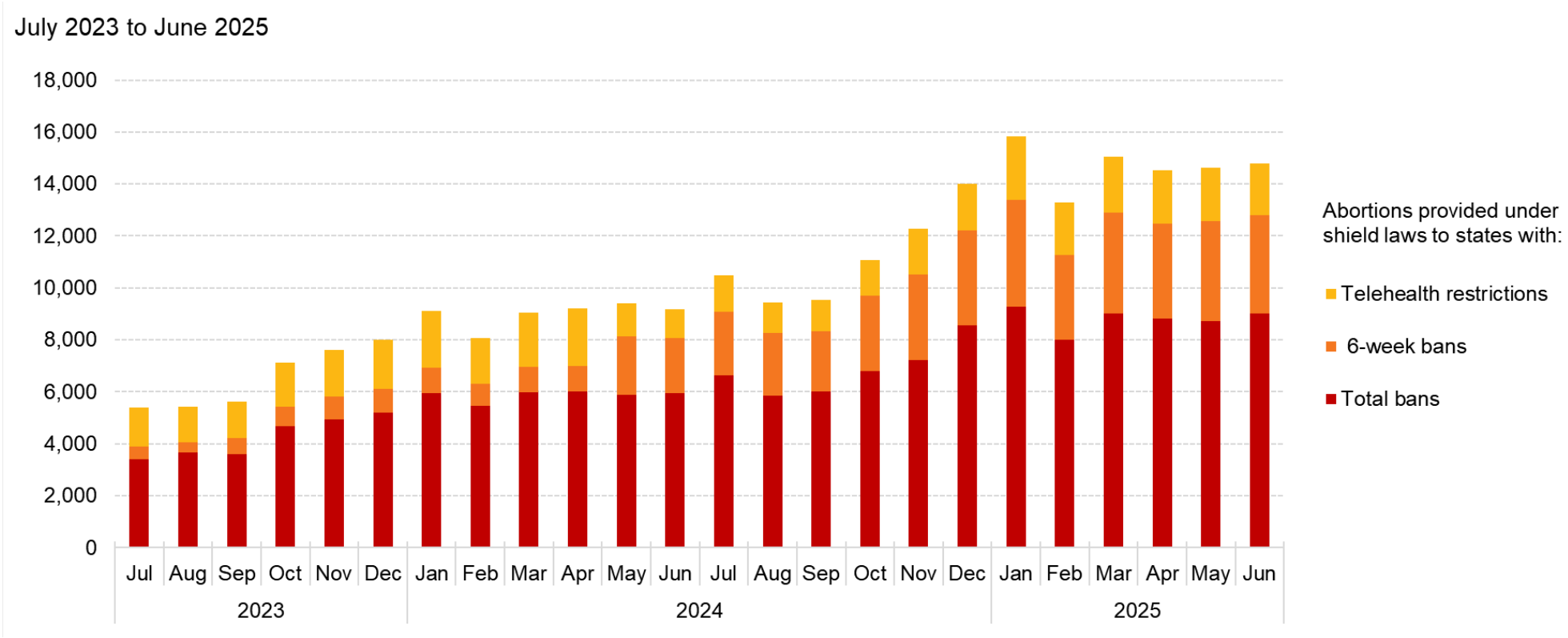
Source: Society of Family Planning, December 2025

A growing share of telehealth abortions are provided under shield laws



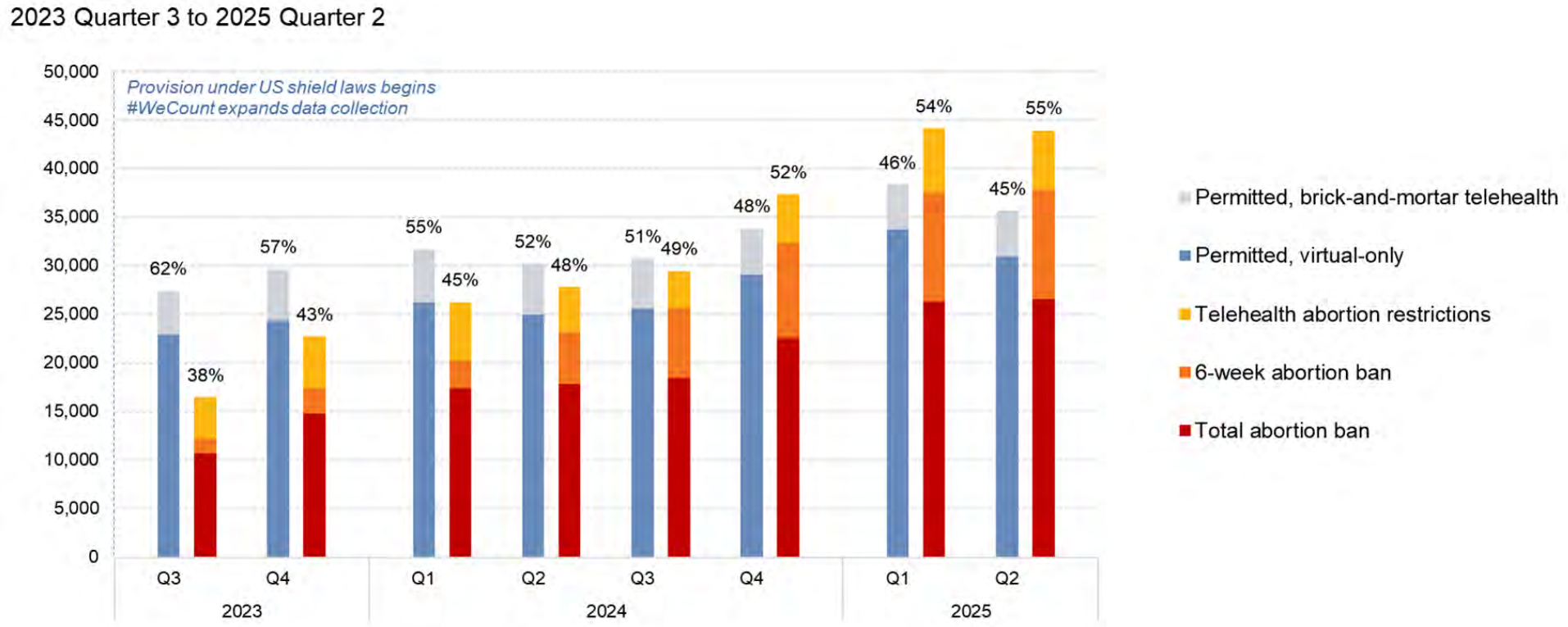
Source: Society of Family Planning, December 2025

Number of abortions provided via shield laws is increasing



Source: Society of Family Planning, December 2025

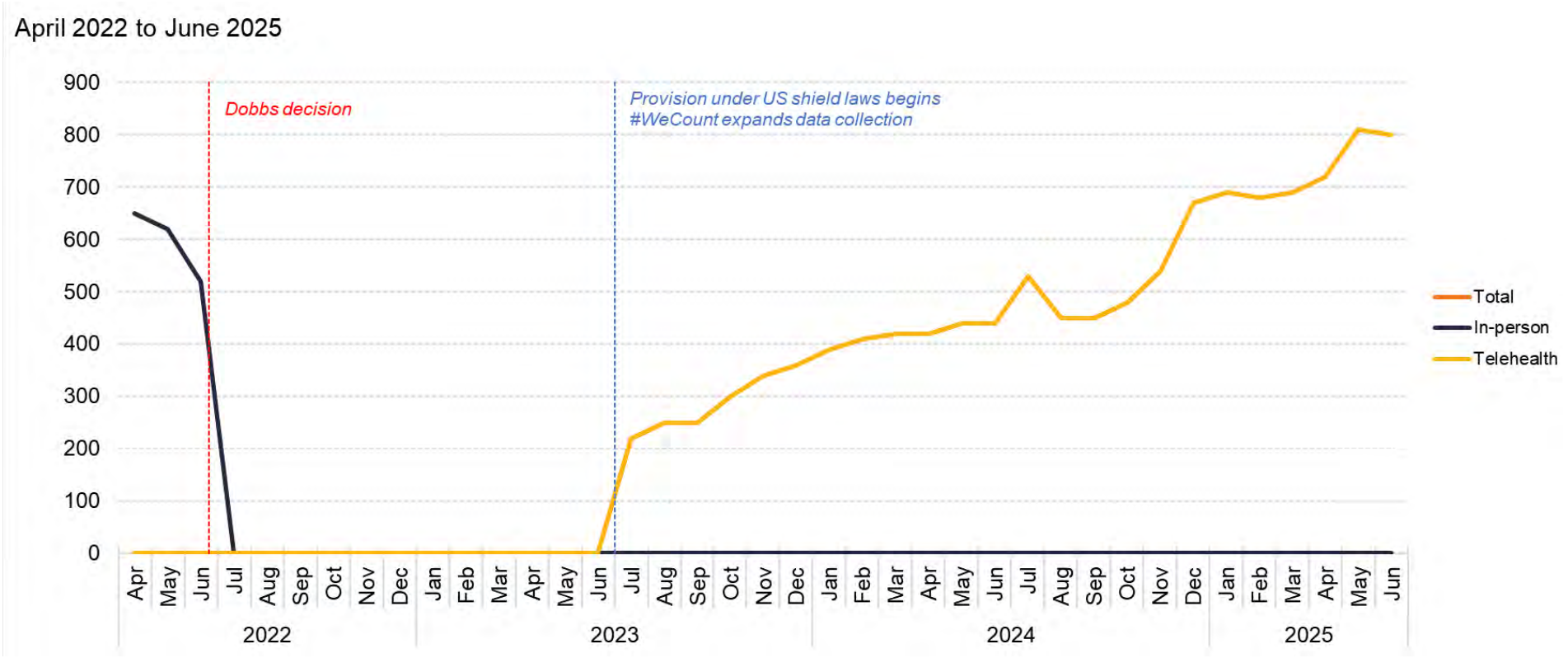
Abortions provided under shield laws account for a growing share of all telehealth abortions



Source: Society of Family Planning, December 2025

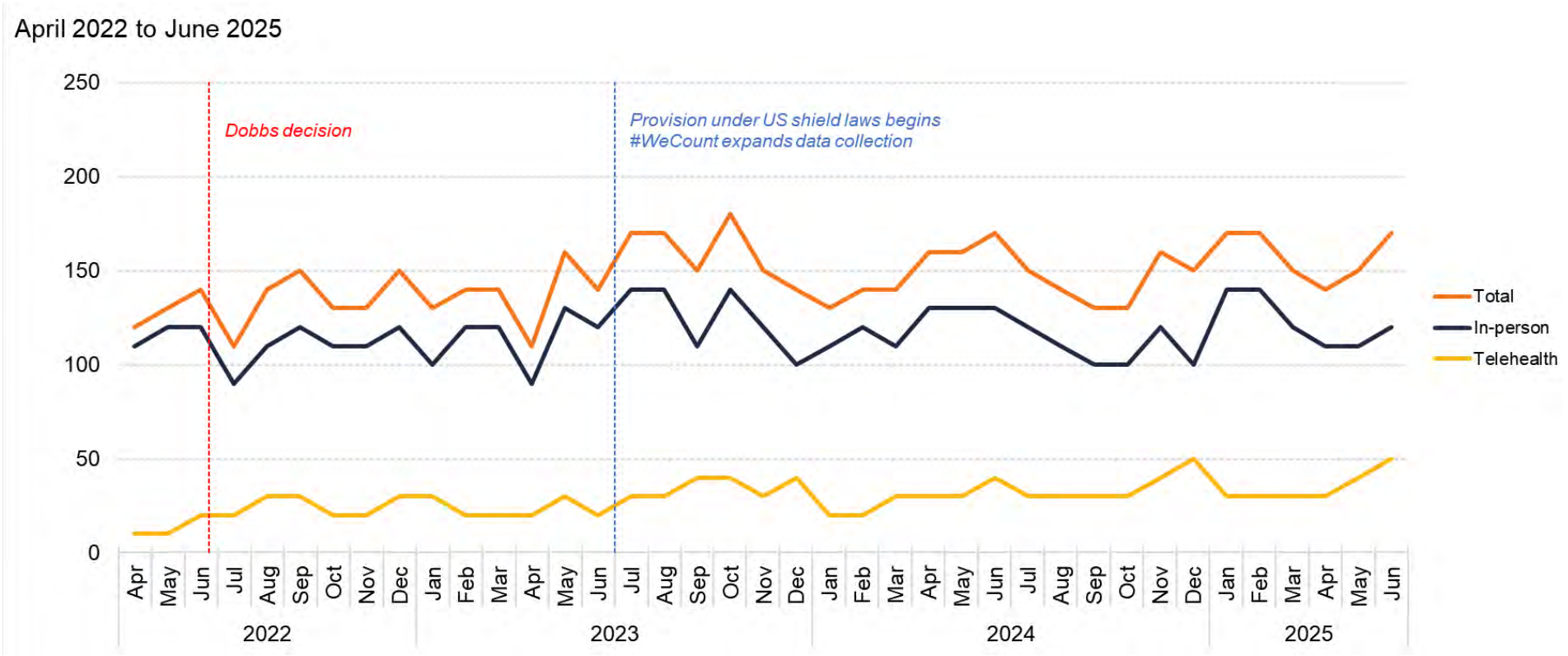
State-level findings

Alabama



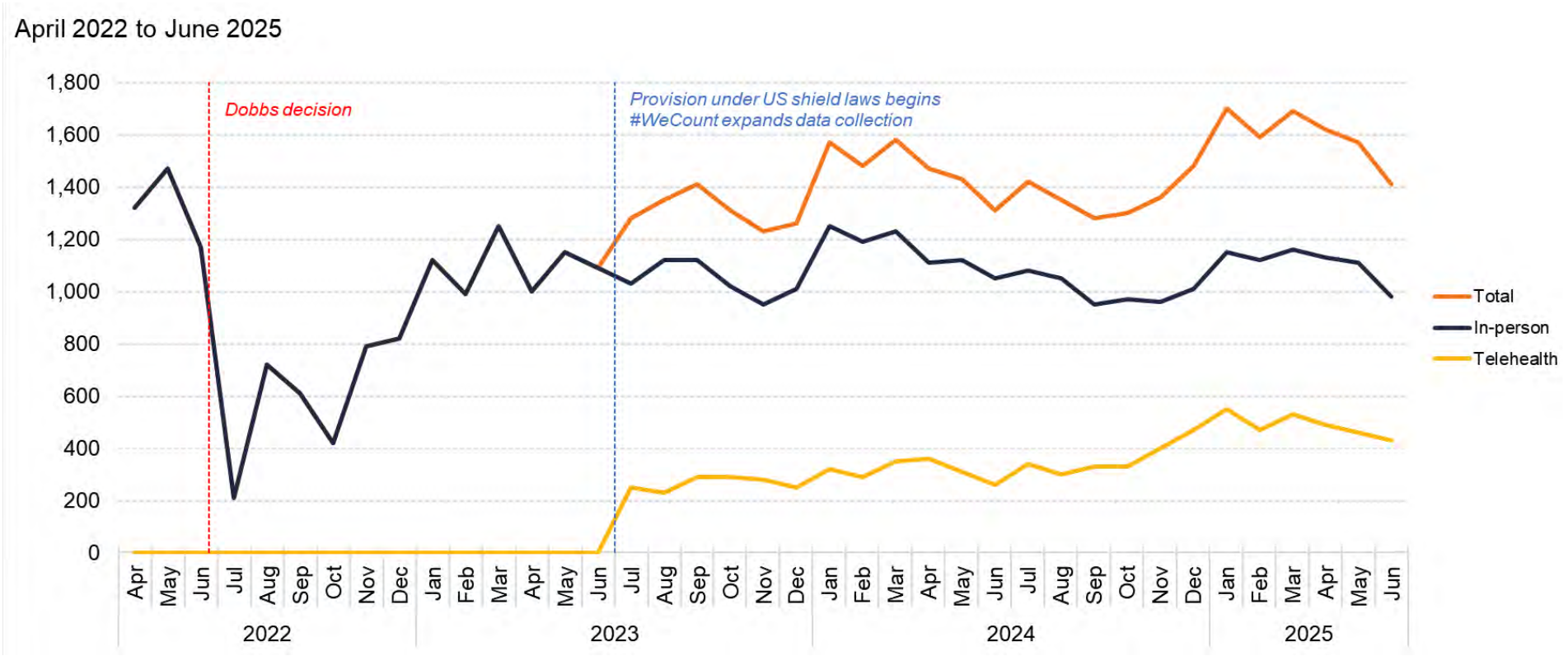
Source: Society of Family Planning, December 2025

Alaska



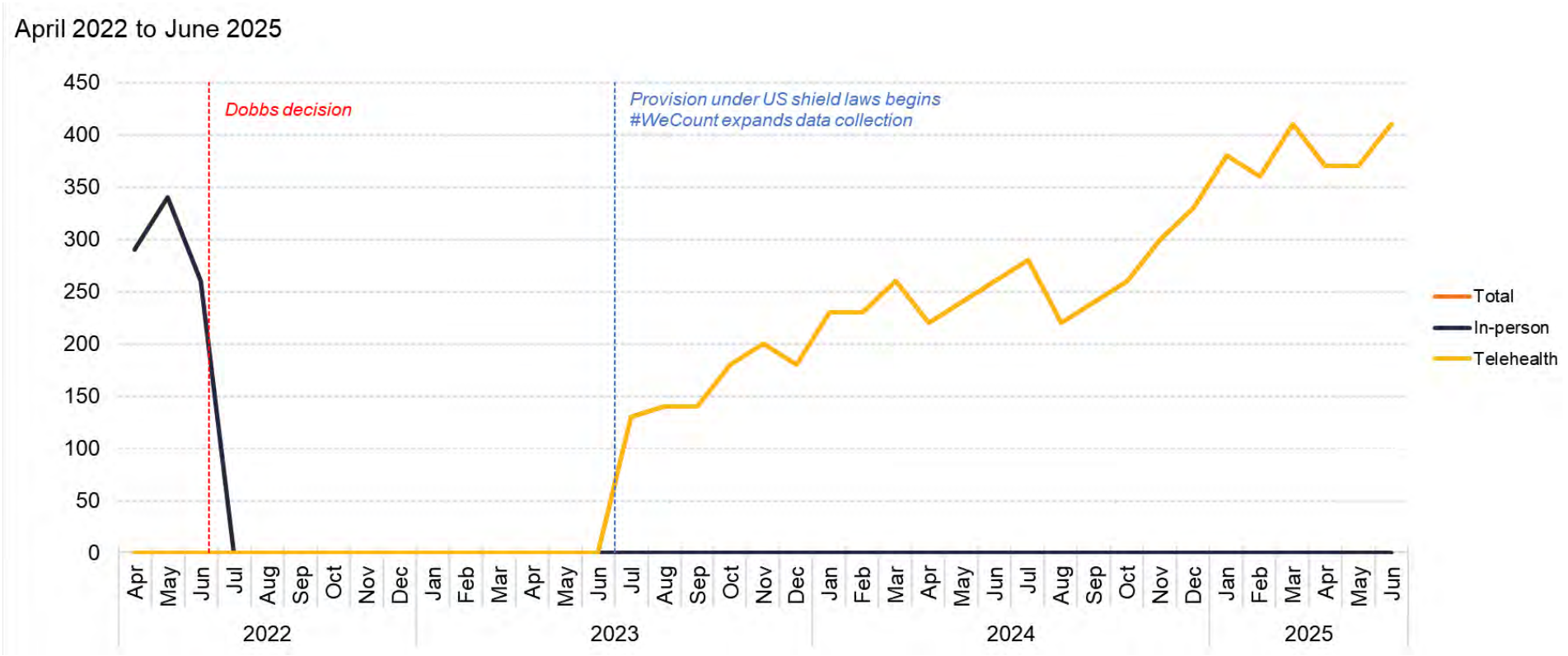
Source: Society of Family Planning, December 2025

Arizona



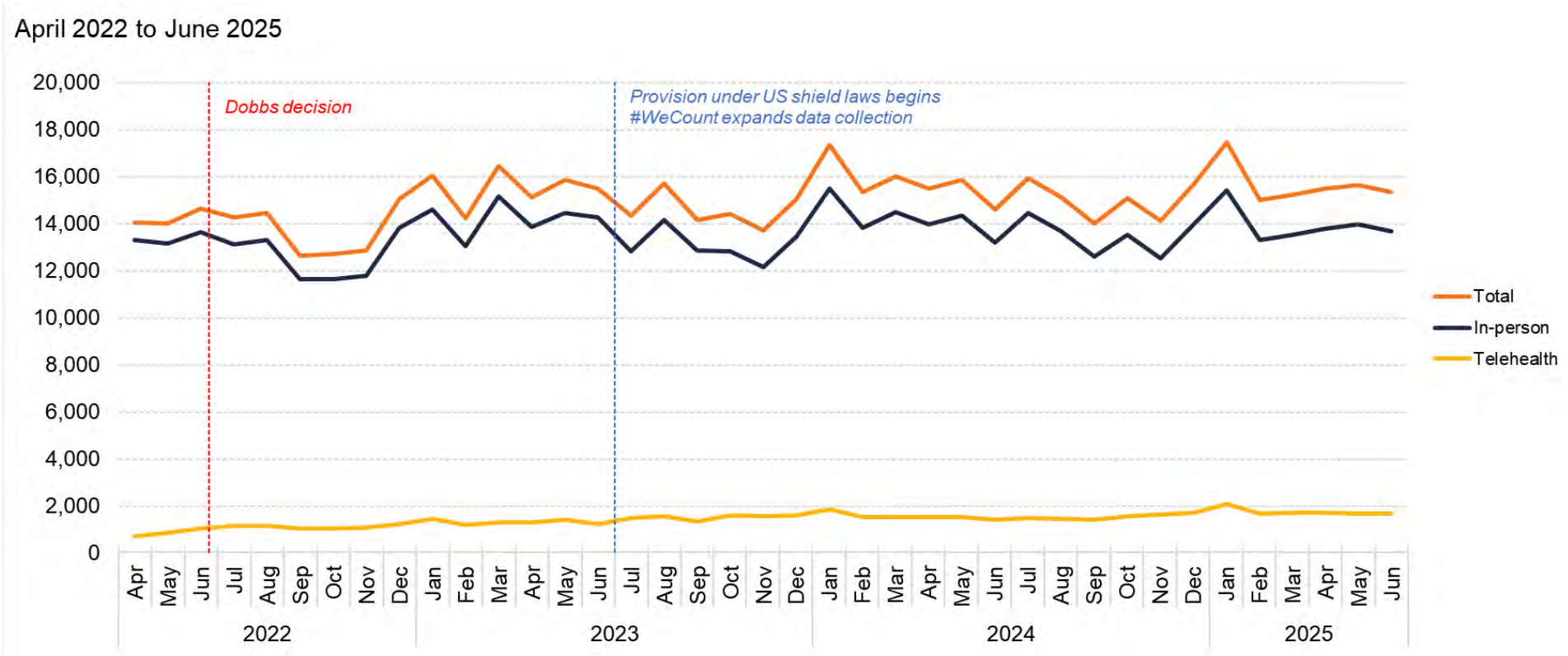
Source: Society of Family Planning, December 2025

Arkansas



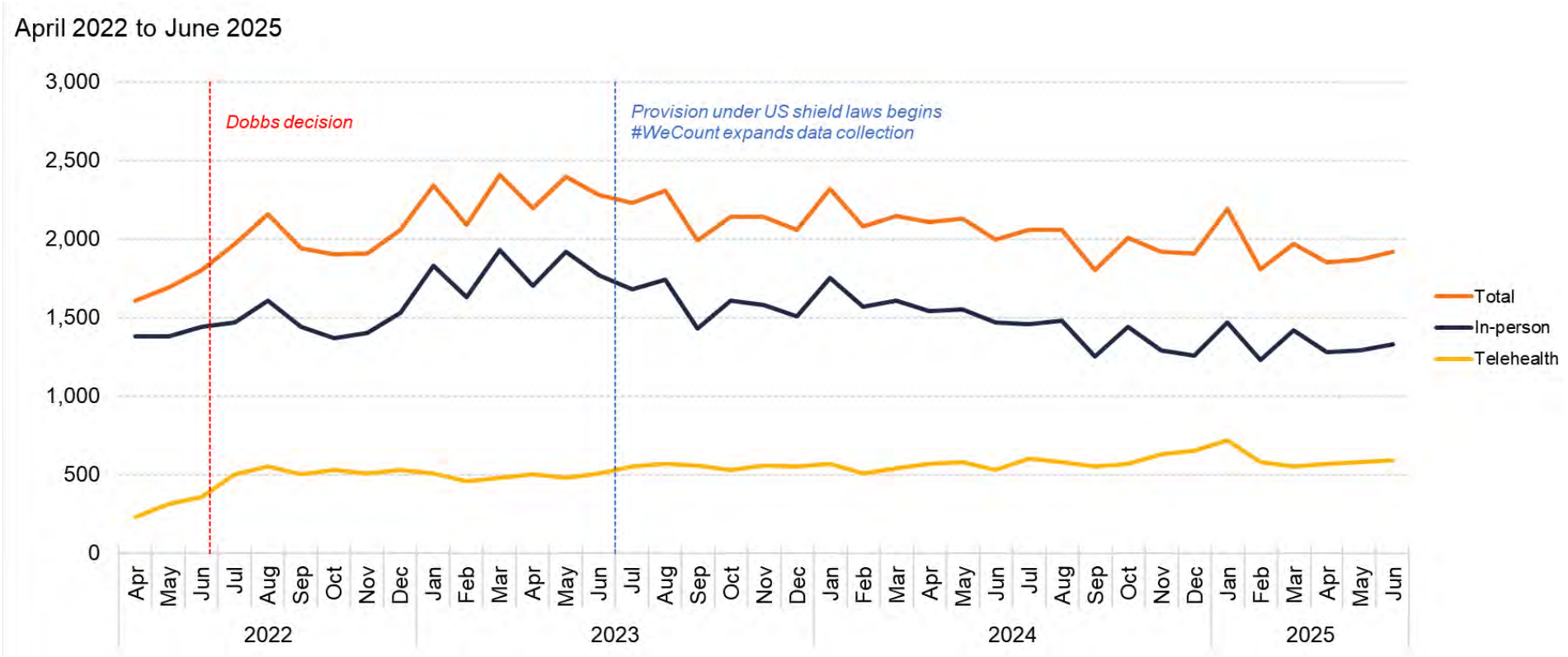
Source: Society of Family Planning, December 2025

California



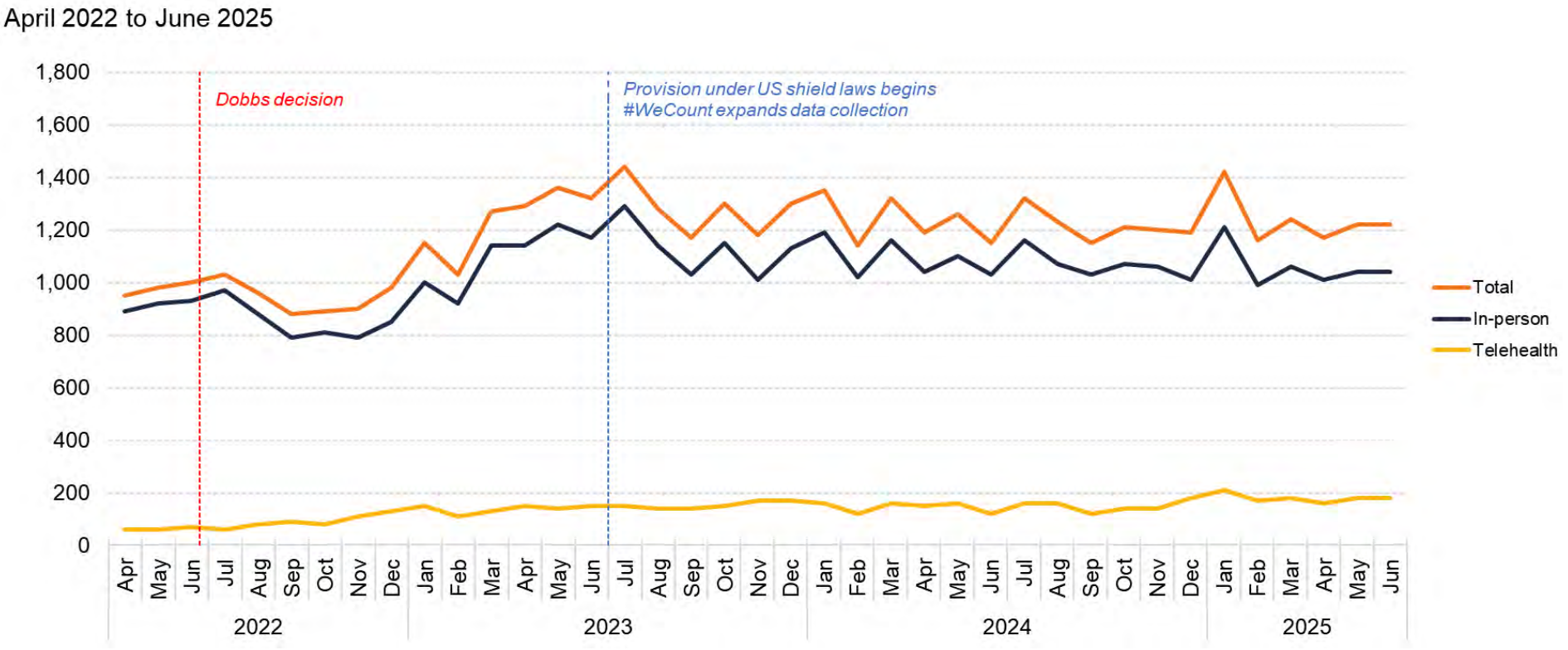
Source: Society of Family Planning, December 2025

Colorado



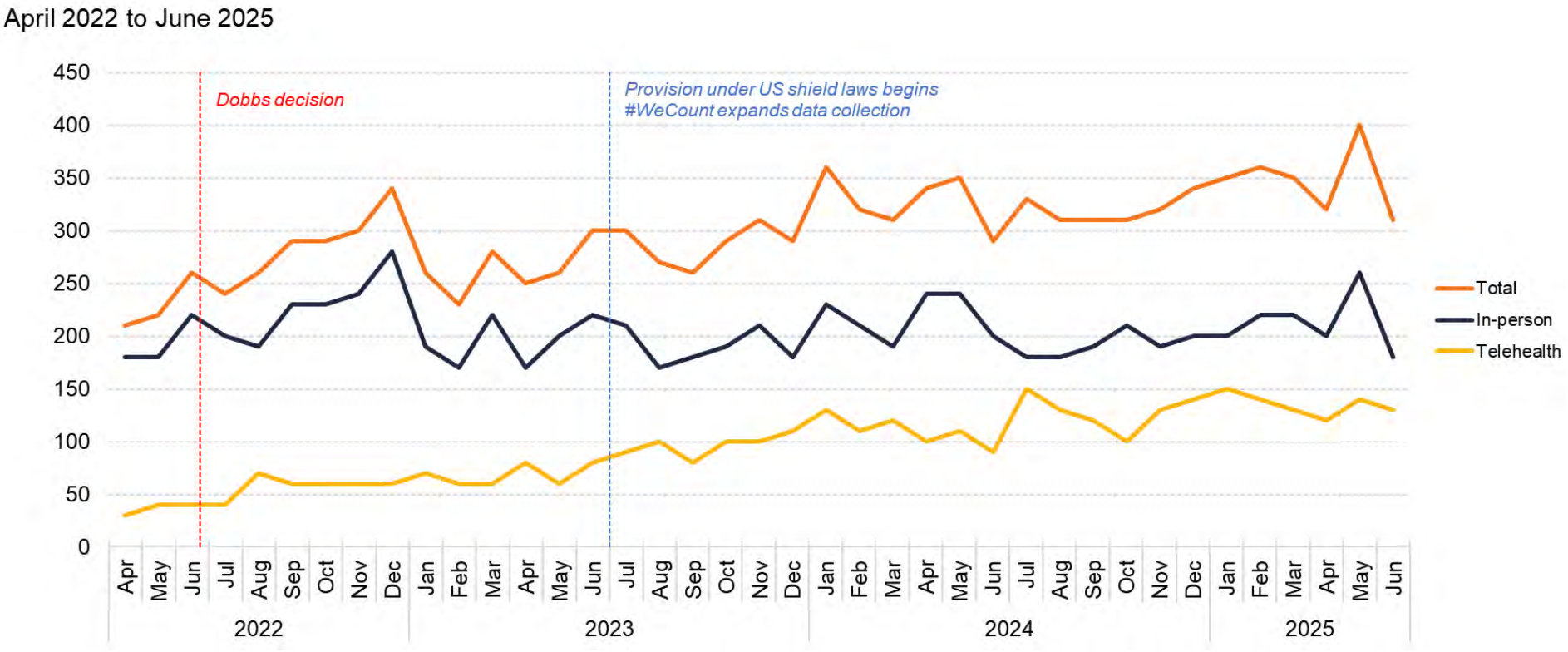
Source: Society of Family Planning, December 2025

Connecticut



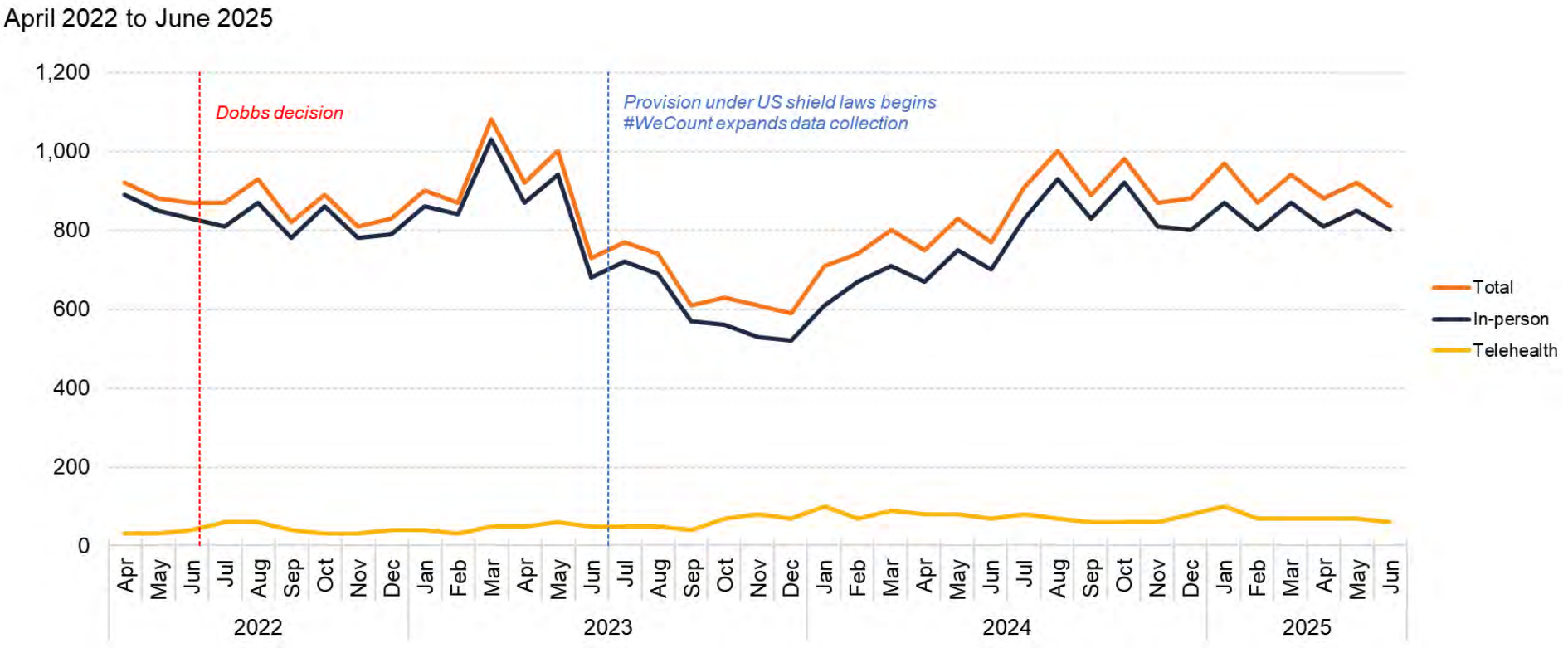
Source: Society of Family Planning, December 2025

Delaware



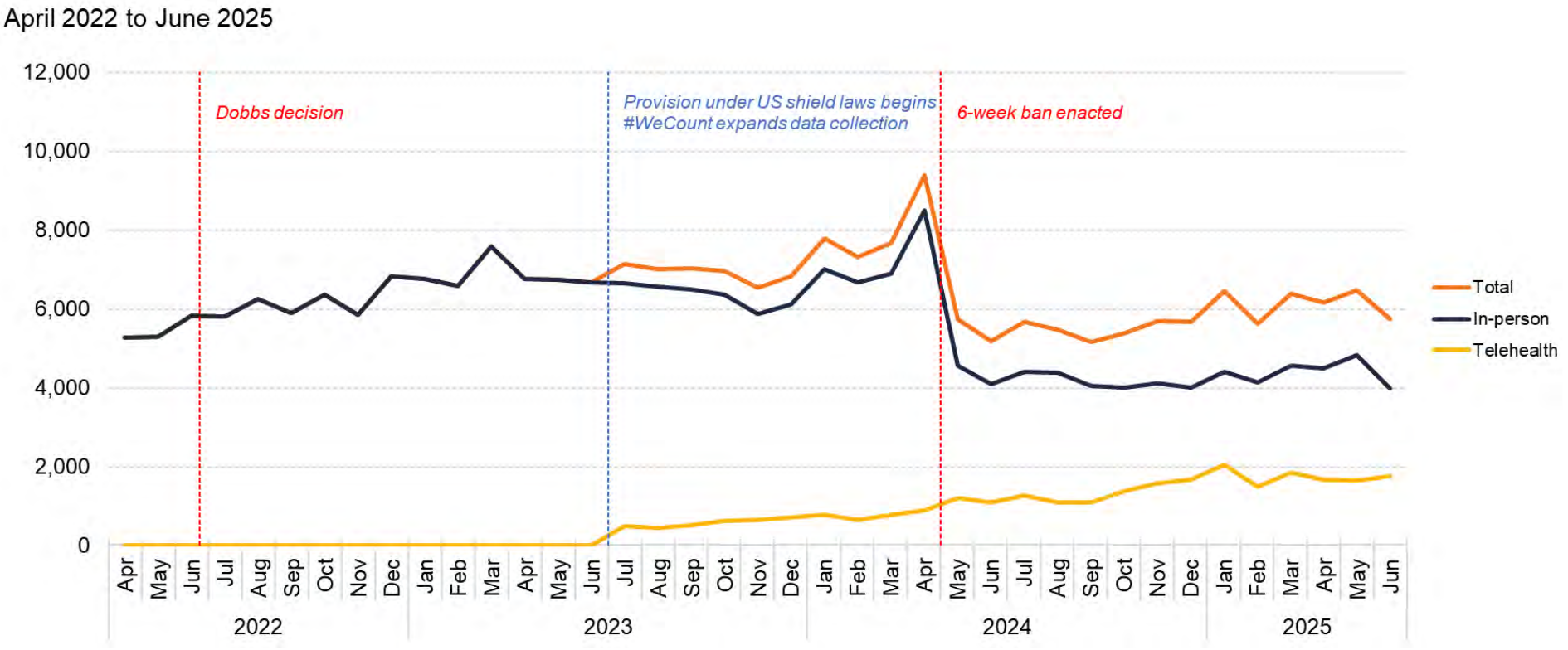
Source: Society of Family Planning, December 2025

District of Columbia



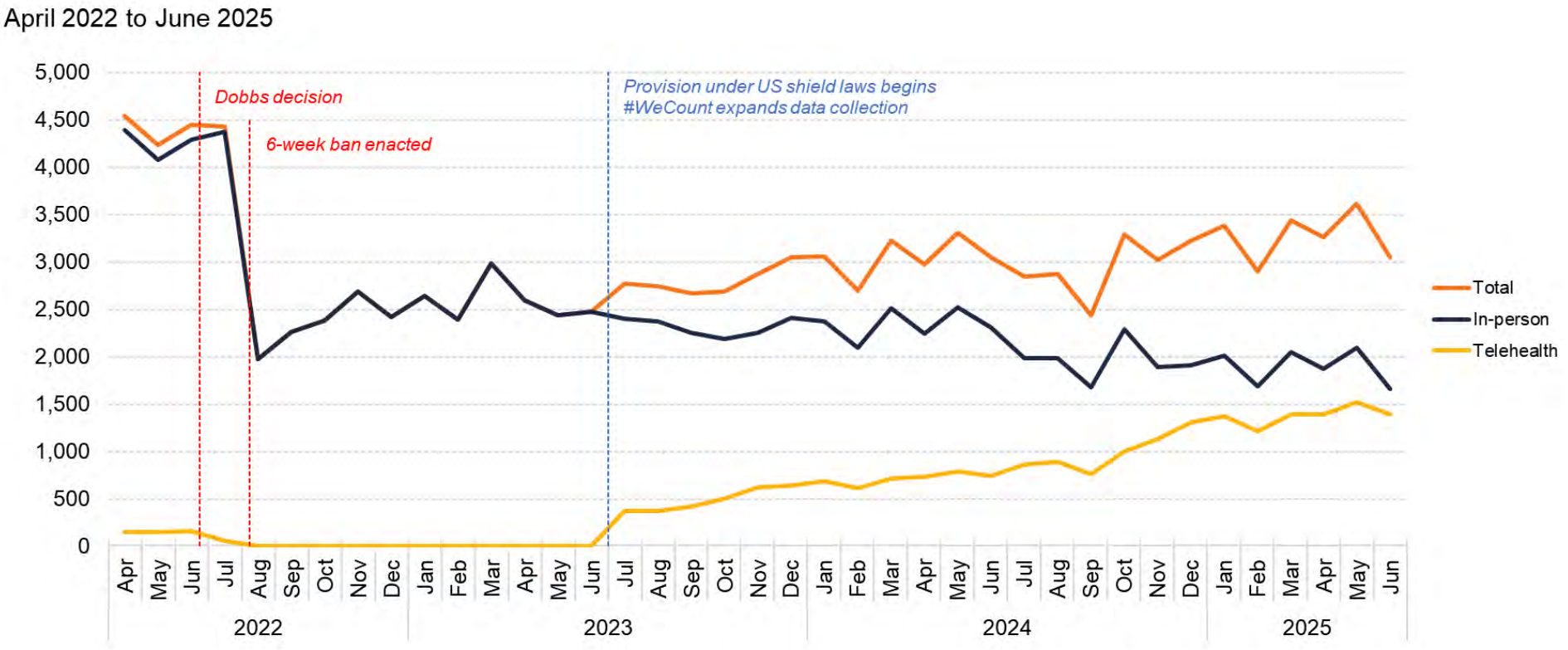
Source: Society of Family Planning, December 2025

Florida



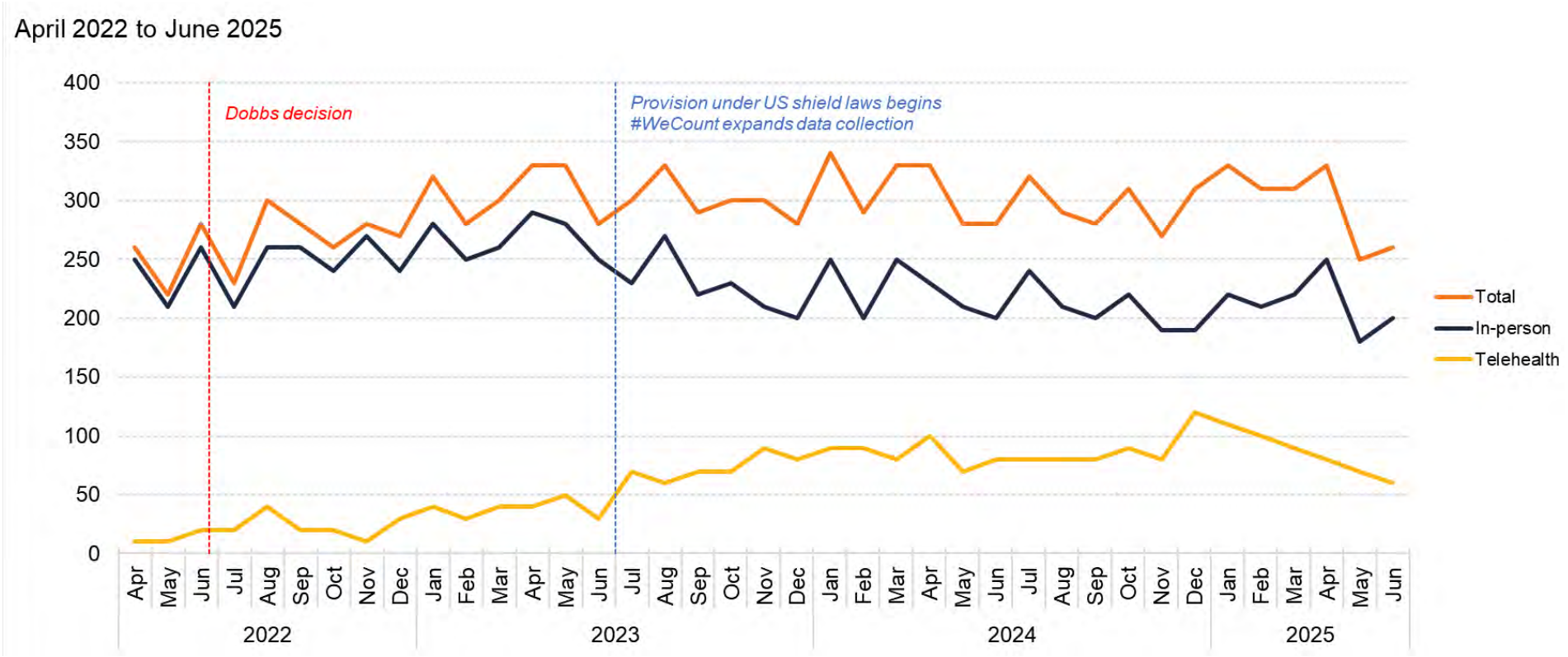
Source: Society of Family Planning, December 2025

Georgia



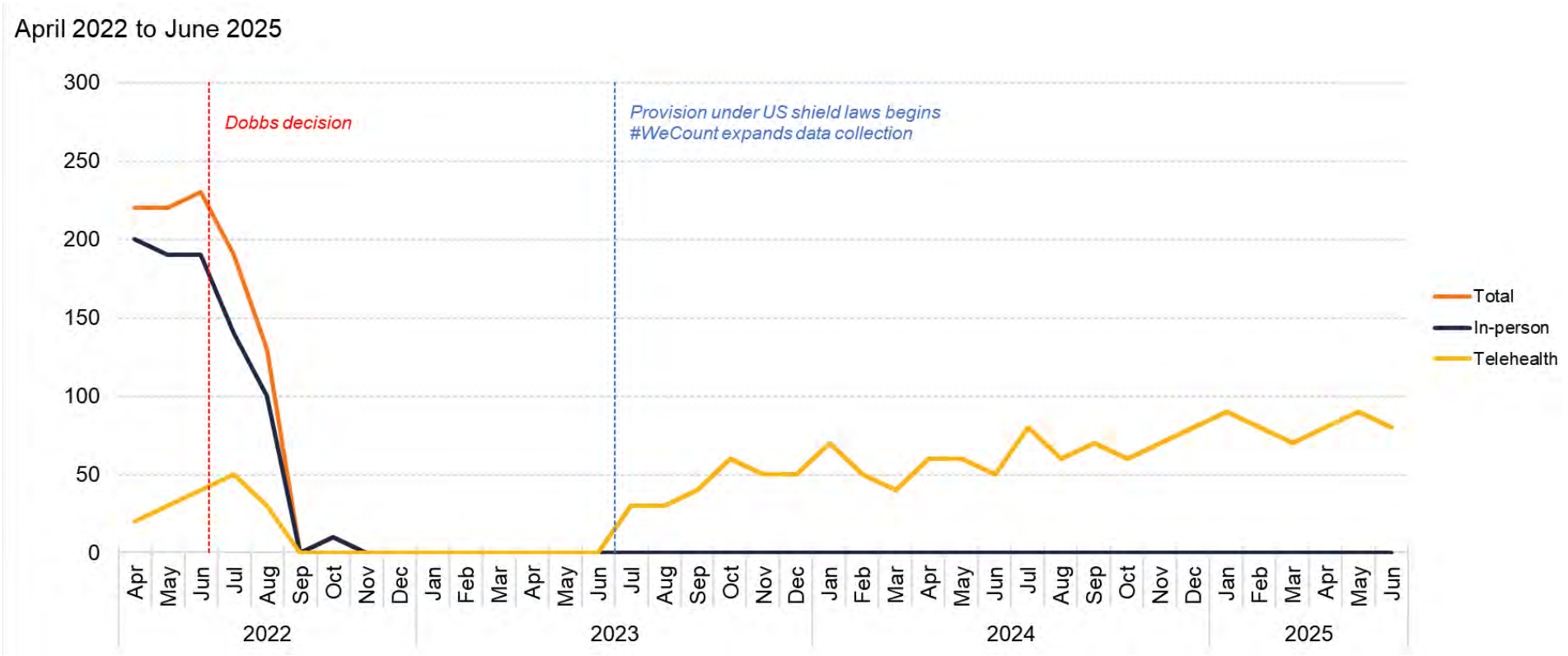
Source: Society of Family Planning, December 2025

Hawaii



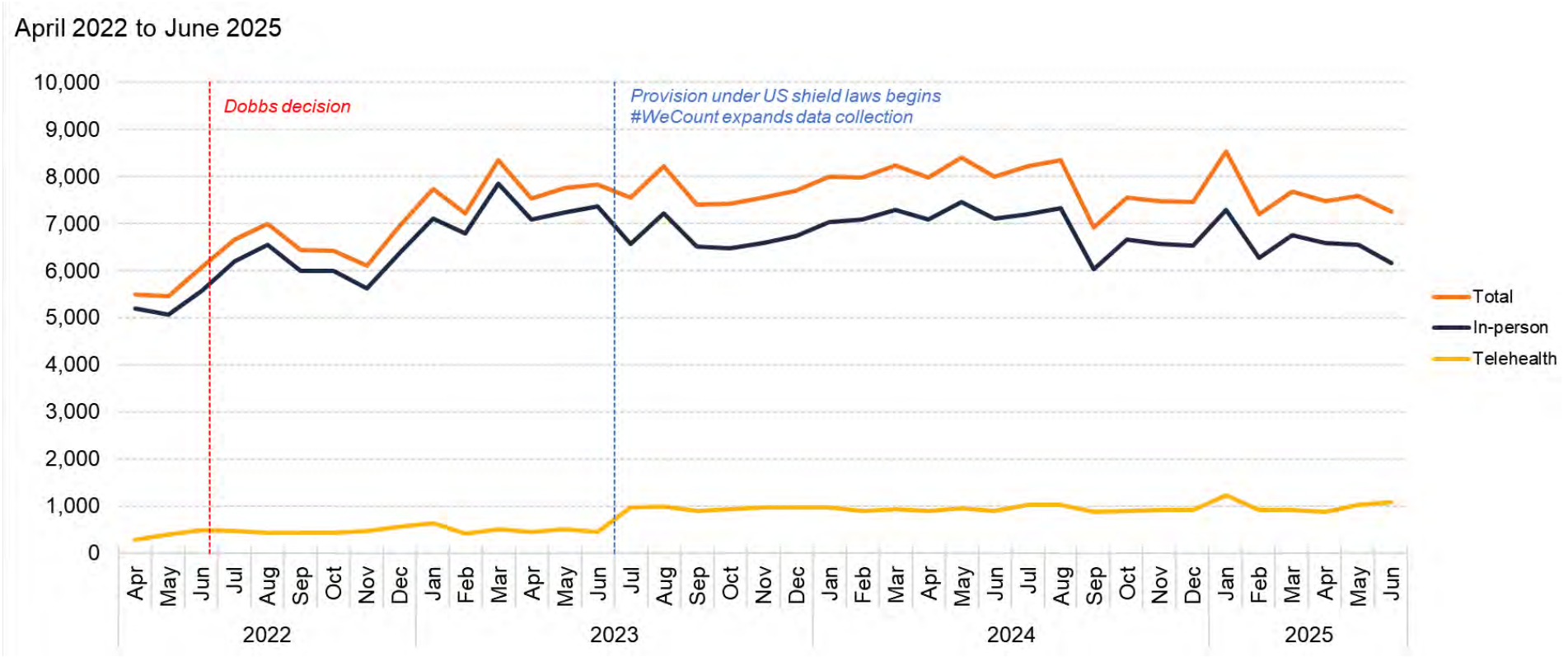
Source: Society of Family Planning, December 2025

Idaho



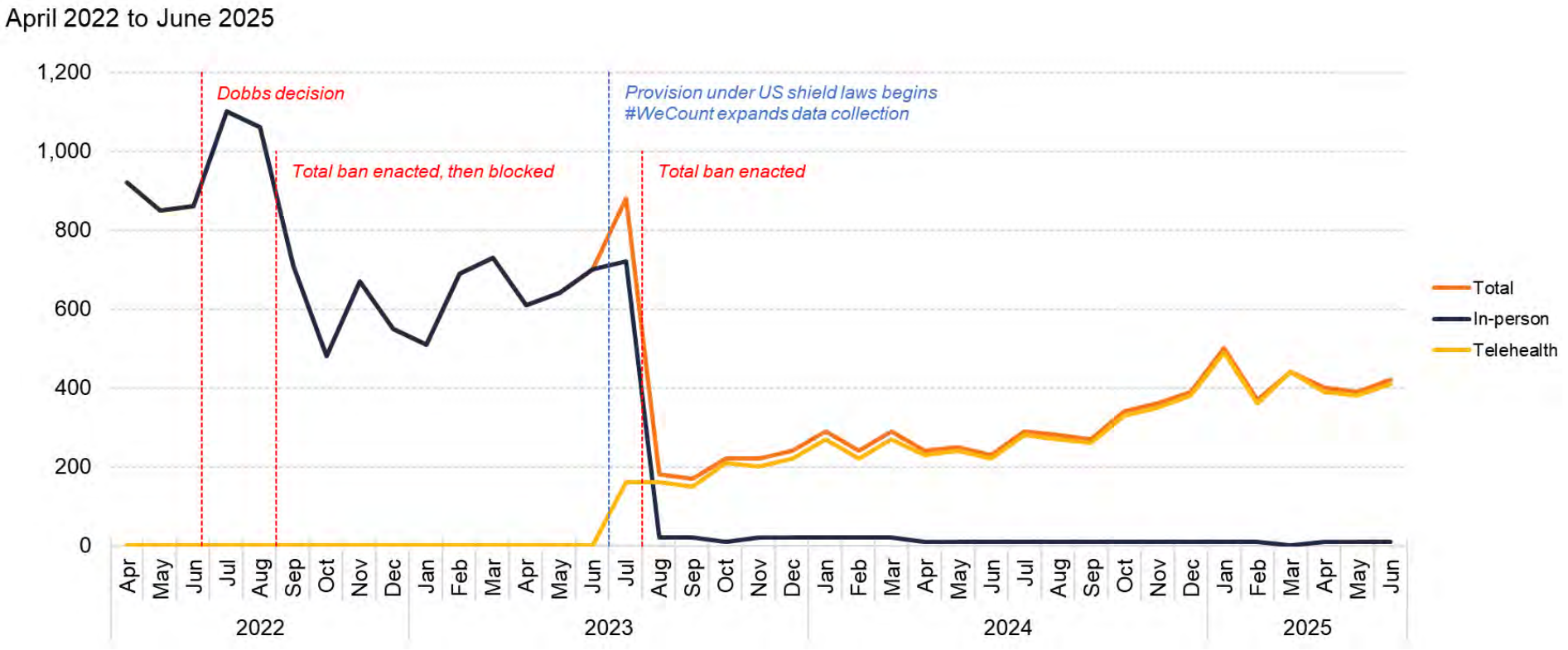
Source: Society of Family Planning, December 2025

Illinois



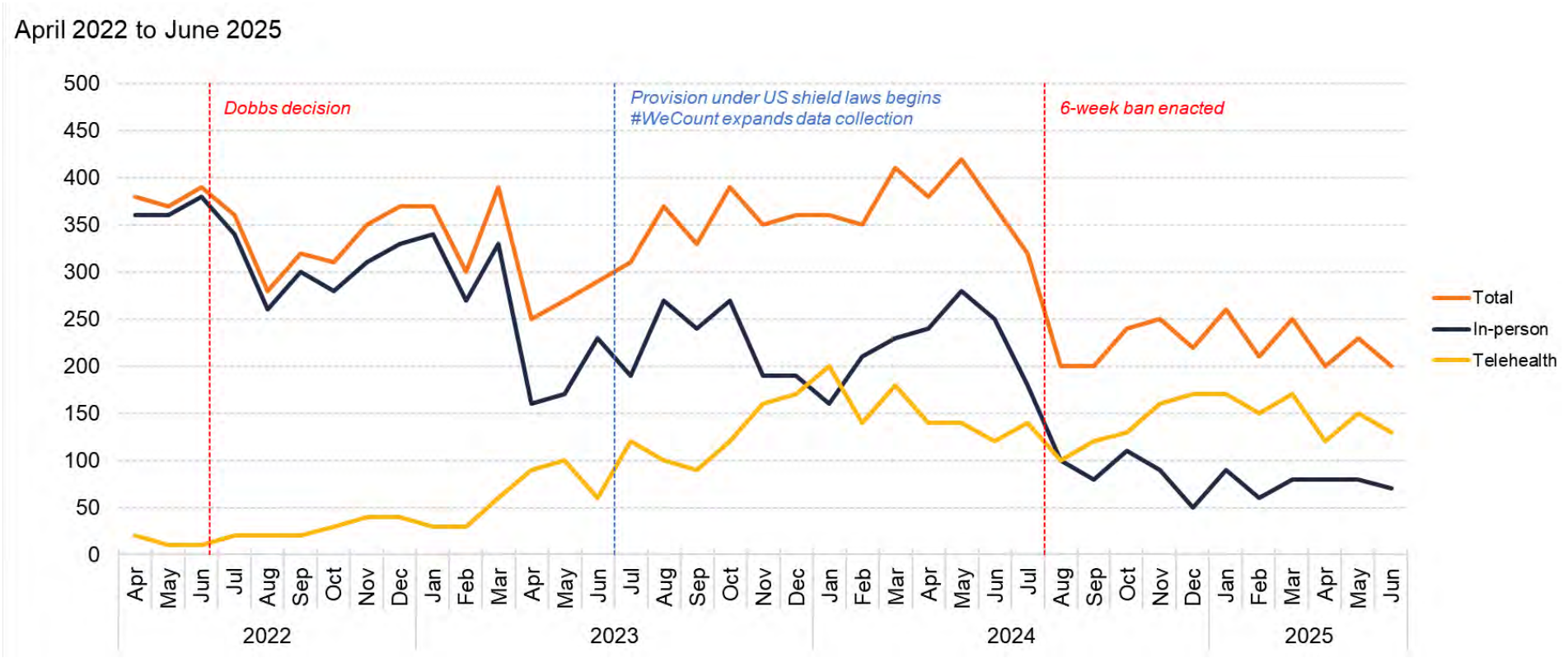
Source: Society of Family Planning, December 2025

Indiana



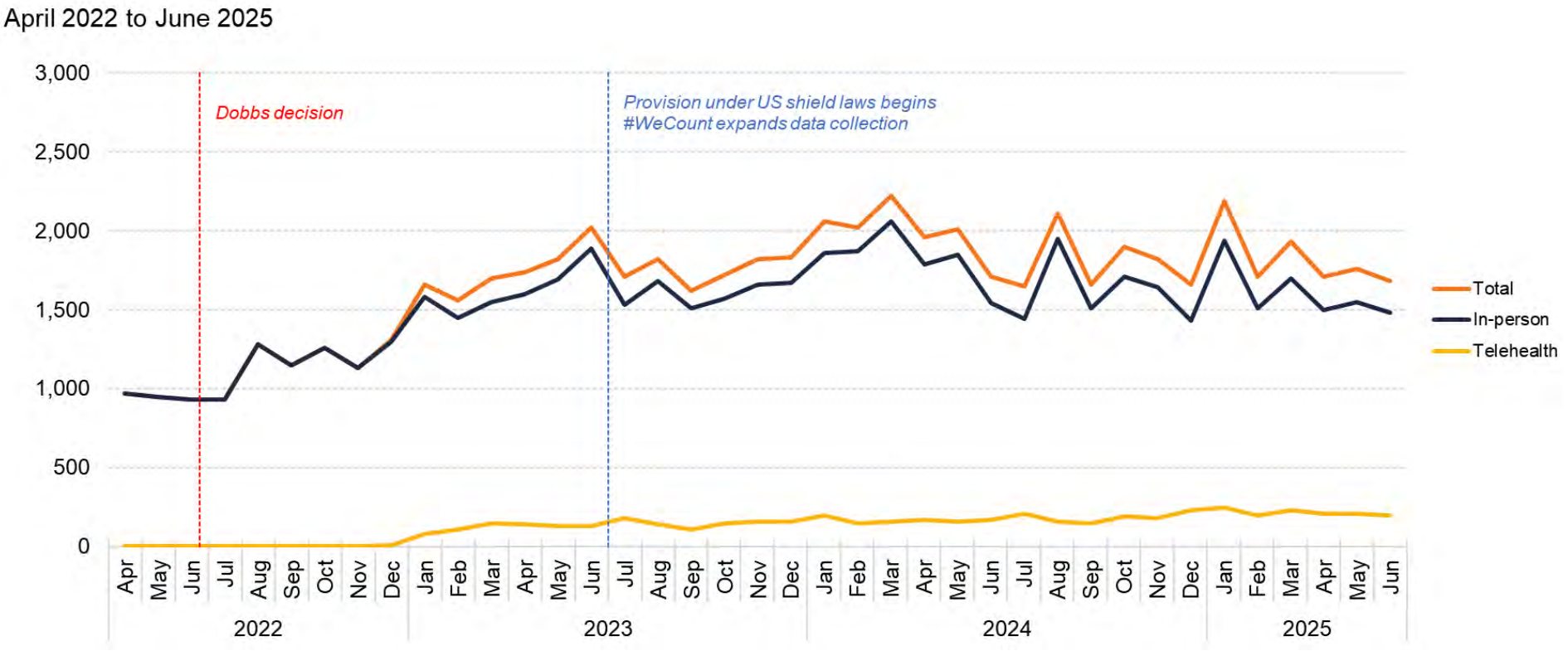
Source: Society of Family Planning, December 2025

Iowa



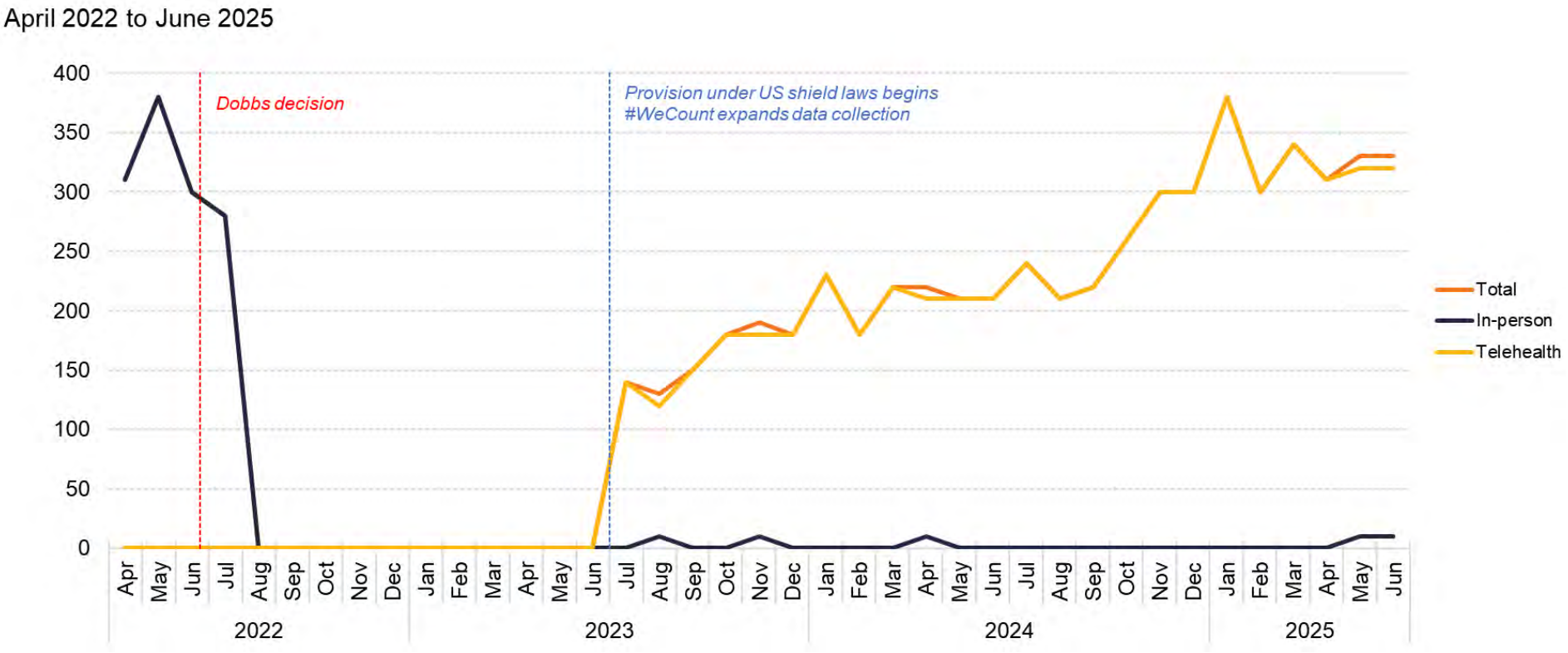
Source: Society of Family Planning, December 2025

Kansas



Source: Society of Family Planning, December 2025

Kentucky



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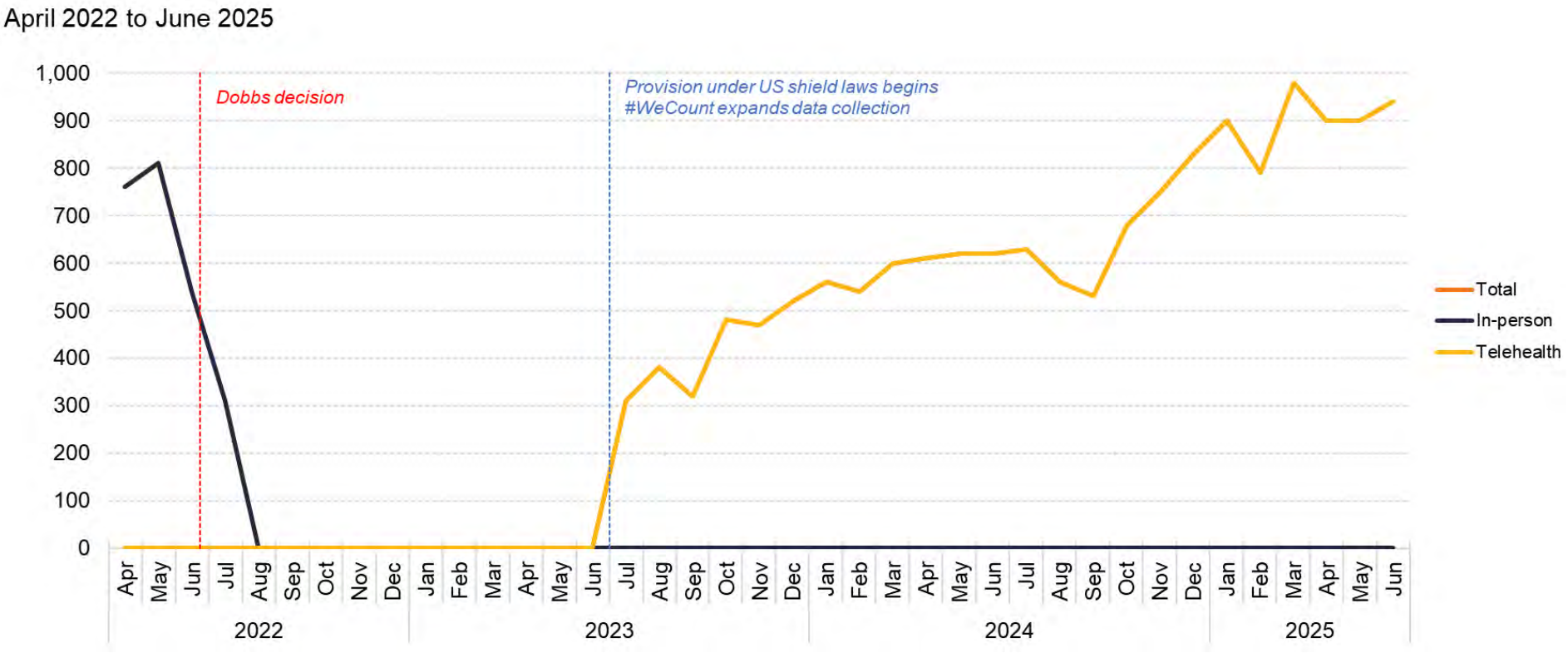
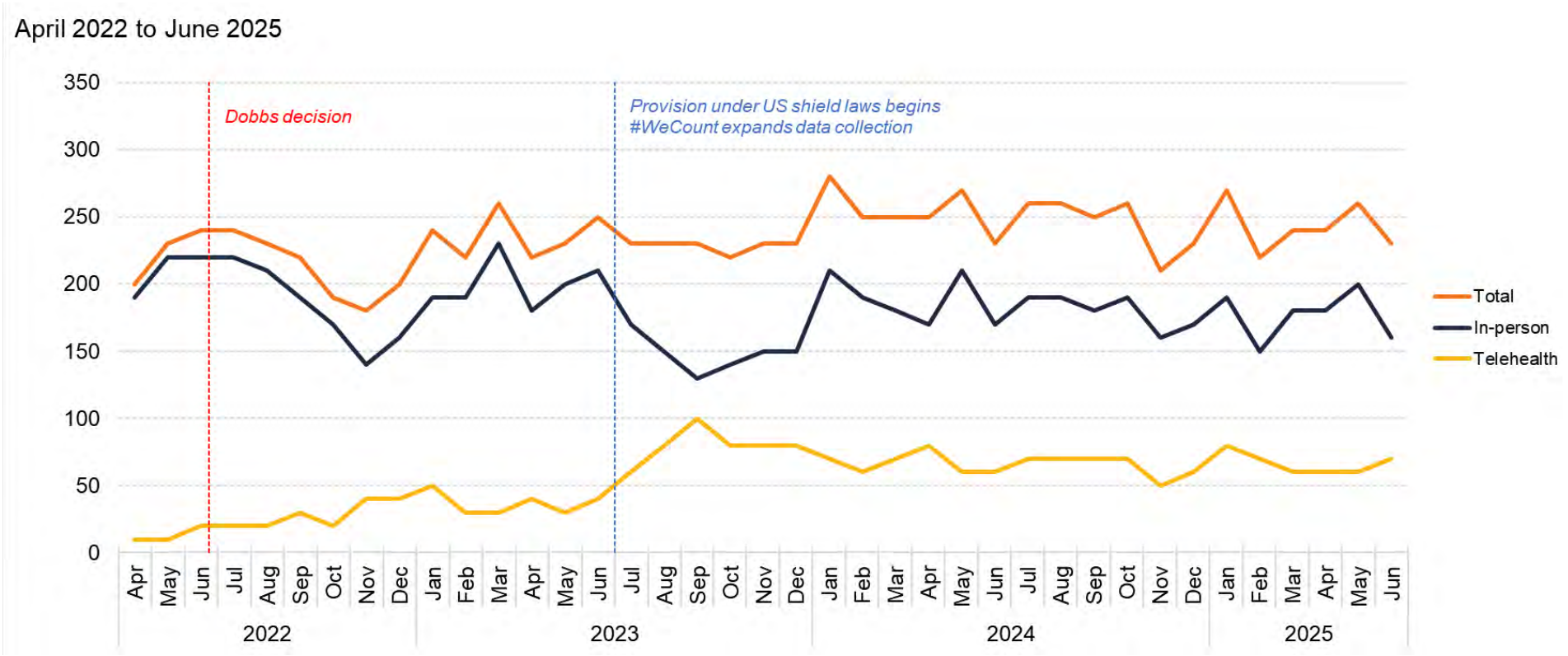
Louisiana



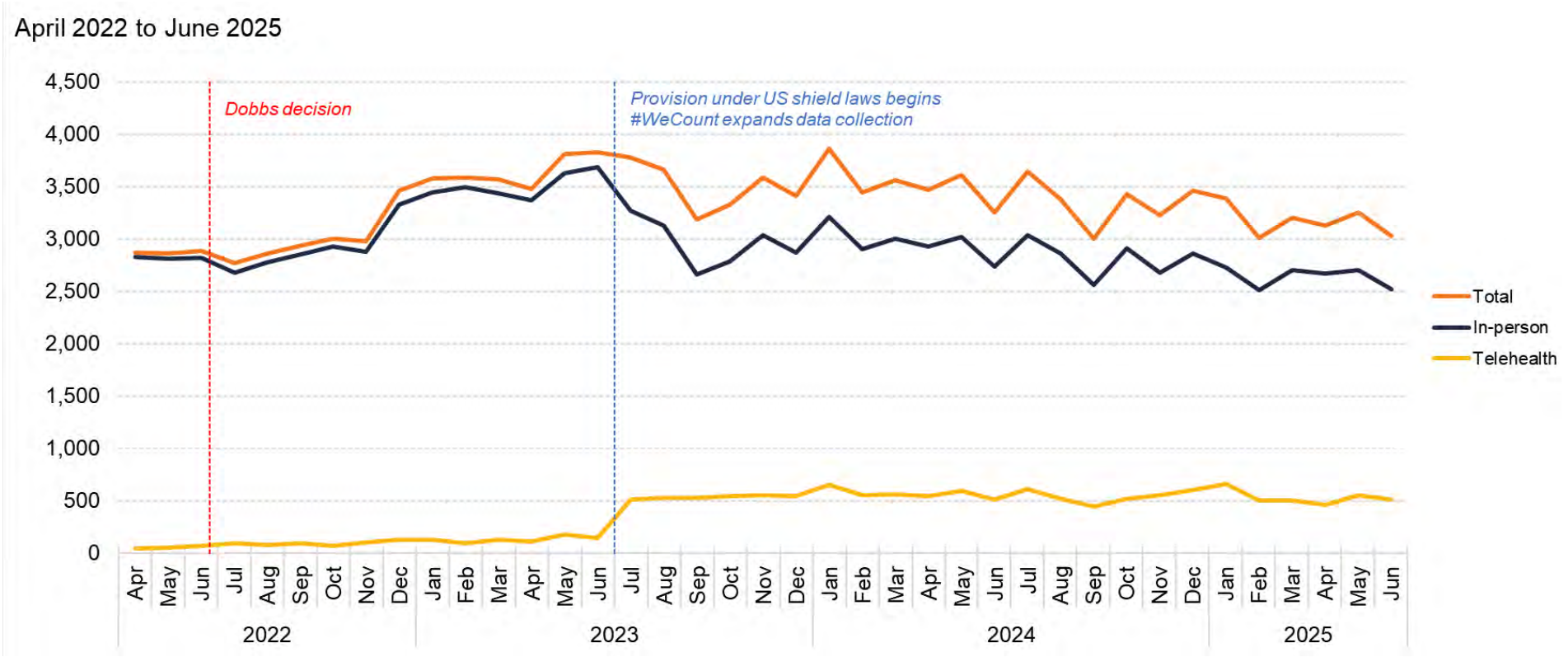
Source: Society of Family Planning, December 2025

Maine



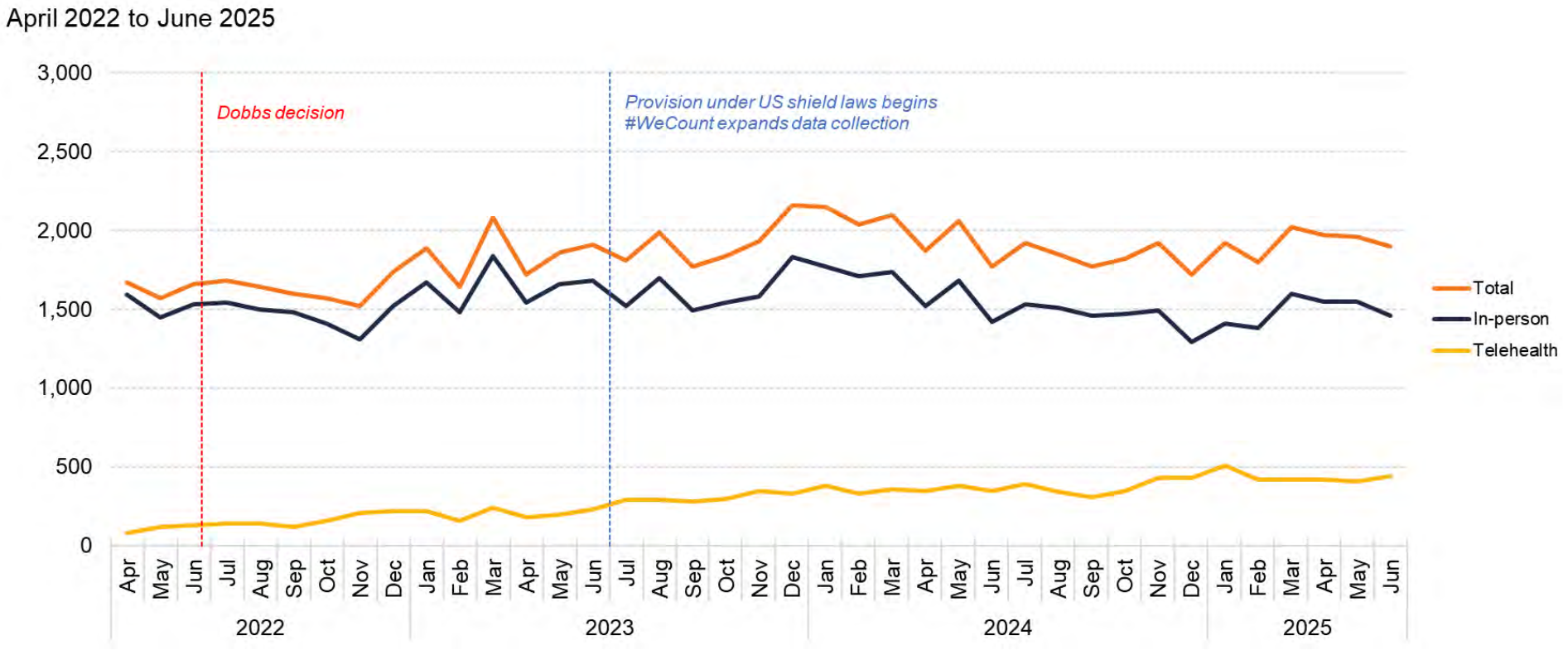
Source: Society of Family Planning, December 2025

Maryland



Source: Society of Family Planning, December 2025

Massachusetts



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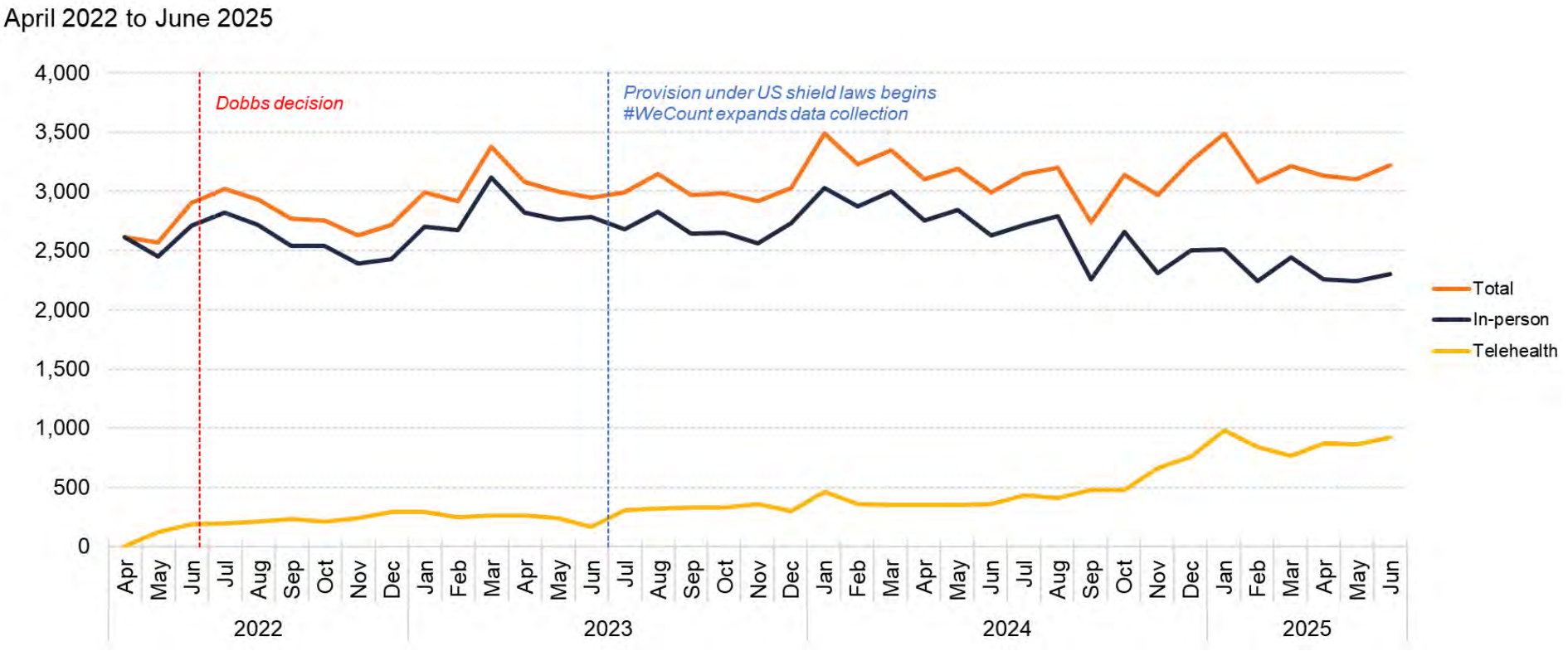
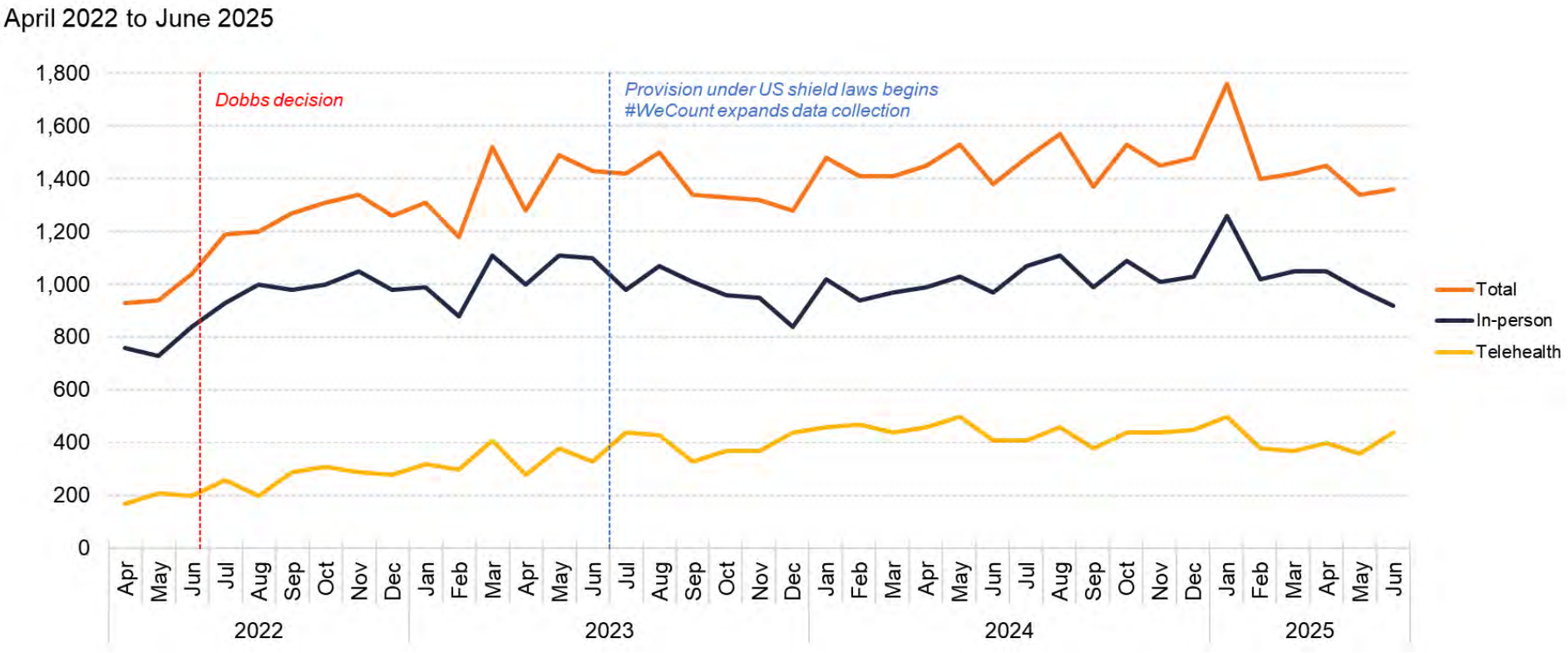
Michigan



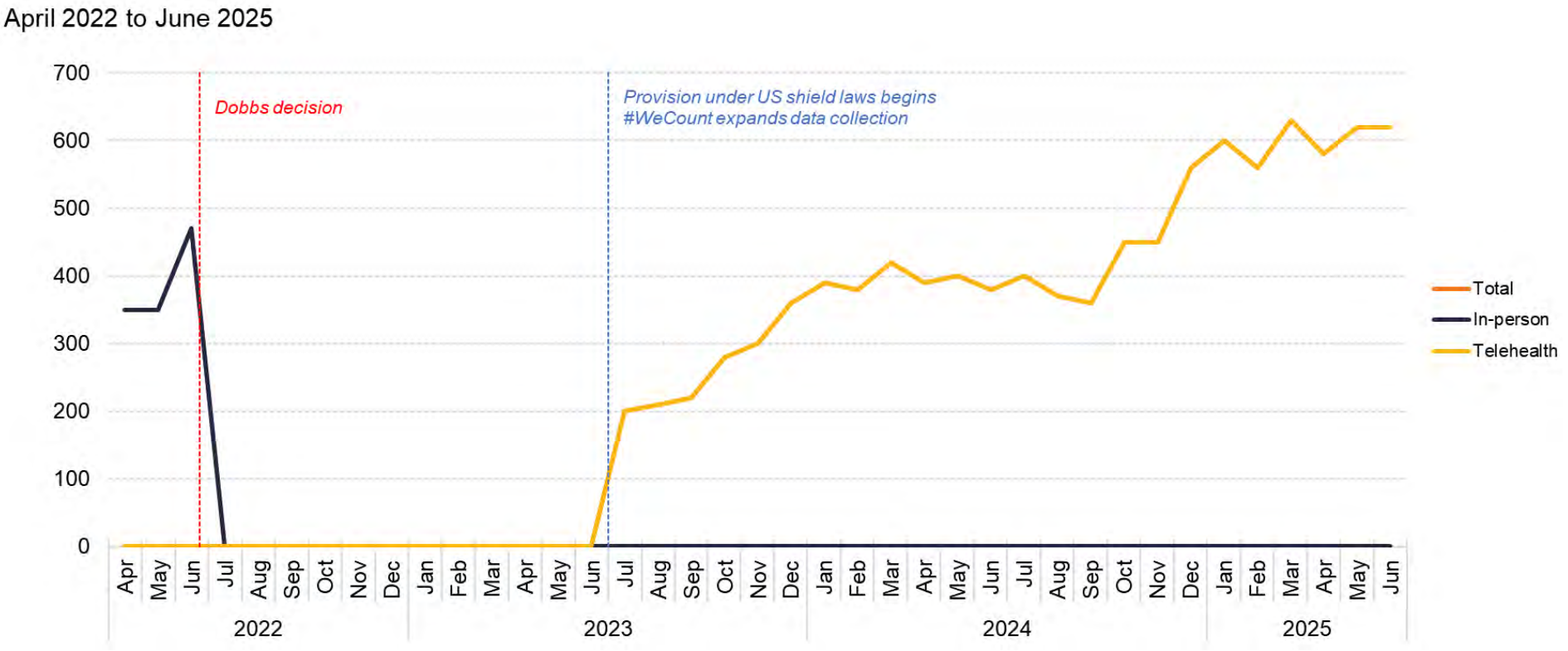
Source: Society of Family Planning, December 2025

Minnesota



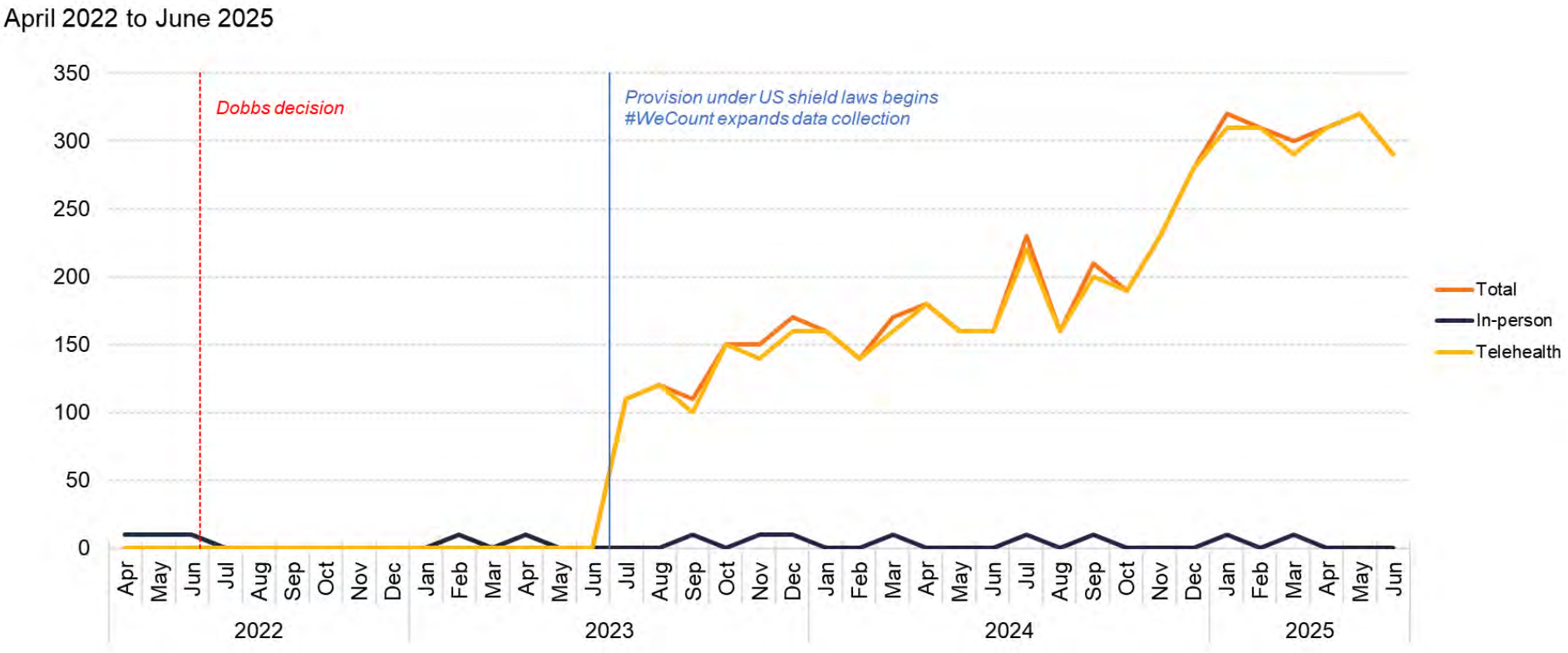
Source: Society of Family Planning, December 2025

Mississippi



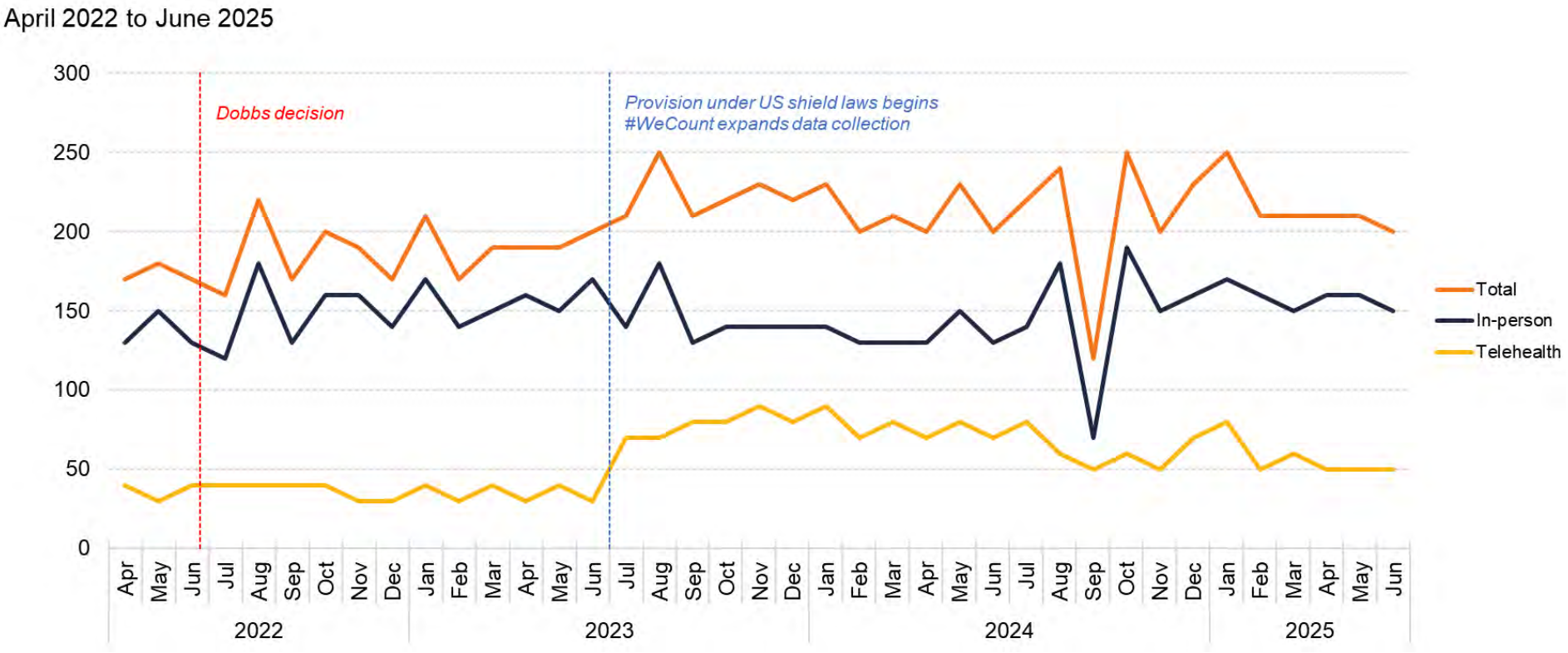
Source: Society of Family Planning, December 2025

Missouri



Source: Society of Family Planning, December 2025

Montana



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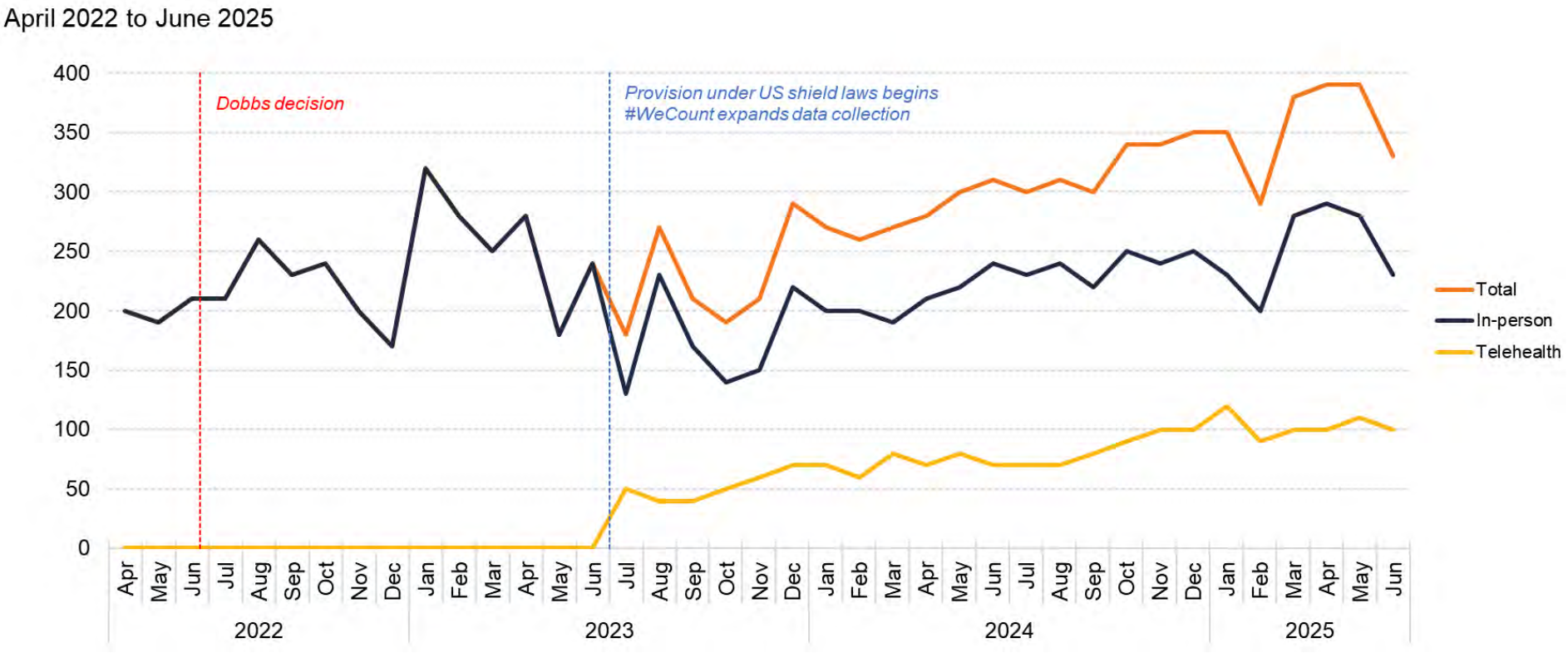
Nebraska



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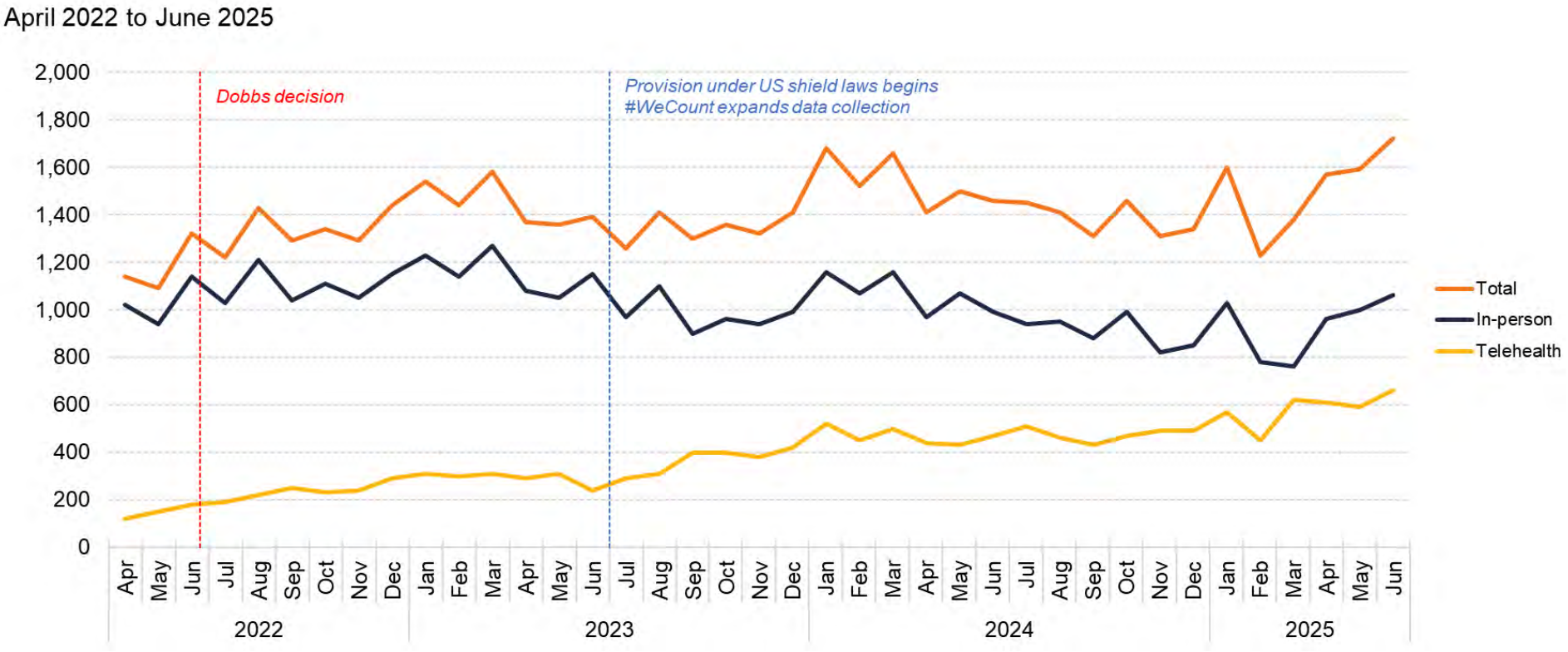
Nevada



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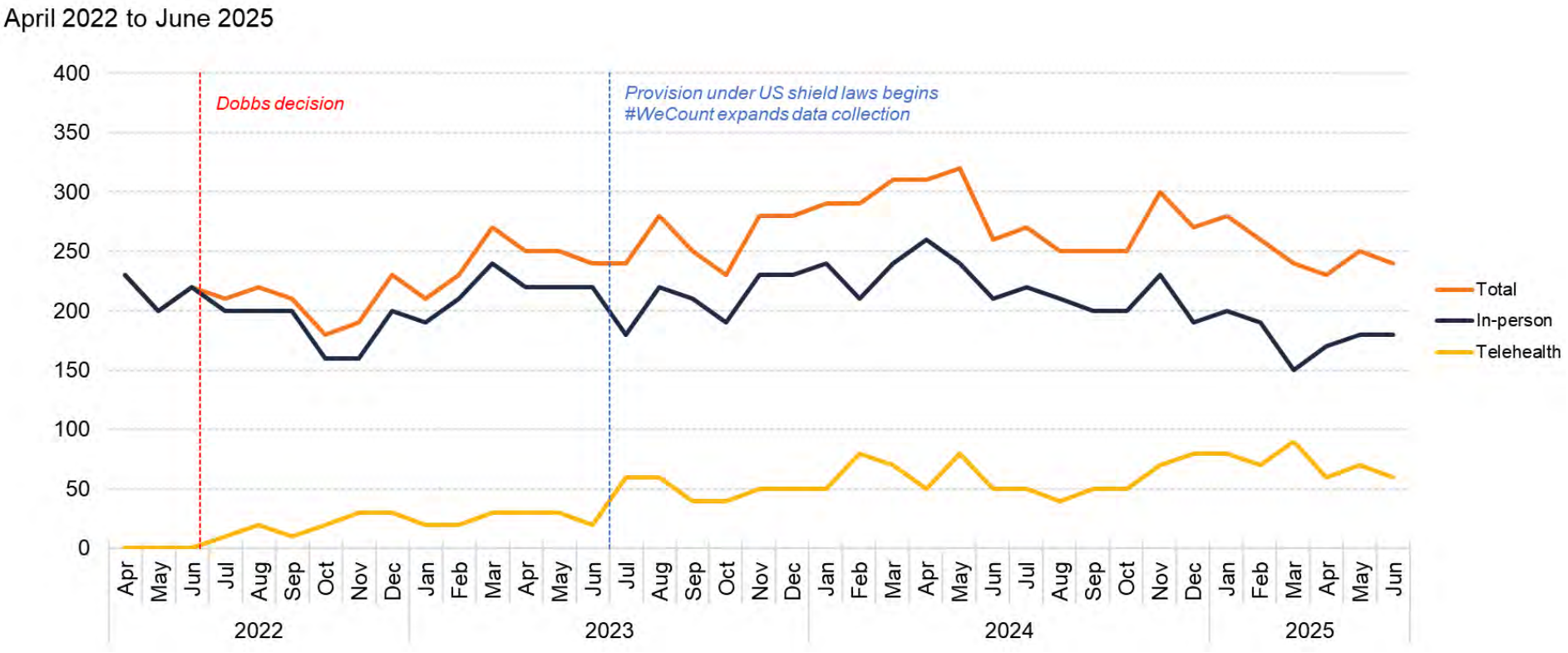
New Hampshire



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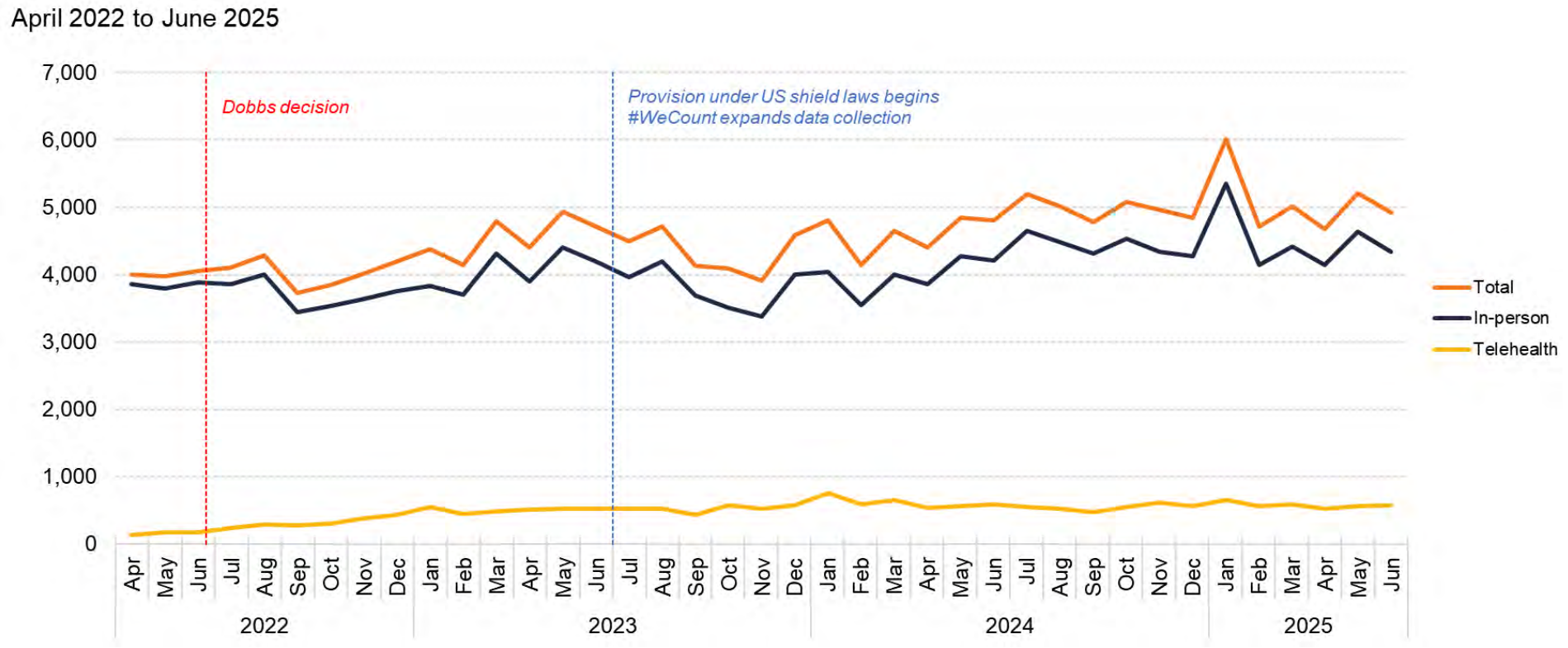
New Jersey



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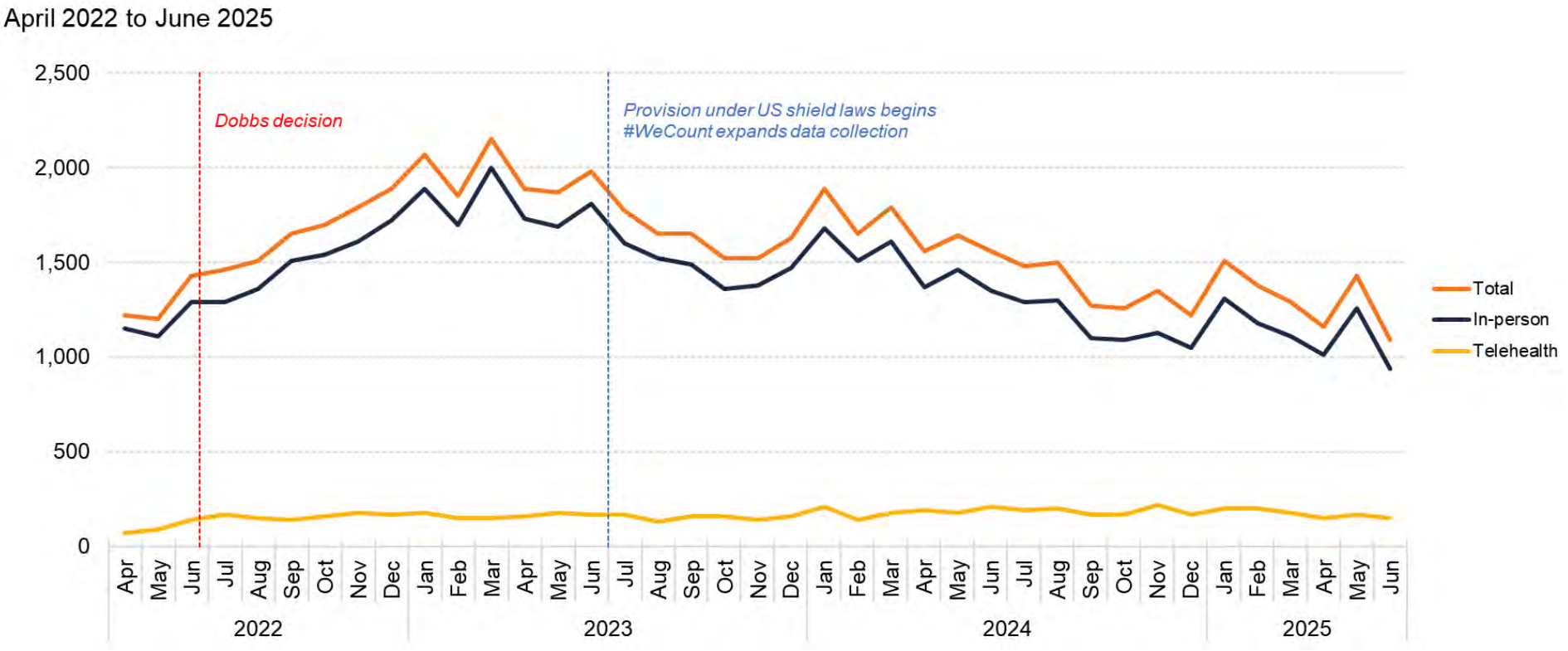
New Mexico



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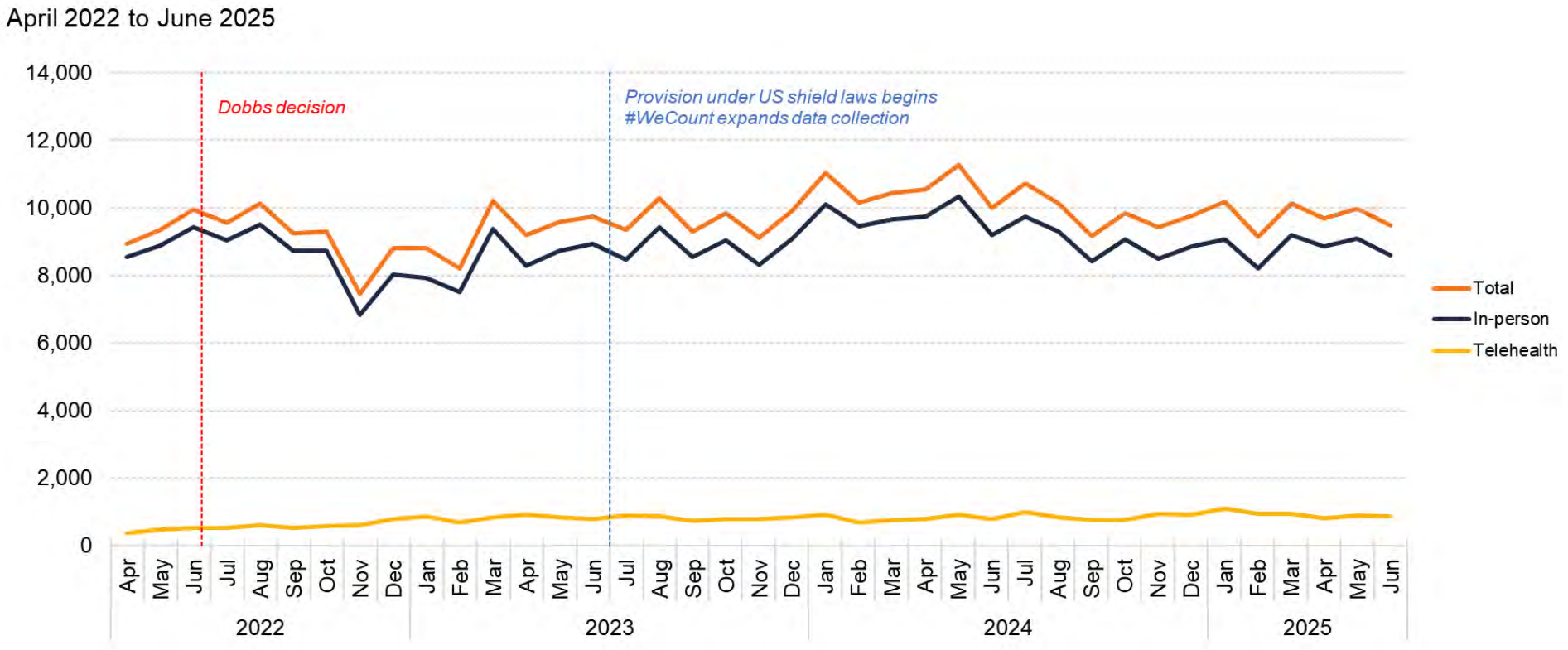
New York



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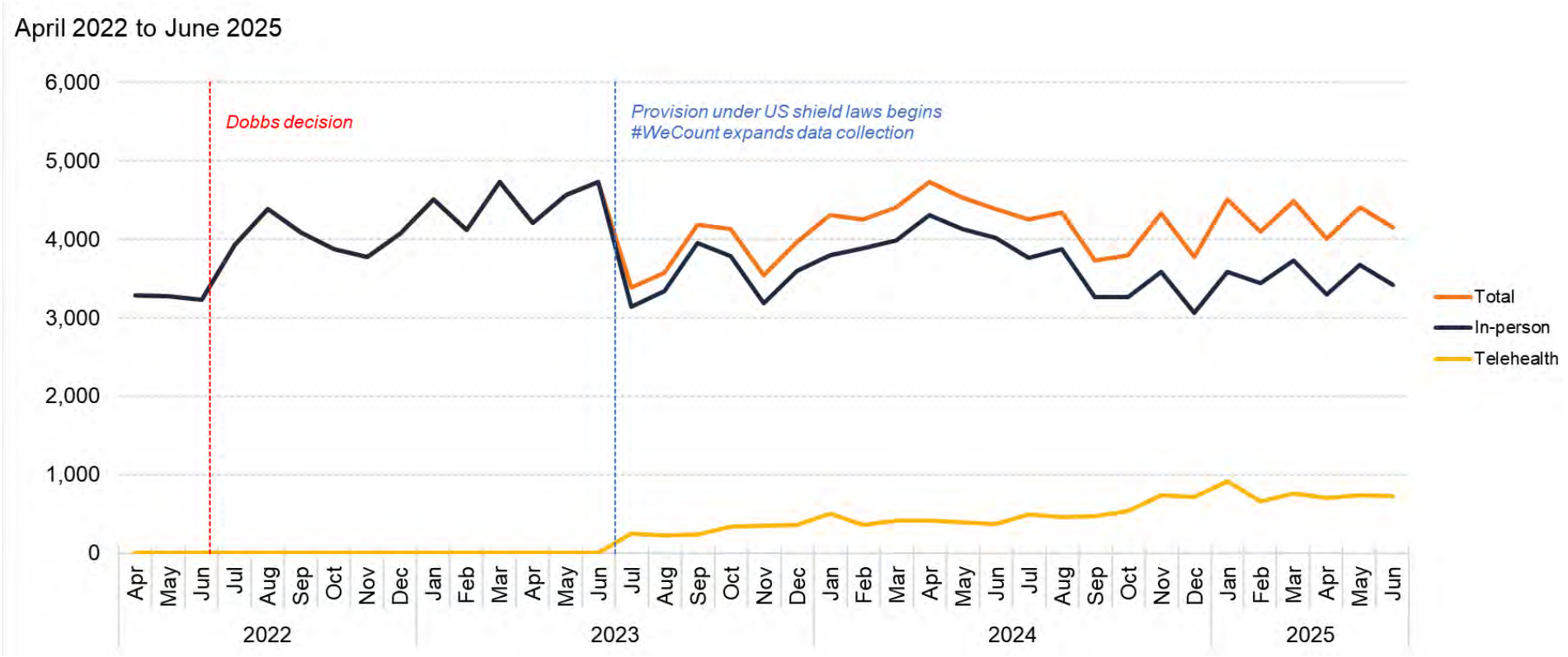
North Carolina



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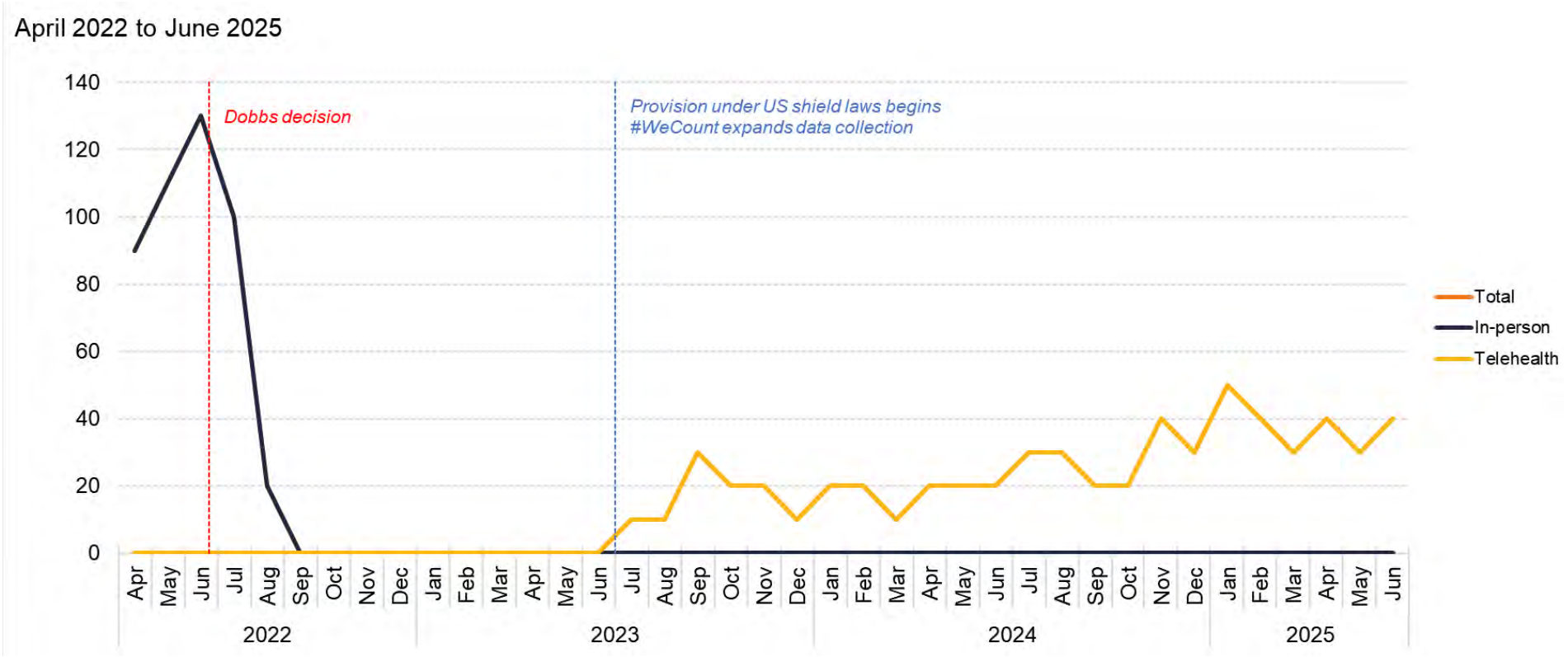
North Dakota



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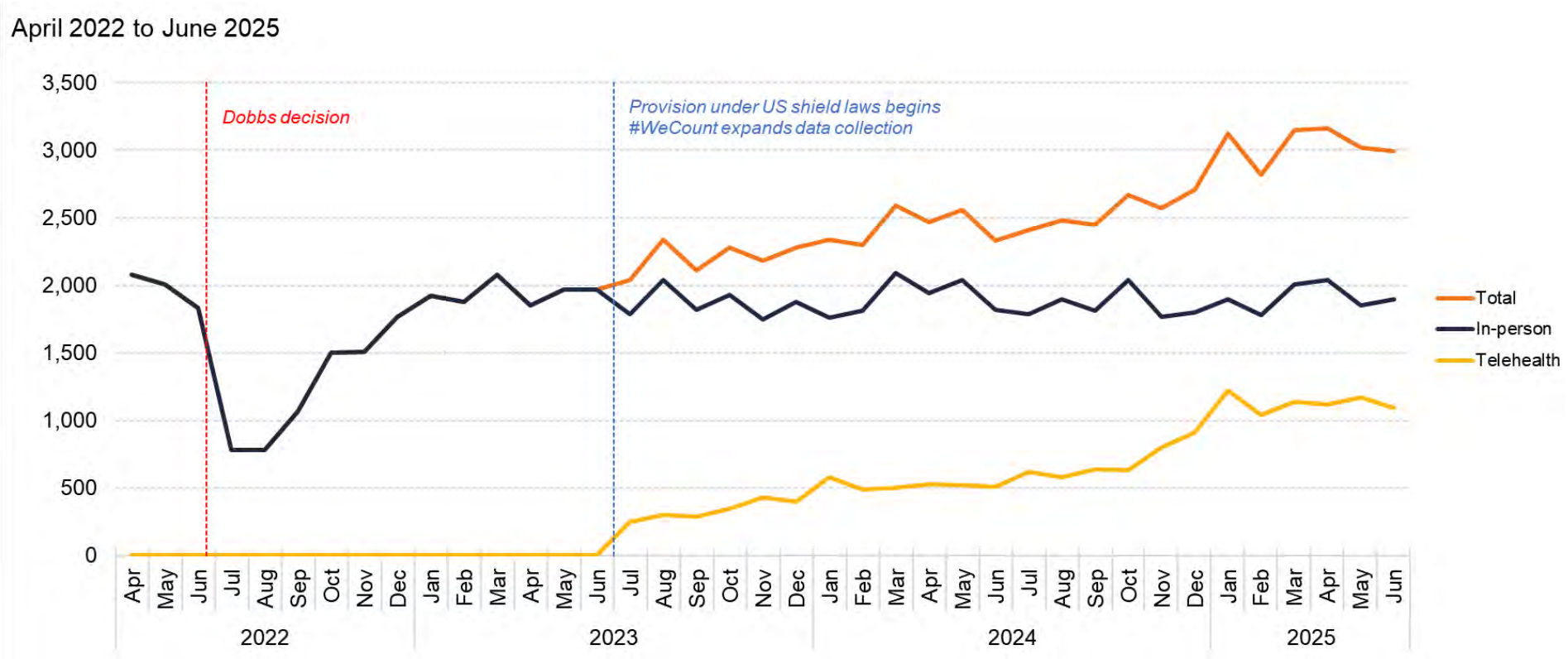
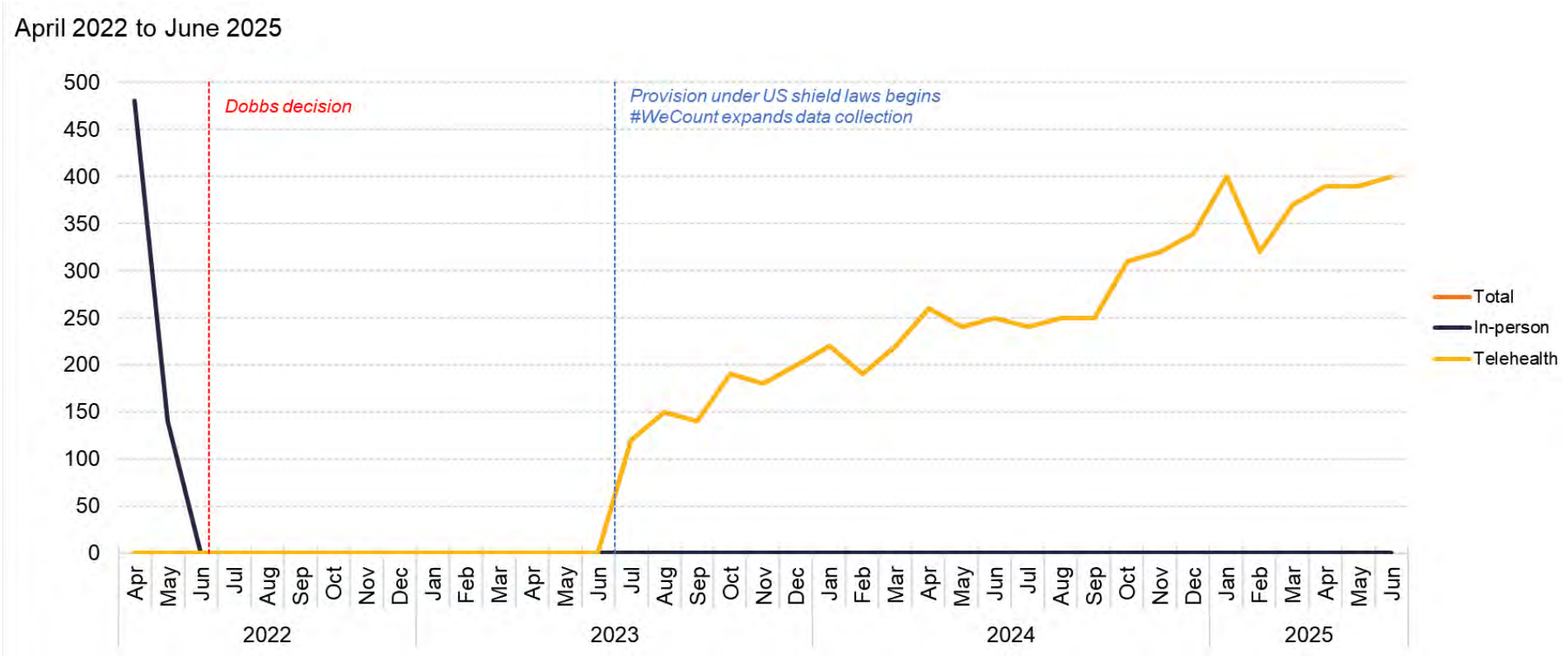
Ohio



Source: Society of Family Planning, December 2025

Oklahoma



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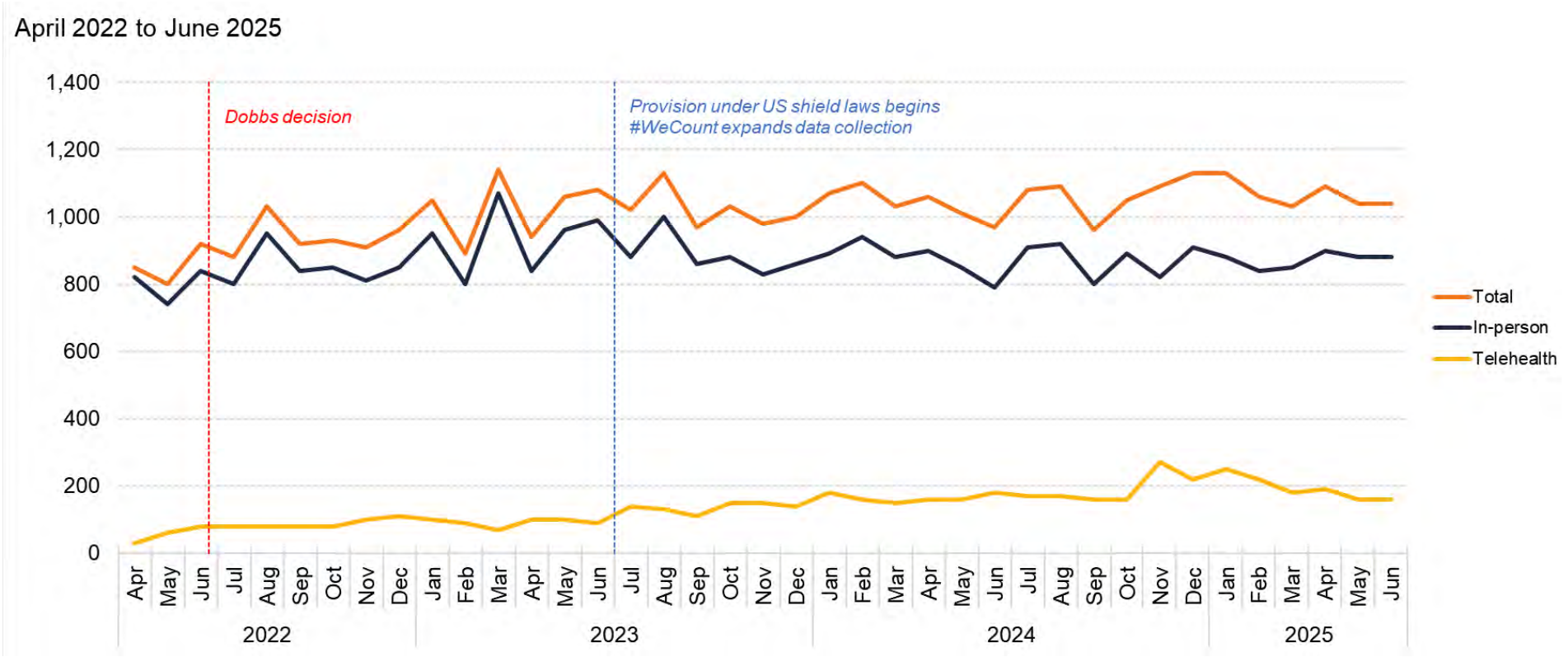
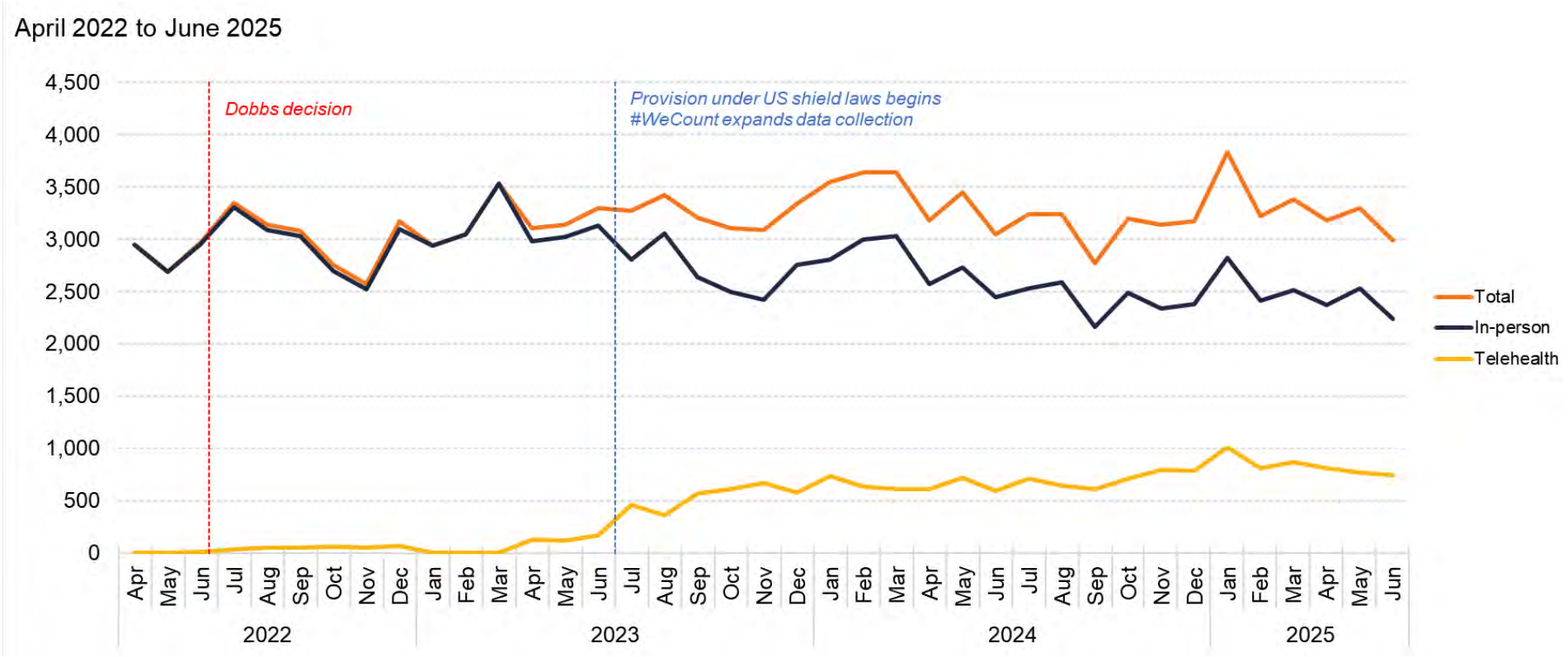
Oregon



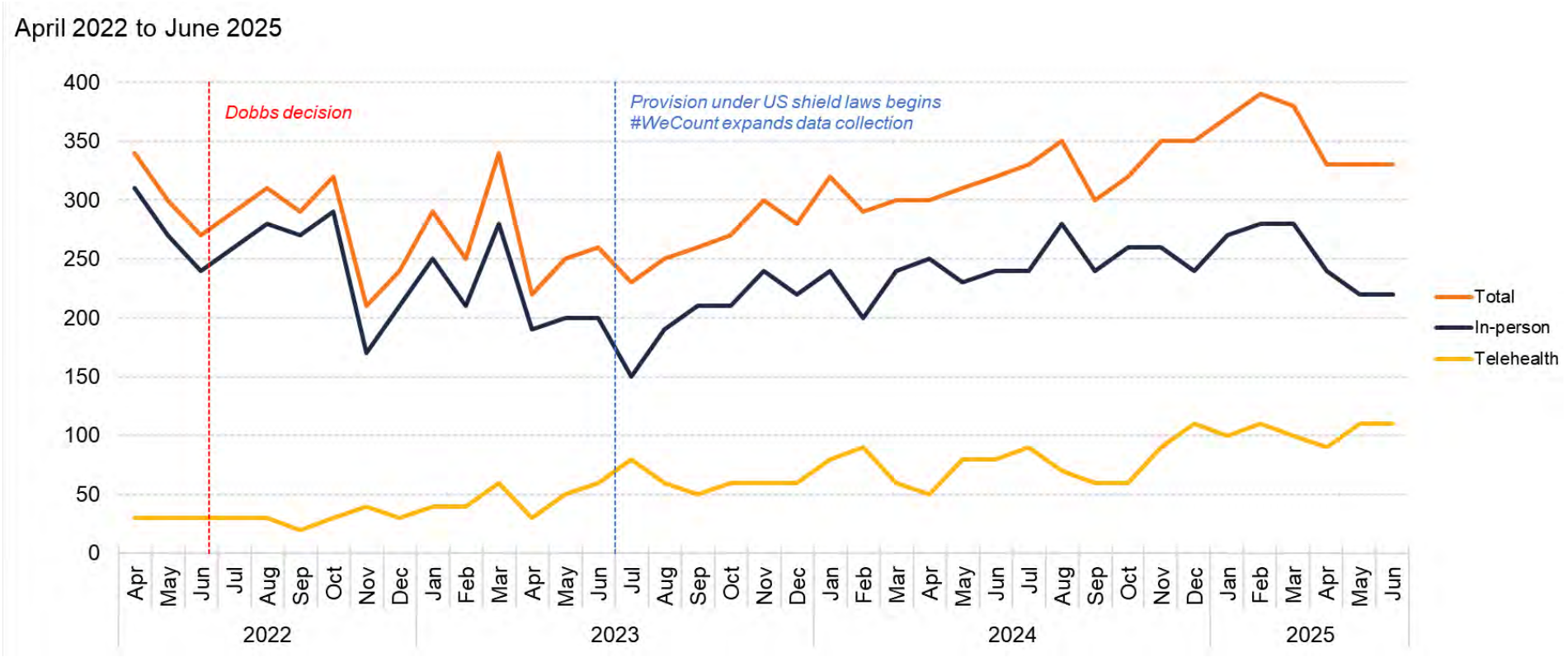
Source: Society of Family Planning, December 2025

Pennsylvania



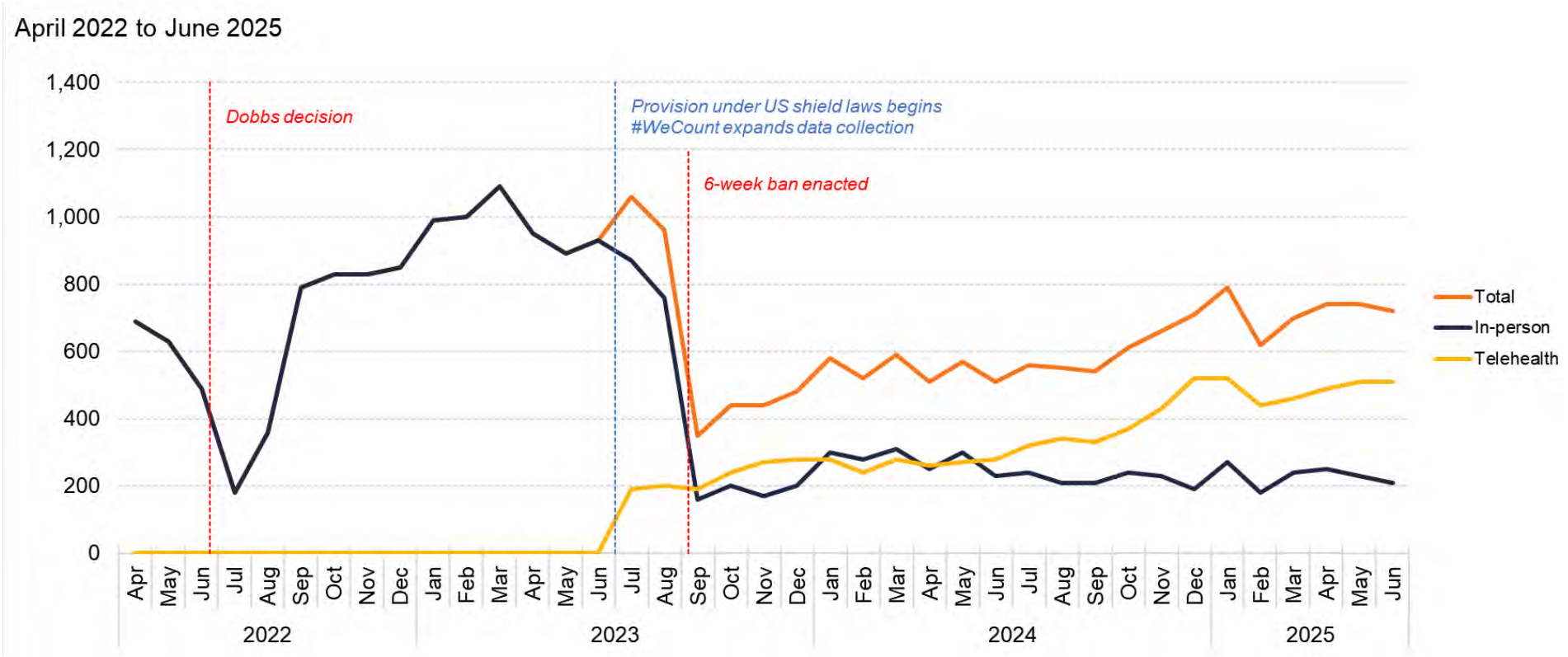
Source: Society of Family Planning, December 2025

Rhode Island



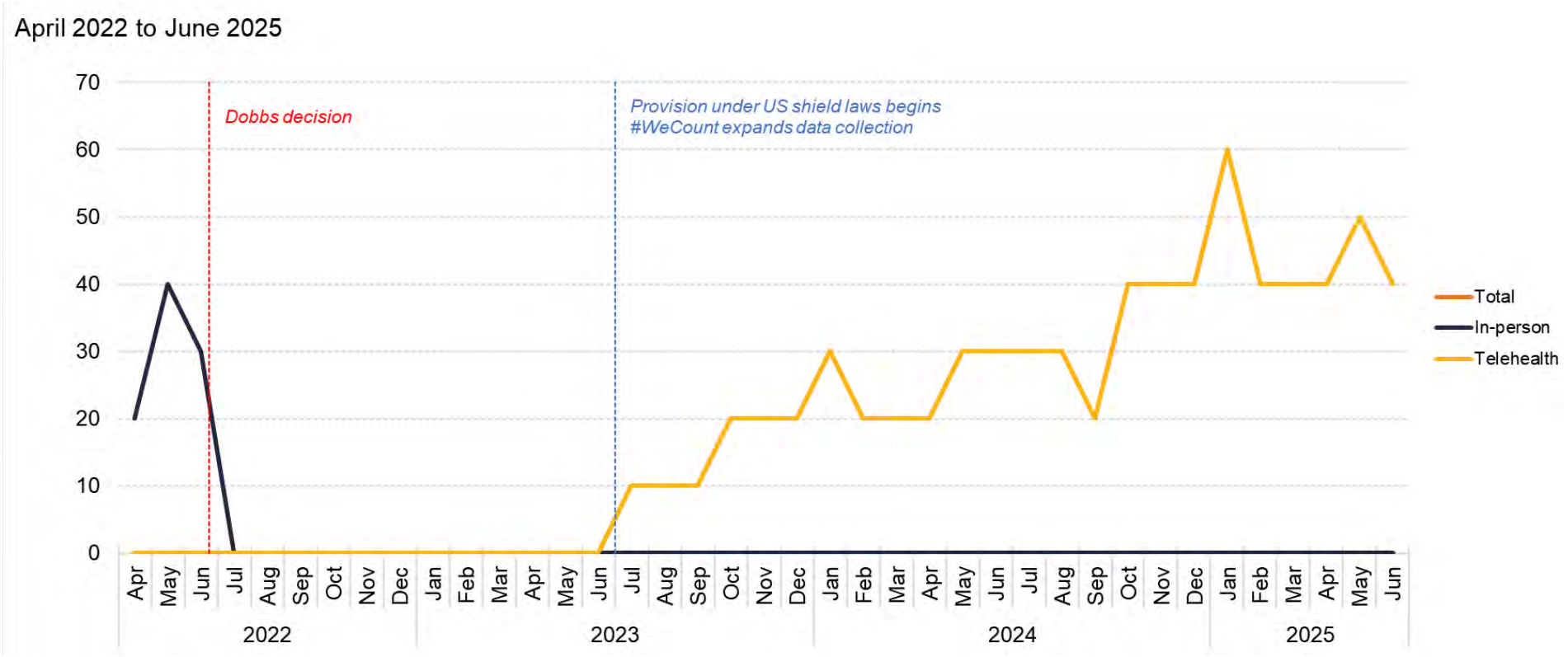
Source: Society of Family Planning, December 2025

South Carolina



Source: Society of Family Planning, December 2025

South Dakota



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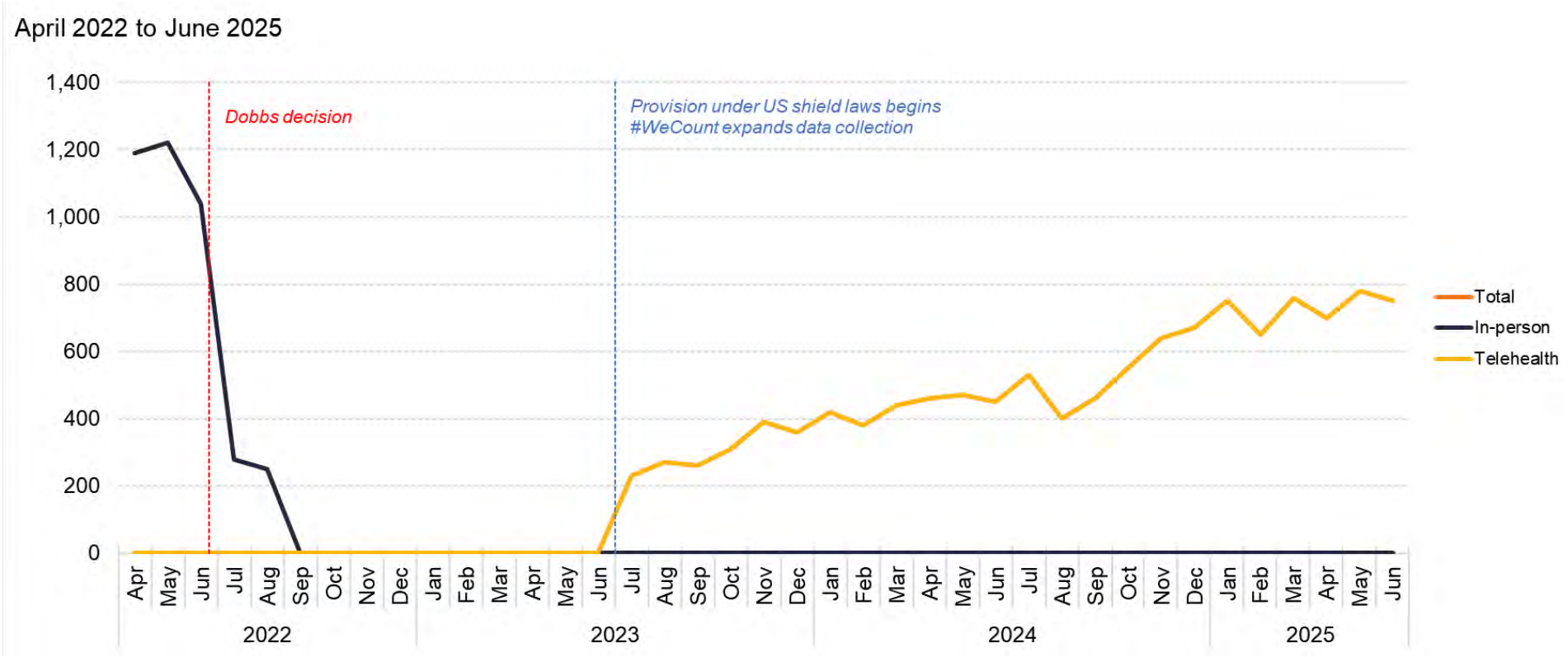
Tennessee



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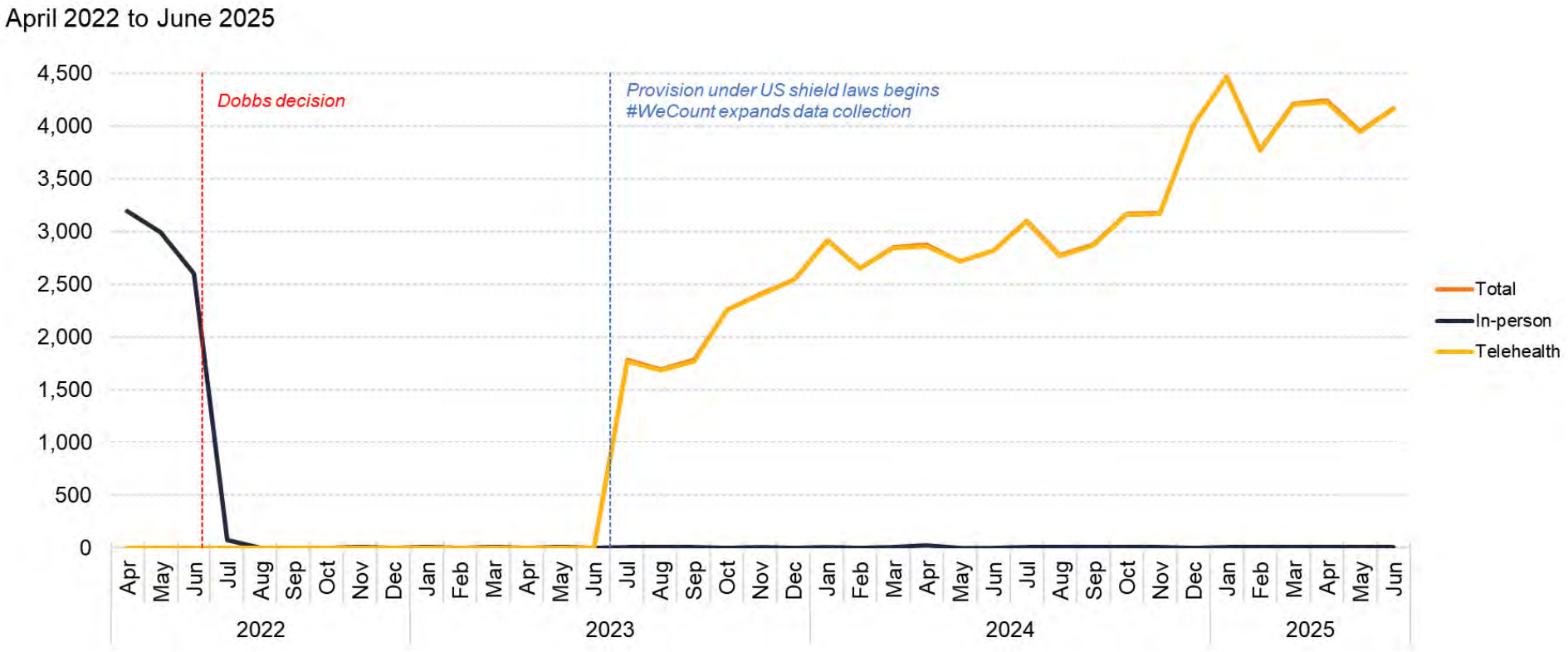
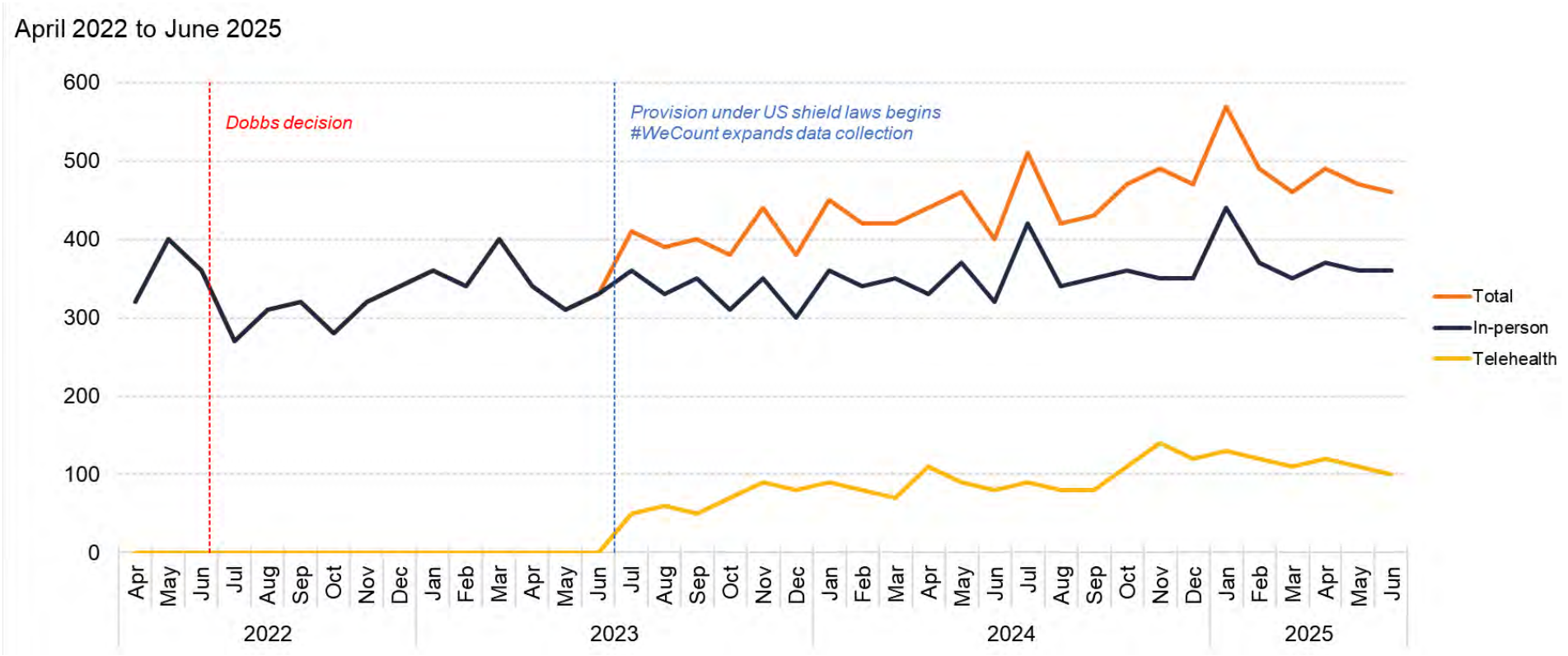
Texas



Source: Society of Family Planning, December 2025

Utah



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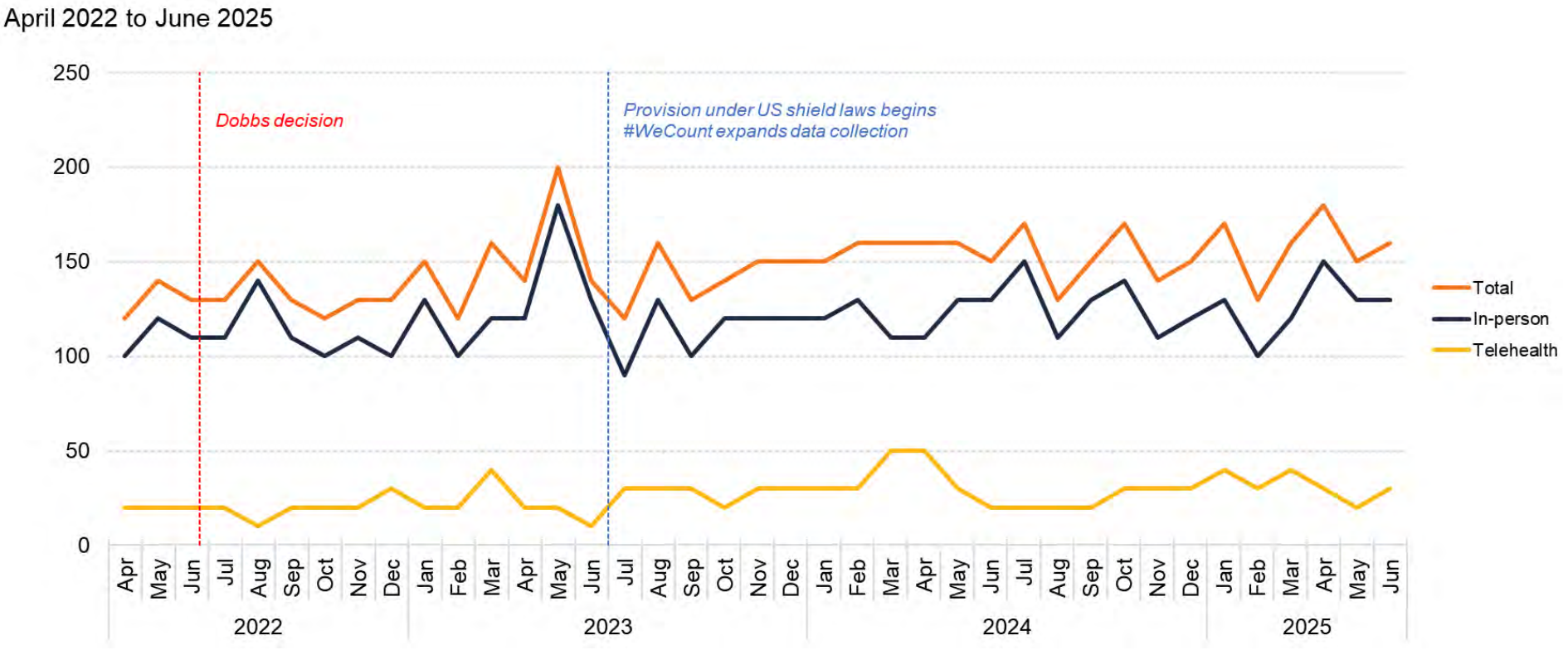

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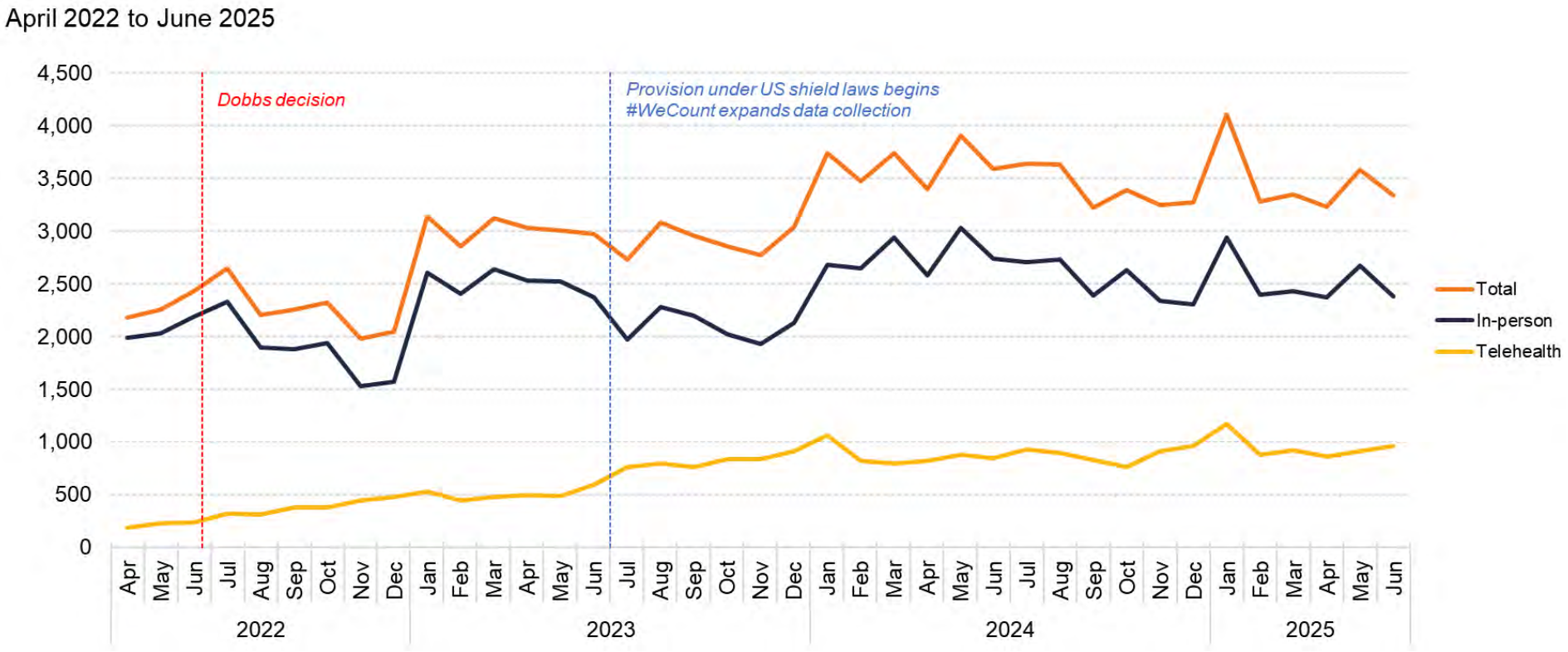

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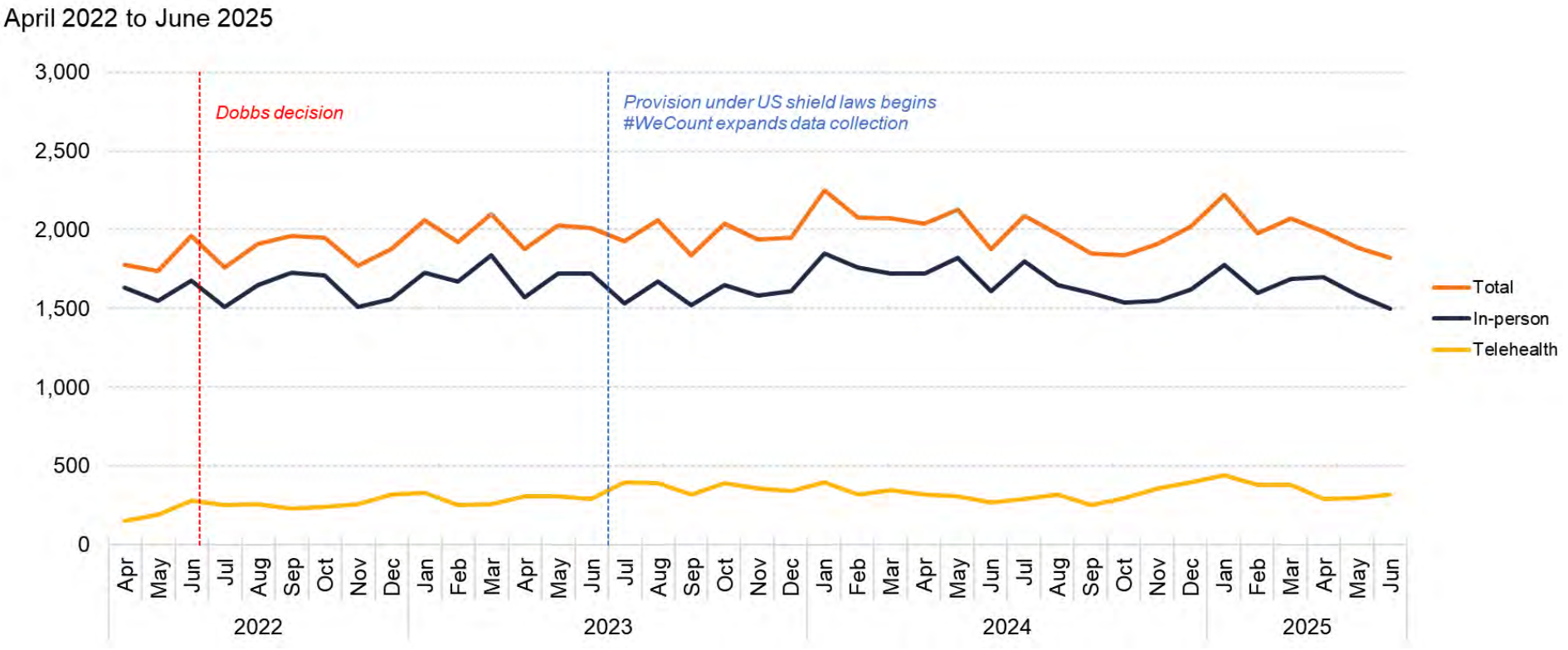

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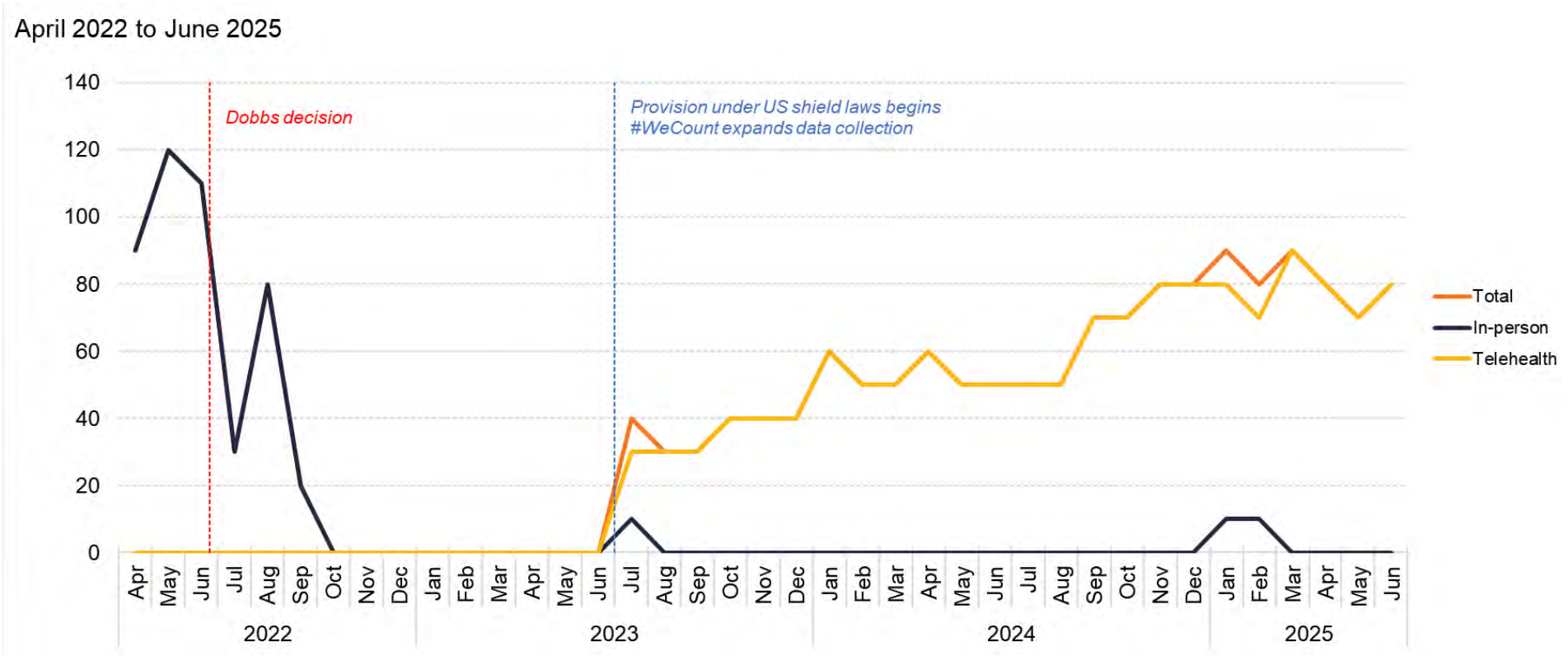

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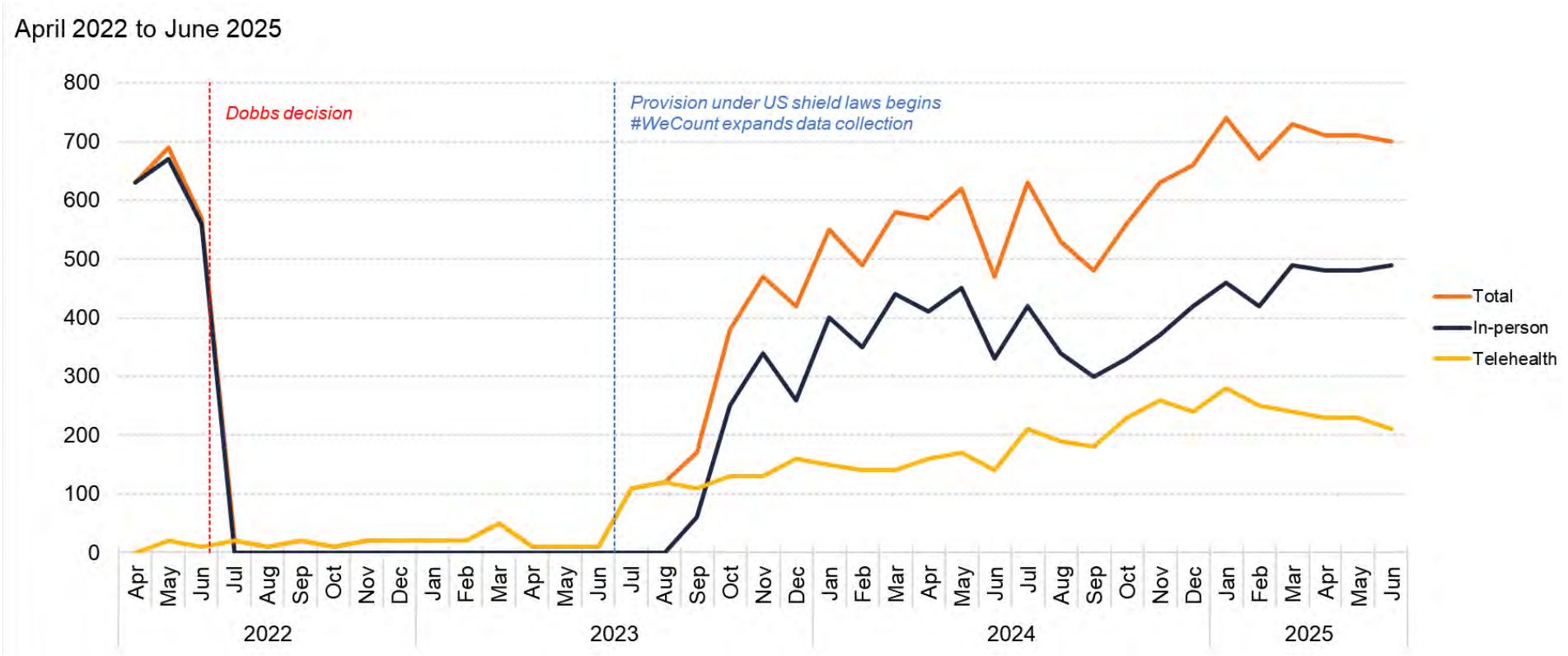

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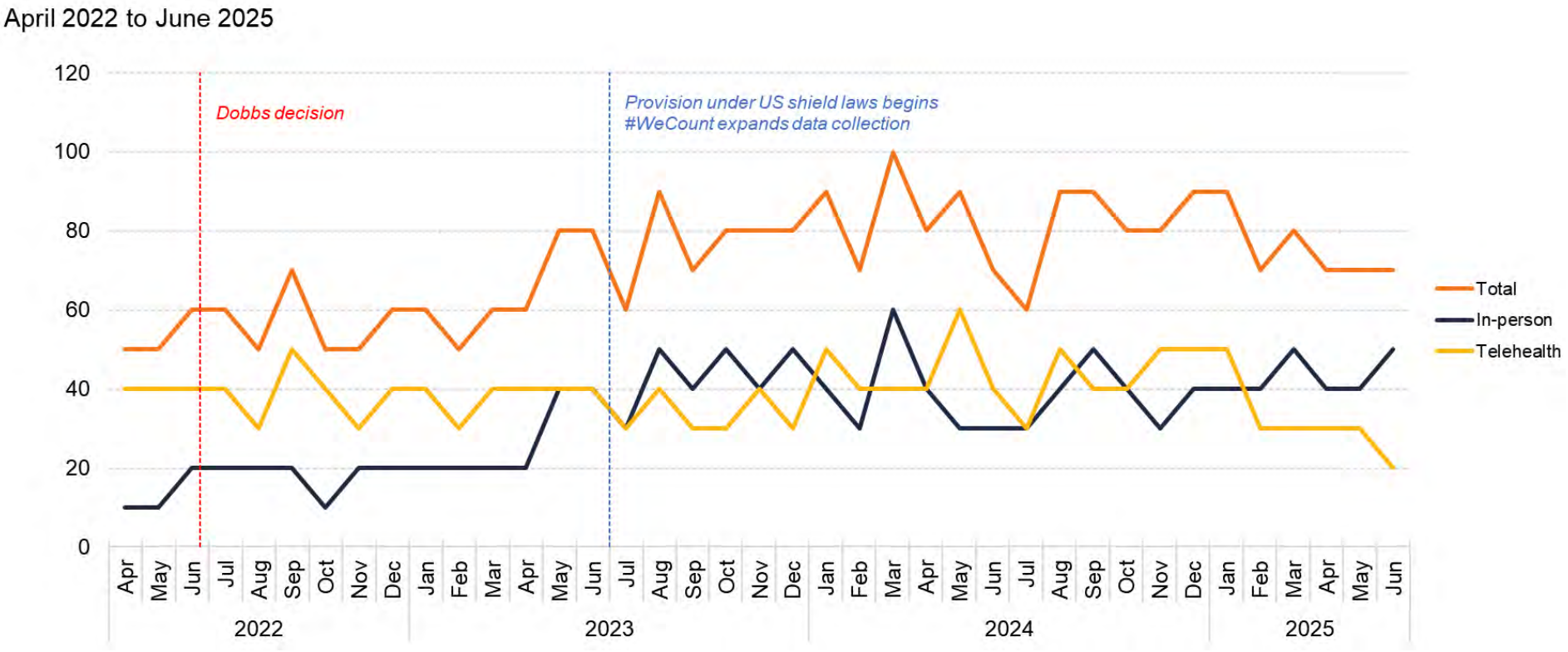

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EXHIBIT 4

Robin Wallace et al, *P040 - Expanding Access to Abortion with Mifepristone and Misoprostol Through 84 Days Estimated Gestational Duration*, 151 Contraception 111117 (Nov. 2025)

Results: Higher perceived abortion stigma predicted greater symptoms of depression, anxiety, and social anxiety. Social support moderated the associations between abortion stigma and symptoms of anxiety and social anxiety. Specifically, such stigma was positively associated with social anxiety symptoms at all levels of partner support (ie, low, moderate, high), but was strongest for those with low partner support. Additionally, perceived abortion stigma was positively associated with symptoms of anxiety and social anxiety for people with moderate and high maternal support (but not low). Abortion disclosure did not moderate the associations between this stigma and mental health symptoms.
Conclusions: This study adds to the emerging literature on perceived abortion stigma and mental health, and findings suggest that the effect of social support on this association may vary based on source.

https://doi.org/10.1016/j.contraception.2025.111116

P040

EXPANDING ACCESS TO ABORTION WITH MIFEPRISTONE AND MISOPROSTOL THROUGH 84 DAYS ESTIMATED GESTATIONAL DURATION

R Wallace
Planned Parenthood Federation of America, New York, NY, US
S Diemert, O Ades-Lawlor, R Topp, H Simons

Objectives: We aimed to assess efficacy and safety of a combined medication abortion regimen, using mifepristone and repeat buccal misoprostol dosing, for patients seeking abortion at 78-84 days estimated gestational duration in an outpatient setting in the US.
Methods: We are conducting a secondary analysis of data from 14 US-based Planned Parenthood affiliates that provided medication abortion for eligible patients with an estimated gestational duration of 78-84 days from April 2024 to December 2024, with additional data through March 2025 expected. Affiliates reported the total number of patients receiving medication abortion at this gestational duration (n = 711) and available outcome data. Among medication abortions with known outcomes (n = 217), we will calculate the incidence rates and 95% confidence intervals for completed abortion, ongoing pregnancy, subsequent procedure, and emergency department or hospital visits associated with medication abortion.
Results: Out of 217 known outcomes of the 711 total medication abortions provided at 78-84 days estimated gestational duration, preliminary raw data includes 27 ongoing pregnancies, 22 aspirations performed for ongoing pregnancies, 10 aspirations performed for other reasons, and 21 visits to an emergency department or hospital.
Conclusions: Use of medication abortion at 78-84 days estimated gestational duration in our study's US-based outpatient health centers resulted in similarly low ongoing pregnancy and need for aspiration as shown by prior research conducted in international inpatient settings. Offering medication abortion with a combined regimen, including mifepristone followed 24-48 hours later by buccal misoprostol every four hours for 2-3 doses, may increase access to safe, effective abortion beyond 77 days of pregnancy.

https://doi.org/10.1016/j.contraception.2025.111117

P042

THE ROLE OF ABORTION RESTRICTIONS IN COUNSELING AT FETAL CARE CENTERS

V Manthena
University of Chicago, Chicago, IL, US
P Gopal, A Akhter, JT Fry, JL Muñoz, J Chor, AF Shaaban, A Premkumar

Objectives: Fetal care centers (FCCs) or hospital-based institutions focused on the diagnosis and management of congenital anomalies have increased over the past decade, but little is known about their abortion care practices including eliciting interest, counseling, and referrals, or how these practices are influenced by institutional or state policies on abortion care.
Methods: We conducted a cross-sectional study across US North American Fetal Therapy Network (NAFTNet) sites, including FCCs in states or institutions with restrictive and permissive abortion policies, as defined by the Guttmacher Institute. Providers were recruited via snowball sampling, and surveys were distributed electronically through REDCap. Semi-structured key interviews were performed among a subgroup of NAFTnet site representatives. Interviews were audio-recorded, transcribed and analyzed using grounded theory, with quantitative data summarized statistically.
Results: Twenty-three providers (3 pediatric surgeons, 20 maternal-fetal medicine (MFM) subspecialists) completed the survey, and 12 providers (1 pediatric surgeon, 11 MFMs) expressed interest in the interview. Among those interviewed, the majority were female (58.3%) and worked at FCCs located in settings with restrictive or partly permissive abortion policies (58.3%). Key themes from interviews by providers located in permissive settings included ease and comfort in abortion counseling, while providers located in hospital systems or states with restrictive abortion policies emphasized counseling practices based on institutional or state restrictions and conscientious provision.
Conclusions: Providers working at FCCs face unique issues in eliciting interest in and counseling about abortion care, which diverge based on institutional and state restrictions. Future research should investigate patient experiences of abortion care after consultation at an FCC.

https://doi.org/10.1016/j.contraception.2025.111118

P043

TRENDS IN MISOPROSTOL PRESCRIBING AND DISPENSING ACROSS NORTH CAROLINA PHARMACIES

L Joudeh
University of North Carolina at Chapel Hill, Chapel Hill, NC, US
C Muir, V Miller, A Schultz

Objectives: The aim of this study is to assess misoprostol dispensing practices across North Carolina pharmacies. We sought to identify trends in misoprostol dispensing in low access healthcare counties, rural counties, and by pharmacy type.
Methods: We used a secret-shopper approach to assess whether pharmacies dispense misoprostol. The secret-shopper called in the role of clinic staff. Chi-squared tests and Fisher's exact tests were used for statistical analysis.
Results: Of the 100 counties in North Carolina, 94 (94%) counties were contacted. Ninety-nine (99%) counties had a chain pharmacy represented and 95 (95%) had an independent pharmacy represented. Some 173 (77.6%) pharmacies dispensed misoprostol, 12 (5.4%) had conditional dispensing practices, and 38 (17.0%) did not

EXHIBIT 6

US FDA Has Delayed Abortion Pill Safety Study,
Bloomberg News Reports,
Reuters (Dec. 8, 2025, at 14:23 PT)

Learn more about LSEG

US FDA has delayed abortion pill safety study, Bloomberg News reports

By **Reuters**

December 8, 2025 2:23 PM PST · Updated December 8, 2025

Feedback

Signage is seen outside of the Food and Drug Administration (FDA) headquarters in White Oak, Maryland, U.S., August 29, 2020. REUTERS/Andrew Kelly/File Photo Purchase Licensing Rights

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Dec 8 (Reuters) - The U.S. Food and Drug Administration has delayed a review of safety data for the abortion drug mifepristone at Commissioner Marty Makary's request, Bloomberg News reported on Monday, citing people familiar with the matter.

Makary has told agency officials to delay the safety review until after the midterm elections, the report said.

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Feedback

"The FDA's comprehensive scientific reviews take the time necessary to get the science right and that's what Dr. Makary is ensuring," Department of Health and Human Services spokesperson Andrew Nixon said.

U.S. Health Secretary Robert F. Kennedy Jr. had said earlier this year that the review of mifepristone is ongoing.

Mifepristone is the first pill, followed by the drug misoprostol, for medication abortion in the first 10 weeks of pregnancy, and won FDA approval in 2000.

Reporting by Mariam Sunny and Sahil Pandey in Bengaluru; Editing by Maju Samuel

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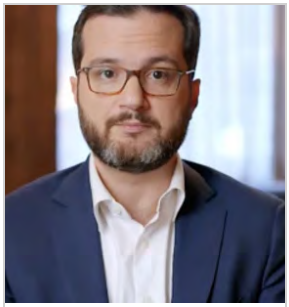

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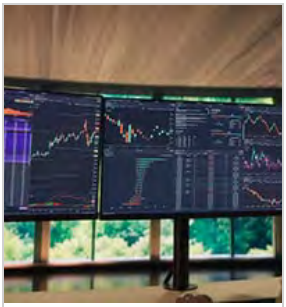

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Business · December 12, 2025 · 9:17 PM PST · 17 mins ago

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EXHIBIT 7

Elizabeth Troutman Mitchell, *EXCLUSIVE: Makary Responds to Report Saying He Slow-Walked Abortion Pill Safety Review*, Daily Signal (Dec. 9, 2025)

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HEALTH CARE NEWS

EXCLUSIVE: Makary Responds to Report Saying He Slow-Walked Abortion Pill Safety Review

Elizabeth Troutman Mitchell December 09, 2025

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Elizabeth Troutman Mitchell is the White House Correspondent for "The Daily Signal." Send her an email.

FIRST ON THE DAILY SIGNAL—Food and Drug Administration Commissioner Dr. Marty Makary said the review of the abortion drug mifepristone is in the “data acquisition phase” following a report saying he is delaying the process.

“We do an ongoing review, but we’re also engaging in a robust study that can serve to validate or not validate other numbers that have been put out there in the literature,” he told The Daily Signal in an exclusive interview.

Makary and Secretary of Health and Human Services Robert F. Kennedy Jr. have pledged to do a review of the safety of abortion drugs following a study from the

English

Ethics and Public Policy Center, which showed 11% of women experience adverse effects after taking the pill regimen. Bloomberg reported that Makary is slow-walking the review, prompting calls from leading pro-life groups for him to be removed from his post.

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English

Makary said he is personally responsible for the review.

”Ultimately, I’m responsible, and so this analysis is going to be done under my auspices, and it’ll be reported up to me,” he said, “and I’m going to be involved.”

The FDA is currently in the “data acquisition phase” of the abortion pill review.

English

“Appropriately, many members of Congress have said, ‘Hey, this is a good time to check in and do a robust study.’ So, part of a robust study is data acquisition,” he said. “And so, we’re in that data acquisition phase to get the right data to be able to do this study.”

Makary said he is unable to predict the “results or the timeframe” of the review.

“The shutdown was a little bit of a setback in that, but we’re gonna do it and whenever the results are available,” he said, “we’re gonna make them public.”

He laid out the plan for the review. Once the data has finished coming in, the FDA will review it and ensure there are no missing data fields that change the way the analysis is designed.

“If there are, then you change the design of the study and you account for how the landscape of the data actually is and the way it presents,” he said. “And then you look at the preliminary exploratory results, and then you change the analysis to account for confounding variables.”

Next, the FDA will “repeat and validate.”

“These are all routine steps in robust data analysis,” he said. “Studies are often repeated, done by multiple reviewers or statisticians. So, we’re going to do it the right way. And look, I know there are a lot of voices in this space, but I’m committed to doing this the right way.”

The former Johns Hopkins professor blamed the rumor mill for Bloomberg’s story saying he has slow-walked the mifepristone review.

“There’s a lot of rumors that are circulating out there,” he said. “We live in a very partisan time, and so you’re going to see the echo chambers of social media sort of magnify rumors, things that are just not true. There has been an ongoing review of mifepristone.”

English

The Risk Evaluation & Mitigation Strategies, or REMS, policy already requires the FDA to perform an ongoing review of medication, Makary said.

“There’s always an ongoing review of that medication, and we need to be open to the fact that maybe there’s a new drug interaction that was not appreciated,” he said.

Makary said it’s possible “there’s a complication that was not recognized previously” with the abortion pill. What the FDA finds in the study will join the “broader discussion nationally,” he said.

“We’re not going to decide what the results are before we’ve done the study,” he said. “We’re doing the study the right way. And when you do the study the right way, and I’ve done dozens of these studies as a Johns Hopkins professor, you gotta do the studies in data the right way with the right pace.”

The Ethics & Public Police Center study found that about 11% of women experience sepsis, infection, hemorrhaging, or another serious adverse event within 45 days following a mifepristone abortion. This has led to calls to reinstate the in-person dispensing requirement for mifepristone.

In April 2021, the Biden administration’s FDA stopped requiring that abortion drugs be dispensed to women in person, which allowed women to receive them through telehealth appointments and by mail. The FDA has not enforced the in-person dispensing requirement ever since.

Seven out of 10 American voters say they don’t think it’s safe for abortion drugs to be sent via mail, according to a McLaughlin & Associates poll.

When asked by The Daily Signal if it’s safe for women to take the abortion pill at home without seeing a doctor first, Makary said the Ethics & Public Police Center study “was done in claims data, so it didn’t have granularity into the patient characteristics in a way that many researchers would want to have.”

“Tha English reasons why we are doing a bigger, more robust study,” he said.

EPPC abortion pill study authors, Ryan T. Anderson and Jamie Bryan Hall, responded that the study they conducted was "the biggest and most robust study conducted thus far—much more so than the studies the FDA has previously relied on—and we are confident that the FDA will find similar results to ours using real-world data."

"However, the FDA need not complete that study to reinstate the in-person doctor visit. We already have seen women coercively poisoned by boyfriends to kill their unborn babies," they told The Daily Signal. "This couldn't happen if the FDA once again required in-person doctor visits as they did during the first Trump administration."

The FDA approved a second generic version of the abortion pill on Oct. 2, shortly before the government shutdown, another move that sparked pro-life backlash. Makary said the FDA had to approve the drug or get sued.

"There's a law that requires the FDA to approve a molecule if it's similar to a branded molecule, so we had no discretion," Makary told The Daily Signal. "If we chose to look at that application and say, no, we're not going to approve this, we'd 100% get sued, and we'd 100% lose."

"It would all happen very quickly because the law is very clear now with drugs that we approve as new branded drugs," he said. "It's a very different law. So we have discretion to weigh risks and benefits. But when it comes to generic compounds, the law is pretty clear."

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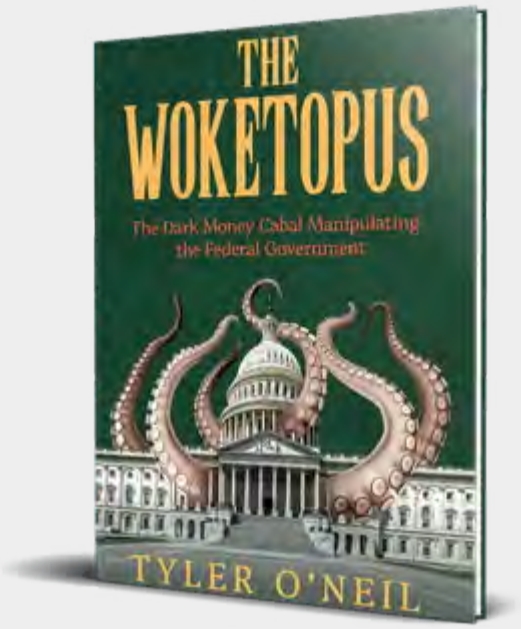

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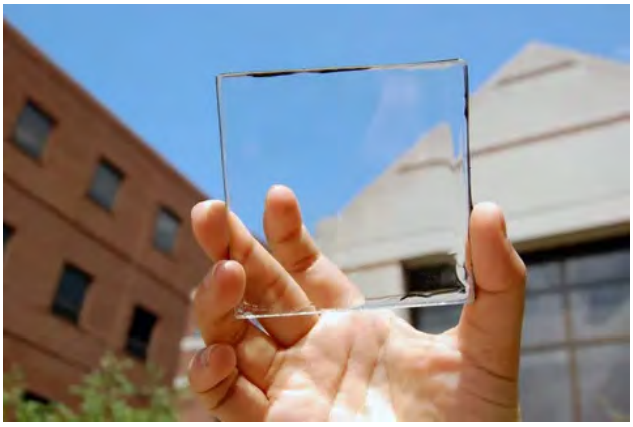

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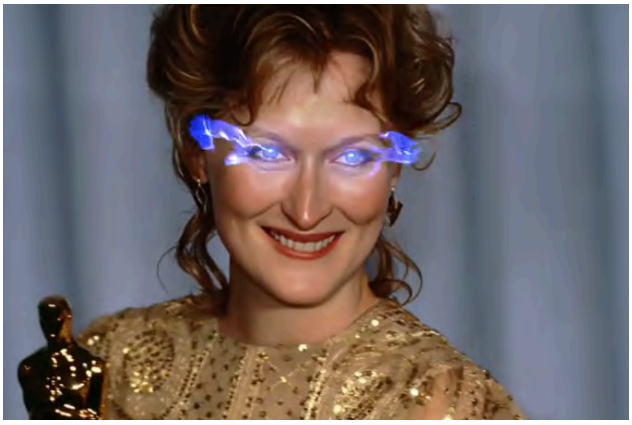

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EXHIBIT 16

FDA, REMS Single Shared System for Mifepristone 200MG (May 2021)

Initial Shared System REMS approval: 04/2019
Most Recent Modification: 05/2021

Mifepristone Tablets, 200 mg

Progestin Antagonist

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

SINGLE SHARED SYSTEM FOR MIFEPRISTONE 200MG

I. GOAL

The goal of the REMS for mifepristone is to mitigate the risk of serious complications associated with mifepristone by:

a) Requiring healthcare providers who prescribe mifepristone to be certified in the Mifepristone REMS Program.

b) Ensuring that mifepristone is only dispensed in certain healthcare settings by or under the supervision of a certified prescriber.

c) Informing patients about the risk of serious complications associated with mifepristone.

II. REMS ELEMENTS

A. Elements to Assure Safe Use

1. Healthcare providers who prescribe mifepristone must be specially certified.
   a. To become specially certified to prescribe mifepristone, healthcare providers must:
      i. Review the Prescribing Information for mifepristone.
      ii. Complete a *Prescriber Agreement Form*. By signing a *Prescriber Agreement Form*, prescribers agree that:
         1) They have the following qualifications:
            a) Ability to assess the duration of pregnancy accurately
            b) Ability to diagnose ectopic pregnancies
            c) Ability to provide surgical intervention in cases of incomplete abortion or severe bleeding, or to have made plans to provide such care through others, and ability to assure patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary.
         2) They will follow the guidelines for use of mifepristone (see b.i-v below).
   b. As a condition of certification, healthcare providers must follow the guidelines for use of mifepristone described below:
      i. Review the *Patient Agreement Form* with the patient and fully explain the risks of the mifepristone treatment regimen. Answer any questions the patient may have prior to receiving mifepristone.

Reference ID: 4799010

ii. Sign the *Patient Agreement Form* and obtain the Patient's signature on the *Form*

iii. Provide the patient with a copy of the *Patient Agreement Form* and Medication Guide.

iv. Place the signed *Patient Agreement Form* in the patient's medical record.

v. Record the serial number from each package of mifepristone in each patient's record.

vi. Report any deaths to the Mifepristone Sponsor that provided the mifepristone, identifying the patient by a non- identifiable reference and the serial number from each package of mifepristone.

c. Mifepristone Sponsors must:

i. Ensure that healthcare providers who prescribe their mifepristone are specially certified in accordance with the requirements described above and de-certify healthcare providers who do not maintain compliance with certification requirements

ii. Provide the Prescribing Information and their *Prescriber Agreement Form* to healthcare providers who inquire about how to become certified.

The following materials are part of the REMS and are appended:

- *Prescriber Agreement Form for Danco Laboratories, LLC*
- *Prescriber Agreement Form for GenBioPro, Inc.*
- *Patient Agreement Form*

2. Mifepristone must be dispensed to patients only in certain healthcare settings, specifically clinics, medical offices, and hospitals, by or under the supervision of a certified prescriber.

a. Mifepristone Sponsors must:

i. Ensure that their mifepristone is available to be dispensed to patients only in clinics, medical offices and hospitals by or under the supervision of a certified prescriber.

ii. Ensure that their mifepristone is not distributed to or dispensed through retail pharmacies or other settings not described above.

3. Mifepristone must be dispensed to patients with evidence or other documentation of safe use conditions.

a. The patient must sign a *Patient Agreement Form* indicating that the patient has:

i. Received, read and been provided a copy of the *Patient Agreement Form*.

ii. Received counseling from the prescriber regarding the risk of serious complications associated with mifepristone.

B. Implementation System

1. Mifepristone Sponsors must ensure that their mifepristone is only distributed to clinics, medical offices and hospitals by or under the supervision of a certified prescriber by:

a. Ensuring that distributors who distribute their mifepristone comply with the program requirements for distributors. The distributors must:

Reference ID: 4799010

i. Put processes and procedures in place to:

a. Complete the healthcare provider certification process upon receipt of a Prescriber Agreement Form.

b. Notify healthcare providers when they have been certified by the Mifepristone REMS Program.

c. Ship mifepristone only to clinics, medical offices, and hospitals identified by certified prescribers in their signed *Prescriber Agreement Form*.

d. Not ship mifepristone to prescribers who become de-certified from the Mifepristone REMS Program.

e. Provide the Prescribing Information and their Prescriber Agreement Form to healthcare providers who (1) attempt to order mifepristone and are not yet certified, or (2) inquire about how to become certified.

ii. Put processes and procedures in place to maintain a distribution system that is secure, confidential and follows all processes and procedures, including those for storage, handling, shipping, tracking package serial numbers, proof of delivery and controlled returns of mifepristone.

iii. Train all relevant staff on the Mifepristone REMS Program requirements.

iv. Comply with audits by Mifepristone Sponsors, FDA or a third party acting on behalf of Mifepristone Sponsors or FDA to ensure that all processes and procedures are in place and are being followed for the Mifepristone REMS Program. In addition, distributors must maintain appropriate documentation and make it available for audits.

b. Ensuring that distributors maintain secure and confidential distribution records of all shipments of mifepristone.

2. Mifepristone Sponsors must monitor their distribution data to ensure compliance with the REMS Program.

3. Mifepristone Sponsors must audit their new distributors within 90 calendar days after the distributor is authorized to ensure that all processes and procedures are in place and functioning to support the requirements of the Mifepristone REMS Program. Mifepristone Sponsors will take steps to address their distributor compliance if noncompliance is identified.

4. Mifepristone Sponsors must take reasonable steps to improve implementation of and compliance with the requirements of the Mifepristone REMS Program based on monitoring and assessment of the Mifepristone REMS Program.

5. Mifepristone Sponsors must report to FDA any death associated with mifepristone whether or not considered drug-related, as soon as possible but no later than 15 calendar days from the initial receipt of the information by the applicant. This requirement does not affect the applicants other reporting and follow-up requirements under FDA regulations.

C. Timetable for Submission of Assessments

The NDA Sponsor must submit REMS assessments to FDA one year from the date of the initial approval of the REMS (04/11/2019) and every three years thereafter. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 calendar days before the submission date for that assessment. The NDA Sponsor must submit each assessment so that it will be received by the FDA on or before the due date.

Reference ID: 4799010

PRESCRIBER AGREEMENT FORM

Mifeprex® (Mifepristone) Tablets, 200 mg

Mifeprex* (Mifepristone) Tablets, 200 mg, is indicated, in a regimen with misoprostol, for the medical termination of intrauterine pregnancy through 70 days gestation. Please see Prescribing Information and Medication Guide for complete safety information.

To set up your account to receive Mifeprex, you must:
1. complete, 2. sign, and 3. fax page 2 of this form to the distributor.

If you will be ordering for more than one facility, you will need to list each facility on your order form before the first order will be shipped to the facility.

Prescriber Agreement: By signing page 2 of this form, you agree that you meet the qualifications below and will follow the guidelines for use. You also understand that if you do not follow the guidelines, the distributor may stop shipping Mifeprex to you.

Mifeprex must be provided by or under the supervision of a healthcare provider who prescribes and meets the following qualifications:

- Ability to assess the duration of pregnancy accurately.
- Ability to diagnose ectopic pregnancies.
- Ability to provide surgical intervention in cases of incomplete abortion or severe bleeding, or to have made plans to provide such care through others, and ability to assure patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary.
- Has read and understood the Prescribing Information of Mifeprex. The Prescribing Information is available by calling our toll free number, 1-877-4 Early Option (1-877-432-7596), or logging on to our website, www.earlyoptionpill.com.

In addition to meeting these qualifications, you also agree to follow these guidelines for use:

- Review the Patient Agreement Form with the patient and fully explain the risks of the Mifeprex treatment regimen. Answer any questions the patient may have prior to receiving Mifeprex.
- Sign and obtain the patient's signature on the Patient Agreement Form.
- Provide the patient with a copy of the Patient Agreement Form and the Medication Guide.
- Place the signed Patient Agreement Form in the patient's medical record.
- Record the serial number from each package of Mifeprex in each patient's record.
- Report deaths to Danco Laboratories, identifying the patient by a non-identifiable patient reference and the serial number from each package of Mifeprex.

ACCOUNT SETUP MIFEPREX® (Mifepristone) Tablets, 200 mg; NDC 64875-001-01

TO SET UP YOUR ACCOUNT:

1. Read the Prescriber Agreement on page 1 of this form.
2. Complete and sign this form.
3. Fax this page to the Danco distributor at 1-866-227-3343. Your account information will be kept strictly confidential.
4. The distributor will call to finalize your account setup and take your initial order.
5. Subsequent orders may be phoned or faxed and are usually shipped within 24 hours.

Mifeprex® (Mifepristone) Tablets, 200 mg
THE ORIGINAL EARLY OPTION PILL

BILLING INFORMATION

Bill to Name _____

Address _____

City _____ State _____ ZIP _____

Phone _____ Fax _____

Attention _____

SHIPPING INFORMATION ☐ *Check if same as above*

Ship to Name _____

Address _____

City _____ State _____ ZIP _____

Phone _____ Fax _____

Attention _____

ADDITIONAL SITE LOCATIONS *I will also be prescribing Mifeprex® at these additional locations:*

Name _____ Address _____

City _____ State _____ ZIP _____

Phone _____ Fax _____

Name _____ Address _____

City _____ State _____ ZIP _____

Phone _____ Fax _____

(Any additional sites may be listed on an attached sheet of paper.)

REQUEST ADDITIONAL MATERIALS

☐ Medication Guides ☐ State Abortion Guides ☐ Patient Brochures ☐ Patient Agreement Form

ESTABLISHING YOUR ACCOUNT *(required only with first order)*

Each facility purchasing Mifeprex must be included on this form (*see additional site locations box above*) before the distributor can ship the product to the facility.

By signing below, you agree that you meet the qualifications and that you will follow the guidelines for use on page 1 of the Prescriber Agreement.

Print Name _____ Signature _____

Medical License # _____ Date _____

FAX THIS COMPLETED FORM TO THE AUTHORIZED DISTRIBUTOR. FAX: 1-866-227-3343

Please fax any questions to the above number or call 1-800-848-6142.

*MIFEPREX is a registered trademark of Danco Laboratories, LLC.

Reference ID: 3909592
Reference ID: 4795916

Mifepristone Tablets, 200 mg, is indicated, in a regimen with misoprostol, for the medical termination of intrauterine pregnancy through 70 days gestation. Please see Prescribing Information and Medication Guide for complete safety information.

To set up your account to receive mifepristone, you must:
1. complete, 2. sign and 3. fax page 2 of this form to the distributor.

If you will be ordering for more than one facility, you will need to list each facility on your order form before the first order will be shipped to the facility.

Prescriber Agreement: By signing page 2 of this form, you agree that you meet the qualifications below and will follow the guidelines for use. You also understand that if you do not follow the guidelines, the distributor may stop shipping mifepristone to you.

Mifepristone must be provided by or under the supervision of a healthcare provider who prescribes and meets the following qualifications:

- Ability to assess the duration of pregnancy accurately.
- Ability to diagnose ectopic pregnancies.
- Ability to provide surgical intervention in cases of incomplete abortion or severe bleeding, or to have made plans to provide such care through others, and ability to assure patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary.
- Has read and understood the Prescribing Information for mifepristone. The Prescribing Information is available by calling our toll free number, 1-855-MIFE-INFO (1-855-643-3463), or logging on to our website, www.MifeInfo.com.

In addition to having these qualifications, you also agree to follow these guidelines for use:

- Review the Patient Agreement Form with the patient and fully explain the risks of the mifepristone treatment regimen. Answer any questions the patient may have prior to receiving mifepristone.
- Sign and obtain the patient's signature on the Patient Agreement Form.
- Provide the patient with a copy of the Patient Agreement Form and the Medication Guide.
- Place the signed Patient Agreement Form in the patient's medical record.
- Record the serial number from each package of mifepristone in each patient's record.
- Report deaths to GenBioPro, identifying the patient by a non-identifiable patient reference and the serial number from each package of mifepristone.

ACCOUNT SETUP

Mifepristone Tablets, 200 mg; NDC 43393-001-01

TO SET UP YOUR ACCOUNT:

1. **Read the Prescriber Agreement on Page 1 of this form.**
2. **Complete and sign this form.**
3. **Fax this page to the GenBioPro distributor at 1-877-239-8036.**
   Your account information will be kept strictly confidential.
4. **The distributor will call to finalize your account setup and take your initial order.**
5. **Subsequent orders may be phoned or faxed and are usually shipped within 24 hours**

BILLING INFORMATION

Bill to Name _____

Address _____

City _____ State _____ ZIP _____

Phone _____ Fax _____

Attention _____

SHIPPING INFORMATION ☐ *Check if same as above*

Ship to Name _____

Address _____

City _____ State _____ ZIP _____

Phone _____ Fax _____

Attention _____

ADDITIONAL SITE LOCATIONS *I will also be prescribing mifepristone at these additional locations:*

Name _____ Address _____

City _____ State _____ ZIP _____

Phone _____ Fax _____

Name _____ Address _____

City _____ State _____ ZIP _____

Phone _____ Fax _____

(Any additional sites may be listed on an attached sheet of paper)

REQUEST ADDITIONAL MATERIALS

☐ **Medication Guides** ☐ **State Abortion Guides** ☐ **Patient Brochures** ☐ **Patient Agreement Form**

ESTABLISHING YOUR ACCOUNT *(required only with first order)*

Each facility purchasing mifepristone tablets must be included on this form (*see additional site locations box above*) before the distributor can ship the product to the facility.
By signing below, you agree that you meet the qualifications and that you will follow the guidelines for use on page 1 of the Prescriber Agreement.

Print Name _____ Signature _____

Medical License # _____ Date _____

FAX THIS COMPLETED FORM TO THE AUTHORIZED DISTRIBUTOR. FAX: 1-877-239-8036

Please fax any questions to the above number or call 1-877-239-8036

Reference ID: 4798946

PATIENT AGREEMENT FORM — Mifepristone Tablets, 200mg

Healthcare Providers: *Counsel the patient on the risks of mifepristone. Both you and the patient must sign this form.*

Patient Agreement:

1. I have decided to take mifepristone and misoprostol to end my pregnancy and will follow my provider's advice about when to take each drug and what to do in an emergency.
2. I understand:
   a. I will take mifepristone on Day 1.
   b. My provider will either give me or prescribe for me the misoprostol tablets, which I will take 24 to 48 hours after I take mifepristone.
3. My healthcare provider has talked with me about the risks, including:
   - heavy bleeding
   - infection
   - ectopic pregnancy (a pregnancy outside the womb)
4. I will contact the clinic/office right away if in the days after treatment I have:
   - a fever of 100.4°F or higher that lasts for more than four hours
   - severe stomach area (abdominal) pain
   - heavy bleeding (soaking through two thick full-size sanitary pads per hour for two hours in a row)
   - stomach pain or discomfort, or I am "feeling sick," including weakness, nausea, vomiting, or diarrhea, more than 24 hours after taking misoprostol
5. My healthcare provider has told me that these symptoms could require emergency care. If I cannot reach the clinic or office right away, my healthcare provider has told me who to call and what to do.
6. I should follow up with my healthcare provider about 7 to 14 days after I take mifepristone to be sure that my pregnancy has ended and that I am well.
7. I know that, in some cases, the treatment will not work. This happens in about 2 to 7 out of 100 women who use this treatment. If my pregnancy continues after treatment with mifepristone and misoprostol, I will talk with my provider about a surgical procedure to end my pregnancy.
8. If I need a surgical procedure because the medicines did not end my pregnancy or to stop heavy bleeding, my healthcare provider has told me whether they will do the procedure or refer me to another healthcare provider who will.
9. I have the MEDICATION GUIDE for mifepristone. I will take it with me if I visit an emergency room or a healthcare provider who did not give me mifepristone so that they will understand that I am having a medical abortion with mifepristone.
10. My healthcare provider has answered all my questions.

Patient Signature: _____ Patient Name (print): _____ Date: _____

The patient signed the PATIENT AGREEMENT in my presence after I counseled the patient and answered all questions. I have given the patient the MEDICATION GUIDE for mifepristone.

Provider's Signature: _____ Name of Provider (print): _____ Date: _____

After the patient and the provider sign this PATIENT AGREEMENT, give 1 copy to the patient before the patient leaves the office and put 1 copy in the medical record.

EXHIBIT 18

Declaration of John Voltz, M.D.
(Nov. 17, 2025)

UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF LOUISIANA
LAFAYETTE DIVISION

THE STATE OF LOUISIANA, by and through its Attorney General, LIZ MURRILL, and ROSALIE MARKEZICH, *Plaintiffs*, v. U.S. FOOD AND DRUG ADMINISTRATION, *et al.*, *Defendants*.	Case No.: 6:25-cv-01491-DCJ-DJA Judge David C. Joseph Magistrate Judge David J. Ayo

DECLARATION OF DR. JOHN VOLTZ

I, John Voltz, M.D., a citizen of the United States of America and a resident of the State of Louisiana, declare under penalty of perjury under 28 U.S.C. § 1746 that the following is true and correct to the best of my knowledge.

1. I am over eighteen years old and make this declaration on personal knowledge. I am fully competent to make this declaration. If called to testify, I could and would testify competently to these facts.
2. I am a board-certified obstetrician and gynecologist. I graduated from Menard High School in Alexandria in 2006. I attended Louisiana State University, graduating in Civil Engineering in 2010. After graduation, I served as a full-time uniform Patrol Deputy in the East Baton Rouge Sheriff's Office.
3. I received my medical degree from Louisiana State University Health Sciences Center–Shreveport in 2018 and completed my residency at Saint Louis University in 2022. I returned home to Louisiana after residency, and I have practiced medicine in Louisiana since 2022.
4. I am a practicing obstetrician and gynecologist with admitting privileges at a large local general medical center in Lafayette, Louisiana.
5. I provide general OB/GYN care. I provide, among other things, labor and delivery care, prenatal care, preventative care, preconception counseling, and minimally invasive and vaginal gynecologic surgery, along with treatment for abnormal bleeding, infertility, pelvic pain, and menopause. I specialize in multiple births, high-risk pregnancies, and vaginal births after a cesarean section. I deliver approximately 300 babies per year.
6. I am on call as an emergency room consultant at the local general medical center in Lafayette.
7. Seventy percent of my patients are enrolled in Medicaid and pay for my services through Medicaid.

8. I have witnessed firsthand how the abortion drug mifepristone has hurt women in Louisiana.

9. I have treated a Louisiana patient who suffered complications after taking mifepristone in 2025.

10. The patient I treated was at five weeks gestation. I performed a dilation and curettage procedure due to an incomplete abortion and severe bleeding. This patient was on private insurance.

11. I presume this patient received the mifepristone by out-of-state mail because abortion drugs are illegal in Louisiana and no in-state provider could dispense the drugs in Louisiana.

12. Another patient—pregnant in her teenage years—came to my office with her mother. Her mother wanted her to take abortion drugs. At one of her ultrasound appointments, the unborn baby was no longer in the uterus. She had taken prescription mifepristone and misoprostol. The patient and her mother showed me the envelope the drugs were mailed in—with a New York sending address.

Executed this 17TH day of NOVEMBER 2025.

By _____
John Voltz, M.D.

EXHIBIT 19

Declaration of Kathleen Richard, LMSW
(Nov. 12, 2025)

UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF LOUISIANA
LAFAYETTE DIVISION

THE STATE OF LOUISIANA, by and through its Attorney General, LIZ MURRILL, and ROSALIE MARKEZICH, *Plaintiffs*, v. U.S. FOOD AND DRUG ADMINISTRATION, *et al.*, *Defendants*.	Case No.: 6:25-cv-01491-DCJ-DJA Judge David C. Joseph Magistrate Judge David J. Ayo

DECLARATION OF KATHLEEN RICHARD

I, Kathleen Richard, a citizen of the United States of America and a resident of the State of Louisiana, declare under penalty of perjury under 28 U.S.C. § 1746 that the following is true and correct to the best of my knowledge.

1. I am over eighteen years old and make this declaration on personal knowledge. I am fully competent to make this declaration. If called to testify, I could and would testify competently to these facts.
2. I am the executive director of Life Choices of North Central Louisiana, a pregnancy resource center in Ruston, Louisiana. I have witnessed how the abortion drug mifepristone has hurt women in Louisiana. Life Choices encounters women considering abortion and women who have had an abortion—including by mifepristone.
3. Since 2022, Life Choices has regularly encountered women who took abortion drugs, who have received abortion drugs in the mail, and many who sought treatment for complications after taking them.
4. These women are either Louisiana residents or college students living in Louisiana.
5. In 2024, Life Choices encountered approximately 75 abortion-minded or undecided pregnant women. At least 65% of these women had abortion drugs in their possession or knew where they could get the drugs. Most of the women received their drugs from out-of-state providers through the mail. They identified Plan C (https://www.plancpills.org/) as the most common source for the drugs.
6. Women call Life Choices once or twice per month asking for a follow-up ultrasound after taking mifepristone.
7. Life Choices has encountered several Louisiana women who suffered mifepristone complications. Many of them come to Life Choices to share their experiences and seek counseling. For example, mifepristone complications sent one woman to the

emergency room and hospital with excessive bleeding after she passed out. Her abortion-drug provider told her not to tell doctors that she had taken mifepristone. She is on Medicaid.

8. A second woman took mifepristone, suffered from excessive bleeding, and had two ultrasounds at her healthcare provider confirm that products of conception were in her uterus. She is on Medicaid.

9. A third woman who took mifepristone passed out at home but did not go to the emergency room.

Executed this 12 day of Nov, 2025.

By Kathleen B Richard, LMSW
Kathleen Richard, LMSW

EXHIBIT 20

Declaration of Kathleen Willis, M.D.
(Dec. 15, 2025)

UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF LOUISIANA
LAFAYETTE DIVISION

THE STATE OF LOUISIANA, by and through its Attorney General, LIZ MURRILL, and ROSALIE MARKEZICH, *Plaintiffs*, v. U.S. FOOD AND DRUG ADMINISTRATION, *et al.*, *Defendants.*	Case No.: 6:25-cv-01491-DCJ-DJA Judge David C. Joseph Magistrate Judge David J. Ayo

DECLARATION OF KATHLEEN WILLIS, M.D.

Pursuant to 28 U.S.C. § 1746, I, Kathleen Willis, M.D., affirm under penalty of perjury:

1. I am over the age of 18, have personal knowledge of the matters set forth herein, and am competent to make this Declaration.

2. I serve as the Associate Medical Director for Louisiana Medicaid in the Louisiana Department of Health ("LDH"). I completed medical school and residency at LSU School of Medicine in New Orleans and served as Chief Resident of the Internal Medicine Residency Program in my final year. I am board certified in Internal Medicine and a lifetime member of the AOA Honor Medical Society. I've been a physician for 26 years with over 20 years of leadership experience in healthcare delivery, quality improvement, and healthcare administration.

3. I help oversee the clinical and medical policy aspects of the State's Medicaid program, which runs through LDH's Bureau of Health Services Financing. My responsibilities include developing and evaluating medical policies to ensure they are evidence-based and cost-effective; reviewing coverage decisions, prior authorization criteria, and clinical guidelines used by Medicaid and its Managed Care Organizations ("MCOs"); providing clinical guidance to Medicaid leadership on

program operations, benefits, and emerging health issues; and collaborating with MCOs, providers, and LDH divisions to align care standards and address medical or utilization concerns.

4. Louisiana Medicaid provides healthcare coverage to eligible low-income individuals as part of a cooperative effort between the State of Louisiana and the federal government, who jointly fund the program. Louisiana Medicaid covers a broad set of services, including hospital and physician care, prescriptions, labs and imaging, long-term care, behavioral health, and more.

5. Louisiana Medicaid also covers emergency services at *any* hospital emergency room ("ER"), whether or not the hospital is in the patient's Medicaid MCO network. We follow federal Medicaid laws that require LDH to cover emergency care. When an individual covered by Medicaid goes to an ER, the hospital will run the patient's Medicaid ID through the State's electronic eligibility system, but emergency care cannot be delayed while the provider is verifying coverage. As part of Medicaid coverage, and under EMTALA, the ER must, at a minimum, perform a medical screening exam, stabilize the patient, and provide any necessary treatment. Louisiana Medicaid and all MCOs prohibit prior authorization for emergency services: The hospital treats the patient first, bills later. After treatment, the hospital submits the claim to the appropriate MCO (or Medicaid fee-for-service, if applicable), and payment goes directly from the plan/Medicaid to the provider. The patient typically has no copay, unless a small copay applies under their specific plan.

6. In 2021, the Department of Health and Human Services estimated that the average cost of a Medicaid-covered ER visit was $600—a number we can safely assume has increased in the past 4 years due to inflation and rising healthcare costs generally. In June 2023, approximately 2 million people were enrolled in Louisiana Medicaid. As of June 2024, the number dropped slightly to just over 1.6 million, as States across the country have seen the overall number of Medicaid enrollees decline from the extreme uptick during the COVID-19 pandemic. However, the decline has stopped: As of June 2025, the number of Louisiana Medicaid enrollees remained around 1.6 million, a number that

surpasses pre-pandemic data. As of January 1, 2023 (the most recent data of its kind available), 534,294 women from ages 15 to 44 were enrolled and 538,139 women from ages 15 to 44 were recipients.[1]

7. The FY 2025 Medicaid budget for Louisiana is about $21.2 billion, with the State covering about 25% of these costs and the federal government covering the remainder. Louisiana Medicaid accounts for roughly 38% of the State's total budget. In FY 2023 (the most recent data available), Louisiana Medicaid cost the federal and State government a combined $16.6 billion.[2]

8. I am familiar with the U.S. Food & Drug Administration's 2023 Risk Evaluation and Mitigation Strategy ("REMS") for mifepristone. I understand that women who ingest mifepristone may end up in the emergency room to treat and remedy side effects of the drug.

9. When such women are covered by Medicaid, the resulting services are paid for by the State (and the federal government) under Medicaid. The patients often do not absorb the costs.

10. These emergent situations and associated Medicaid costs will continue to be a problem in Louisiana because of mifepristone that is being mailed into Louisiana.

11. In 2025, a Louisiana woman on Medicaid—Jane Doe #1—received emergency medical care at a Louisiana regional medical center after ingesting FDA-approved mifepristone that she received in the mail from AidAccess.org. She delivered a dead fetus in the emergency room. As a result of the services rendered by the Louisiana medical center to Jane Doe #1, the total cost billed to Medicaid was over $17,500 and the total amount paid was over $4,500.

12. In 2025, another Louisiana woman covered by Medicaid—Jane Doe #2—ingested FDA-approved abortion drugs in Louisiana that she received in the mail from AidAccess.org. Two

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[1] The information in this paragraph comes from *Louisiana Medicaid 2023 Annual Report*, Louisiana Department of Health, p.26 (https://ldh.la.gov/assets/medicaid/AnnualReports/MedicaidAnnualReport2023.pdf) (last visited Dec. 9, 2025).

[2] *See, e.g.*, *Medicaid Enrollment Declines*, PAR Louisiana (July 28, 2025) (https://parlouisiana.org/wp-content/uploads/2025/07/Medicaid-Enrollment-Declines2.pdf).

days later, she arrived at a Louisiana emergency room with severe abdominal pain and delivered her baby alive. The baby needed emergency treatment and a prolonged hospitalization. As a result of this emergency room visit, the total cost billed to Medicaid for the mother's treatment was over $24,000 and the total amount paid was over $7,500. The total cost billed for the baby's treatment was over $299,500 and the total amount paid was over $80,000.

13. These women are just two examples of many women believed to have suffered adverse health consequences requiring emergency medical care at Louisiana's hospitals, paid for by Louisiana Medicaid, as a result of ingesting FDA-approved supplies of mifepristone.

14. These figures almost certainly understate the true harm, owing to incomplete hospital reporting, miscoding or false reporting of complications as "miscarriages," and concealed shipments. Louisiana Medicaid covers miscarriage treatment and reimburses for miscarriage treatment and care.[3]

15. Because the amount of mifepristone illegally prescribed and shipped to Louisiana women is unlimited and increasing, there is no doubt that the number of adverse health consequences requiring emergency medical care in Louisiana hospitals will only increase as well, as will the associated costs borne by Louisiana Medicaid.

Executed in Baton Rouge, Louisiana, this 15th day of December, 2025.

Kathleen Willis, M.D.

Kathleen Willis, M.D.

[3] *See LaMOMS*, Louisiana Department of Health (https://ldh.la.gov/medicaid/lamoms) (last visited Dec. 9, 2025).

EXHIBIT 21

Declaration of Christina Francis, M.D.
(Dec. 12, 2025)

UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF LOUISIANA
LAFAYETTE DIVISION

THE STATE OF LOUISIANA, by and through its Attorney General, LIZ MURRILL, and ROSALIE MARKEZICH, *Plaintiffs*, v. U.S. FOOD AND DRUG ADMINISTRATION, *et al.*, *Defendants*.	Case No.: 6:25-cv-01491-DCJ-DJA Judge David C. Joseph Magistrate Judge David J. Ayo

DECLARATION OF CHRISTINA FRANCIS, M.D.

I, Christina Francis, M.D., a citizen of the United States of America and a resident of Indiana, declare as follows:

1. I am over eighteen years old and make this declaration on personal knowledge. I am fully competent to make this declaration. The opinions expressed in this report are my own and do not represent the views of any organization with which I am associated.

I. Background

2. I am a board-certified Obstetrician and Gynecologist (OB/GYN) in good standing and licensed to practice in Indiana and Virginia. I have been practicing for 17 years, and I have been board-certified for thirteen years. I have worked for the last nine years as an OB/GYN Hospitalist in Fort Wayne, Indiana, which is where I work now.

3. I graduated from medical school at Indiana University in 2005 and completed my obstetrics and gynecology residency at St. Vincent Hospital in Indianapolis in 2009.

4. As an OB/GYN Hospitalist, my practice is primarily hospital-based. I manage both high- and low-risk pregnancies and deliveries, obstetric critical care, gynecological emergencies presenting to our Emergency Department, and inpatient obstetric and gynecologic consultations.

5. I am a member of the Board of Directors and the CEO of the American Association of Pro-Life Obstetricians and Gynecologists (AAPLOG), a national professional organization of approximately 8,000 pro-life medical practitioners.

6. AAPLOG is the largest nonsectarian organization of pro-life medical practitioners in the world and is headquartered in Indiana. AAPLOG includes more than 70 members in Louisiana. AAPLOG members oppose elective induced abortion and are committed to the care and well-being of their patients, including both pregnant women and their preborn children. AAPLOG members are concerned about the adverse impacts of chemical abortions—including chemical abortions using mifepristone and misoprostol—on their practice of medicine. I am familiar with AAPLOG, its policy positions, its members, and its members' interests and concerns.

7. I am familiar with chemical abortion drugs, their use, and the complications that accompany chemical abortions. I am also familiar with FDA's regulation of chemical abortion drugs, including mifepristone and misoprostol.

II. Pregnancy and the development of the human person

8. The childbearing years for women typically range from ages 14 to their mid-40s.

9. A new human life begins at the moment of fertilization. It is a scientific fact that a distinct, living, and whole human being comes into existence at the moment of fertilization. At fertilization, a sperm from a male meets an ovum from a female, and their genetic material combines to form a new, unique human being. From the moment of sperm-egg fusion and onward, the embryo exhibits all of the characteristics of a new living organism. Put another way, at fertilization, a new single-celled entity is formed that is distinct from the sperm or the egg, and her development and metabolic activity are radically unlike that of a sperm or egg cell.

10. The sperm and ovum unite to form a single-celled human being called a zygote. The zygote begins dividing immediately and continues developing as an embryo through the first eight weeks of gestation. After the eighth week, the developing human is termed a fetus, a designation that

continues for the remainder of the pregnancy. A pregnancy usually lasts about 280 days, after which a woman gives birth, and the new baby continues growing and developing outside the uterus.

11. At every stage of development—zygote, embryo, and fetus—there is a human being with its own unique DNA. Even a zygote has self-directed growth and development. And, although nutrients and protection are required, the new embryo or fetus is self-integrated and oriented toward her own survival. The organism goes on to have one continuous biological existence throughout her developmental stages, from zygote through embryo, fetus, newborn, toddler, child, teen, adult, and aged adult, until death. Each of us begins our existence as a human embryo. Each of us was carried in our mother's uterus through the early stages of development.

12. As a physician, I recognize that each human life has equal dignity and value from the moment of fertilization throughout her entire lifespan. As a physician, my oath compels me to provide care towards health and healing for all of my patients, regardless of their age or level of development. The age of a human being does not determine her humanity or whether she has value.

13. Intentionally ending the life of any human being goes against the basic tenets of medical ethics that have steered the practice of medicine for millennia. Since its introduction, the Hippocratic Oath has distinguished the practice of medicine from any act intended to end human life. Induced abortion violates the basic tenets of medical ethics because it intentionally takes a human life.

14. As a physician, I know that when I care for pregnant women, I care for two distinct patients. My duty is to protect and preserve both mother and child. Our medical system and our society have a duty to support women throughout and after their pregnancies. All pregnant women and their preborn children deserve excellent healthcare.

15. I understand that many states, like Louisiana, recognize the scientific reality that life begins at the moment of fertilization. They thus protect human life from the moment of fertilization. Through their laws and their healthcare programs, like Medicaid, they ensure that all pregnant women and preborn children are valued and protected.

III. The nature and known risks of mifepristone and misoprostol

16. The FDA-approved chemical abortion regimen involves two drugs: mifepristone and misoprostol.

17. Mifepristone is a synthetic steroid that blocks the release of progesterone, a hormone that is critical for the development of a preborn child. Progesterone is essential to achieve and maintain a healthy pregnancy. It prepares the uterine lining to allow implantation and stimulates glands in the lining to secrete nutrients for the early embryo. During the first 8 weeks of pregnancy, progesterone is produced by the corpus luteum (a cyst on the ovary during pregnancy), but between 8 and 12 weeks the placenta takes over this role and maintains the pregnancy thereafter.[1] Mifepristone binds to progesterone receptors,[2] thereby blocking the action of progesterone. This causes the uterine lining to deteriorate, cutting off oxygen and nutrients to the preborn child and causing her to die.

18. Misoprostol, a prostaglandin analogue, is then taken 24 to 48 hours after mifepristone to induce uterine contractions intended to expel the embryo or fetus and other pregnancy tissue. Bleeding can last from several hours to over 30 days. Chemical abortions of this type are approved by FDA for use through the 10th week of gestation.

19. By removing the in-person dispensing requirement from its chemical abortion-drug protocol, FDA authorized abortion drugs to be prescribed to patients remotely and sent to them via the mail—even without any in-person contact or real-time interaction (even virtual) with a medical professional. FDA also authorized dispensing from certified pharmacies that can ship medications in the mail. This transformed mifepristone from a drug that required visiting a specialized medical site like a clinic, medical office, or hospital, to one that could be obtained from online sites, some of which have minimal or asynchronous medical oversight.

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[1] Arri Coomarasamy et al., *PROMISE: First-Trimester Progesterone Therapy in Women with a History of Unexplained Recurrent Miscarriages—A Randomized, Double-Blind, Placebo-Controlled, International Multicenter Trial and Economic Evaluation*, 20(41) Health Technol. Assess. (May 2016).

[2] Oskari Heikinheimo et al., *The Pharmacokinetics of Mifepristone in Humans Reveal Insights into Differential Mechanisms of Antiprogestin Action*, 68(6) Contraception 421, 421 (Mar. 17, 2003). *Contraception* is a journal affiliated with the Guttmacher Institute and Planned Parenthood, or Obstetrics organizations well known for their abortion advocacy.

IV. The importance of in-person doctor care

20. It is my professional opinion that the proper standard of care is an in-person doctor's visit before receiving mifepristone and misoprostol.

21. It is also my professional opinion that in-person dispensing of abortion drugs enhances the safety and well-being of women taking these drugs and leads to better-informed medical decisions. Requiring an in-person doctor visit ensures that each woman is able to give truly informed consent, can be screened for coercion and potential contraindications to the drugs, and can have her preborn child's gestational age, pregnancy location, and other risks accurately assessed.

22. A pre-abortion ultrasound (or appropriate physical examination) is the best way to rule out ectopic pregnancy and to confirm the gestational age of the preborn child.

23. Eliminating the in-person dispensing requirement increases the risk that an ectopic pregnancy will go undetected. This can cause women serious and life-threatening complications, such as rupture of the fallopian tube and secondary hemorrhage. Ectopic pregnancies are not rare, occurring in 1 in 50 pregnancies. Some emergency room studies have reported a higher incidence of 8–9% of pregnancies.[3] Approximately 50% of women with an ectopic pregnancy will have no risk factors for it, so screening for this condition based on risk factors is not adequate. The symptoms women experience when they have a rupturing ectopic pregnancy (vaginal bleeding and abdominal pain) are the same as those experienced by women undergoing a chemical abortion. This similarity can cause a delay in seeking care if women have taken mifepristone and misoprostol as they will assume these are normal symptoms of a chemical abortion. This delay in care can increase her risk of morbidity and mortality.

24. An in-person test is necessary in early pregnancy to determine a mother's Rh factor. If the mother's Rh factor is negative, she can form antibodies against an Rh-positive baby's blood cells, which can be prevented by administering Rho(D) immunoglobulin (Rhogam) preventatively, after delivery, or after any event that could mix maternal and fetal blood—such as miscarriage, abortion,

[3] Carlos A. Link, M.D. et al., *Diagnosing Ectopic Pregnancy Using Bayes Theorem: A Retrospective Cohort Study*, 119(1) Fertil. Steril. 78, 82 (2023).

ectopic pregnancy, prenatal testing, or trauma. About 15% of North Americans have an Rh-negative blood type.[4] If these women are not appropriately administered Rhogam, they may experience isoimmunization, which threatens future pregnancies. If an Rh-negative woman is left untreated and she becomes isoimmunized, her future baby will have a 14% chance of being stillborn and a 50% chance of suffering neonatal death or a brain injury.[5]

25. In-person care is also important as a way to obtain informed consent and to ensure that there is no coercion. The process of obtaining informed consent involves assessing the individual patient in front of you—her exact clinical situation (gestational age and location of pregnancy, number of fetuses, placental location, etc.) and her individual medical history—to inform her of her specific risks, benefits, and alternatives. This can only truly be done with an in-person assessment to confirm these details.

26. Medical professionals are the first line of defense for women who are being coerced, abused, or trafficked. We regularly screen women for abuse or coercion to ensure decisions are informed and voluntary. If we detect abuse or coercion, we can provide support, secure the patient's safety, or connect the patient with appropriate resources or authorities. Mail-order abortion increases the risk of coerced abortion. When abortion drugs are dispensed in-person, a prescriber can confirm that the person seeking the abortion drugs is actually a pregnant woman. And the prescriber has an opportunity to see whether the pregnant woman is freely choosing to have an abortion or whether she is facing outside pressure or threat.

27. Not so with mail-order abortion. The prescriber may never see the person ordering the abortion drugs and thus cannot determine whether it is a pregnant woman or some other bad actor ordering the drugs. And even if it is a pregnant woman ordering the drugs, there is no way to fully assess whether she is freely choosing to have an abortion and is sure about her decision or is

[4] *American College of Obstetricians and Gynecologists Practice Bulletin No. 181: Prevention of Rh D Alloimmunization*, 130(2) Obstet. Gynecol. e57, e58 (Aug. 2017) (ECF 1-17).

[5] *Id.*

being coerced by a third party. This is music to the ears of abusive boyfriends, rapists, and human traffickers.

28. Mail-order abortion can enable human traffickers and sexual abusers force their victims into getting abortions while preventing the authorities from identifying these victims.[6] In fact, the State of Texas has recognized that "[d]ue to the potentially high number of trafficking victims who undergo abortion procedures, abortion facility employees are uniquely situated to identify and assist victims of sex trafficking."[7] Physicians are trained in ways to screen for trafficking and abuse; part of this involves observing body language and how a patient interacts with her partner (when the partner is with her). In person assessment also gives us the opportunity to ensure we talk to her alone if we suspect abuse or coercion—something that cannot be reliably done through a virtual interaction and certainly not when women have zero interaction with a medical professional.

V. Complications from mifepristone and misoprostol

29. Women who take chemical abortion drugs can experience significant complications.

30. There are many intense side effects for women who take chemical abortion drugs, including labor-like abdominal pain, heavy bleeding, nausea, vomiting, and fevers.[8]

31. FDA's own label states that roughly 1 in 25 women who take mifepristone as directed will end up in the emergency room,[9] with up to 7% requiring a "surgical procedure because the pregnancy did not completely pass from the uterus or to stop bleeding."[10] These statistics apply when

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[6] Laura J. Lederer & Christopher A. Wetzel, *The Health Consequences of Sex Trafficking and Their Implications for Identifying Victims in Healthcare Facilities*, 23 Annals Health L. 61 (2014); *Id.* at 73, 77–78 (noting that survivors in study "reported that they often did not freely choose the abortions they had while being trafficked," these "[s]urvivors [ ] had significant contact with clinical treatment facilities, most commonly Planned Parenthood clinics," and that "these points of contact with healthcare represent rare opportunities for victim identification and intervention.").

[7] House Committee Report, H.B. 3446, 84th Leg., C.S. (Tex. 2015), https://perma.cc/KF4N-P3W2 (a subsequent, similar version was codified at Tex. Health & Safety Code § 245.025).

[8] FDA-Approved Label for Mifepristone (Mifeprex) at 7 (Jan. 2023) (ECF 1-9) ("Mifeprex 2023 Label") ("Uterine bleeding and cramping are expected consequences of the action of MIFEPREX and misoprostol as used in the treatment procedure. Most patients can expect bleeding more heavily than they do during a heavy menstrual period.").

[9] *Id.* at 8, Table 2.

[10] *Id.* at 17.

a woman has had an in-person evaluation before taking mifepristone—something that is not occurring in many cases today. The label also includes a black box warning that "[s]erious and sometimes fatal infections and bleeding" may occur.[11]

32. FDA also agrees that the risks of complications and emergency surgeries increase with gestational age.[12] FDA's label notes that the percentage of surgical interventions for ongoing pregnancies is ten times higher for women at 64–70 days' gestation than for women at less than or equal to 49 days' gestation.[13] And one study on which FDA previously relied[14] found that—as compared to those who take mifepristone before nine weeks' gestation—almost four times as many women who take it after nine weeks' gestation experience an incomplete abortion, nearly twice as many suffer an infection, and over six times as many require surgical evacuation.[15] In fact, the study suggests that upwards of 10% of women who take these drugs will need follow-up medical treatment for an incomplete or failed chemical abortion.[16] An average of 39% of women require surgery if taken in the second trimester.[17]

33. One study showed that nearly 14% of women who took this mifepristone-misoprostol combination from 10–11 weeks required surgical intervention.[18] This is consistent with larger studies, which show that the further along in pregnancy a woman is when she takes these drugs, the higher

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[11] *Id.* at 1.

[12] 2021 FDA Letter to AAPLOG and Am. Coll. of Pediatricians denying in part and granting in part 2016 Citizen Petition, Docket No. FDA-2019-P-1534 at 9 (Dec. 16, 2021) (ECF 1-10) ("We agree that the failure rate of medical abortion regimens, including the currently approved regimen, generally increases with increasing gestational age."); Mifeprex 2023 Label, *supra* note 8, at 13, Table 4.

[13] Mifeprex 2023 Label, *supra* note 8, at 13, Table 4.

[14] Center for Drug Evaluation and Research, Application Number: 020687Orig1s020 Summary Review at 19 (Mar. 29, 2016) ("FDA 2016 Summary Review") (ECF 1-11).

[15] Maarit Niinimäki et al., *Comparison of Rates of Adverse Events in Adolescent and Adult Women Undergoing Medical Abortion: Population Register Based Study*, 342 BMJ 5 (April 20, 2011) (ECF 1-12).

[16] *Id.* at 4.

[17] Maarit J. Mentula et al., *Immediate Adverse Events After Second Trimester Medical Termination of Pregnancy: Results of a Nationwide Registry Study*, 26(4) Hum. Reprod. 927, 931 (Apr. 2011).

[18] Ilana G. Dzuba et al., *A Non-Inferiority Study of Outpatient Mifepristone-Misoprostol Medical Abortion at 64-70 Days and 71-77 Days of Gestation*, 101(5) Contraception 302, 305, Table 2 (2020).

her risk of complications.[19] Mifepristone is in fact known to increase risk of hemorrhage due to its effect on the spiral arteries of the pregnant uterus.[20]

34. A recent review of large-scale insurance claims data concluded that the "real-world rate of serious adverse events following mifepristone abortions is at least 22 times as high as the summary figure of 'less than 0.5 percent' in clinical trials reported on the drug label."[21] Nearly 11% of women "experience sepsis, infection, hemorrhaging, or another serious adverse event within 45 days following a mifepristone abortion."[22] This review provides preliminary information. It warrants serious concern and suggests the need for further investigation. It also suggests that FDA was right when it predicted that women in the real world would experience significant complications from abortion drugs.

35. Another recent study also suggests that the complication rate may in fact be nearly 15%. In that study, "Out of 217 known outcomes of the 711 total medication abortions provided at 78-84 days estimated gestational duration, preliminary raw data includes 27 ongoing pregnancies, 22 aspirations performed for ongoing pregnancies, 10 aspirations performed for other reasons, and 21 visits to an emergency department or hospital."[23] Medical professionals and regulatory agencies like FDA should follow important safety signals like this. This study suggests that mifepristone's complication rate in the real world is much higher than what is indicated on the label.

36. Of the women who end up in the emergency room after taking abortion drugs, many suffer severe injuries. A study testing the severity of emergency department visits for Medicaid-eligible women following various pregnancy outcomes found that "an [emergency department (ED)] visit following a [mifepristone] abortion was significantly more likely to have a severe or critical acuity

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[19] Mentula, *supra* note 17, at 927–32.

[20] Ralph Miech, *Pathopharmacology of Excessive Hemorrhage in Mifepristone Abortions*, 41(12) Ann. Pharmacother. 2000, 2004 (Dec. 2007).

[21] Jamie Bryan Hall & Ryan T. Anderson, *The Abortion Pill Harms Women: Insurance Data Reveals One in Ten Patients Experiences a Serious Adverse Event* 1, Ethics & Pub. Pol'y Ctr. (Apr. 28, 2025) (ECF 1-13).

[22] *Id.*

[23] Robin Wallace et al., *P040 - Expanding Access to Abortion with Mifepristone and Misoprostol Through 84 Days Estimated Gestational Duration*, 151 Contraception 111117 (Nov. 2025).

rating than a visit following surgical abortion, live birth, or an ED visit at any time by a woman who was never pregnant."[24] The study also found that ED visits coded severe or critical for women who underwent a chemical abortion increased by 4,041.1% between 2004 and 2015, compared to a 450.6% increase for surgical abortion subjects and 20.9% for live birth subjects.[25]

37. All of this assumes accurate reporting in the ED, notwithstanding that some abortion activists encourage women to tell emergency room staff that they are having a miscarriage if they suffer abortion-drug complications requiring urgent care. I know that many women suffering complications from chemical abortions tell their doctors that they are experiencing miscarriages.[26] This phenomenon—regardless of why it occurs—means that doctors cannot be certain of what their patients have taken or are experiencing. This kind of inaccurate information also means that the true number of incidences of complications from chemical abortions are significantly underreported or not fully known.

38. FDA used to require that women seeking care for an abortion drug complication bring the Medication Guide with them to the ED. Removing this requirement places women at heightened risk of cascading complications and impedes physicians' ability to treat them. The Medication Guide protection ensures that physicians have critical information that helps them recognize and manage adverse effects, reduce delays in treatment, and make safer and more informed decisions for patient care. Without the Medication Guide, it is harder for physicians to treat complications because these patients also do not present with their medical records from a pre-abortion visit or document what they were given. This is, in fact, crucial because of the unique risk of clostridial sepsis from mifepristone that is not present in women having first-trimester miscarriages (and is what precipitated the black box warning for infection on the mifepristone label). This is a very difficult infection to

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[24] James Studnicki et al., *Comparative Acuity of Emergency Department Visits Following Pregnancy Outcomes Among Medicaid Eligible Women, 2004–2015*, 5(2) Int'l J. Epidemiol. & Pub. Health Rsch. 1, 1 Aug. 20, 2024 (ECF. No. 1-14).

[25] *Id.* at 2.

[26] *Will a Doctor Be Able to Tell if You've Taken Abortion Pills?*, Women Help Women Blog (Sep. 23, 2019), (ECF 1-15); *How Do You Know if You Have Complications and What Should You Do?*, Aid Access (ECF 1-16).

diagnose, requiring physicians to have a high index of suspicion—something they can only do if they know a woman has taken mifepristone.[27]

39. Claims that mifepristone is "safer than Tylenol" have no basis in reality. *First*, acetaminophen (Tylenol) toxicity is nearly exclusively caused by not following the directions—for example, not taking the FDA-approved dose.[28] Not so for mifepristone. *Second*, mifepristone still has a black box warning attached to it due to the risk of hemorrhage and infection (specifically sepsis from clostridium sordellii which causes an insidious sepsis picture and has caused the deaths of several women who took mifepristone).[29] Tylenol has no such warning. *Third*, FDA's own data shows that approximately 1 in 25 women who take mifepristone for an induced abortion as directed by the label will seek care for complications in the ED—and this was when women were still being evaluated in person prior to receiving this.[30]

40. In addition, beyond the known physical risks, women have described their abortion-drug experiences as harming their mental health and leaving them feeling unprepared, silenced, regretful, or trapped.[31]

41. Remotely-dispensed abortion drugs present even greater risks to women because, without an in-person examination, prescribers cannot confirm and therefore are more likely to misdate the gestational age of a baby or fail to detect an ectopic pregnancy—with potentially fatal consequences. The American College of Obstetricians and Gynecologists (ACOG) states that "A pregnancy without an ultrasound examination ... before 22 0/7 weeks of gestational age should be

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[27] AAPLOG, Dangers of Clostridial Infection after Mifepristone Ingestion for Induced Abortion: A Public Health Concern (Aug. 2025), perma.cc/YK2A-AQZQ.

[28] Suneil Agrawal et al., *Acetaminophen Toxicity*, StatPearls Publishing (April 10, 2025), perma.cc/8XL9-TJVQ.

[29] CDC, Clostridium Sordellii *Toxic Shock Syndrome After Medical Abortion with Mifepristone and Intravaginal Misoprostol—United States and Canada, 2001–2005*, Morbidity & Mortality Weekly Rep. (July 29, 2005), perma.cc/5MVR-HN94.

[30] Mifeprex 2023 Label, *supra* note 8, at 8, Table 2.

[31] Katherine A. Rafferty & Tessa Longbons, #AbortionChangesYou*: A Case Study to Understand the Communicative Tensions in Women's Medication Abortion Narratives*, 36 Health Commc'n 1485 (2021) (ECF 1-18).

considered suboptimally dated."[32] This is because 40–50% of women will be wrong about their gestational age based on their last menstrual period alone.[33] As the number of mifepristone-induced mail-order abortions continues to increase, so will the overall number of women seeking emergency care in hospitals.

VI. My experience with abortion-drug complications

42. Since FDA's 2000 approval of Mifeprex (the chemical abortion drug regimen consisting of mifepristone and misoprostol), medical professionals have needed to treat women and girls who have suffered from chemical abortion and experienced complications.

43. Mifepristone and misoprostol are high-risk drugs that should not be administered in combination for induced abortion without medical supervision. FDA's actions to eliminate the necessary supervision of these drugs harm women and remove fully informed consent.

44. The most common physical complications resulting from chemical abortions are hemorrhage, retained tissue (incomplete abortion), and infection. These often necessitate treatments such as admission to the hospital, intravenous antibiotics, dilation and curettage (D&C) to remove retained tissue or control bleeding, or blood transfusion. Less commonly, more significant surgery can be necessary, such as hysterectomy in the case of clostridial infection.

45. I have seen first-hand the complications that can result from the use of these high-risk drugs. Although Fort Wayne does not have an abortion facility, and the majority of abortions are illegal in Indiana, I personally have seen several women present with complications after seeking chemical abortions with mifepristone and misoprostol, and my group has seen many more.

46. As an example, an AAPLOG-member partner and I cared for a patient who suffered complications from a chemical abortion. I had taken care of her when she was hospitalized for hyperemesis gravidarum at 9 weeks 5 days gestation. She was discharged home in good condition after

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[32] American College of Obstetricians and Gynecologists Committee on Obstetric Practice, *Committee Opinion No. 700: Methods for Estimating the Due Date*, 129(5) Obstet. Gynecol. e150 (May 2017), https://doi.org/10.1097/AOG.0000000000002046.

[33] *Id.*

significant improvement with medications. During that hospital stay, she had an ultrasound, which showed a healthy pregnancy with no apparent complications and a strong fetal heart rate. During her hospitalization, she expressed to me that she was considering abortion because of experiencing hyperemesis, but was unsure. About a week after her discharge, the patient presented back at our emergency room with heavy vaginal bleeding and unstable vital signs as a result of taking chemical abortion drugs. One of my partners was able to detect a fetal heartbeat. However, due to the amount of bleeding that she was experiencing and evidence of hemodynamic instability, my partner had no choice but to perform an emergency D&C. The patient needed to be hospitalized overnight for close observation after the D&C. Not only did my partner need to provide several hours of critical care for this patient, but she also needed to call in a backup physician to care for another critically ill patient. And because the preborn baby still had a heartbeat when the patient presented, my partner felt as though she was forced to participate in something that she did not want to be a part of–completing the abortion.

47. I also cared for a woman who had undergone a chemical abortion approximately one month prior. She had had no follow up with the abortion provider. She presented to our hospital two days before I saw her with complaints of abdominal pain and ongoing vaginal bleeding. One of my partners evaluated her and determined that she had retained tissue from her chemical abortion. She was taken to the operating room for a D&C procedure to complete her abortion and then discharged home after her surgery. She returned to our hospital two days later with persistent abdominal pain as well as worsening nausea and vomiting. Repeat ultrasound did not show any retained tissue, but she had evidence of endometritis on exam as well as a significantly elevated white blood cell count, consistent with a bacterial infection. She required treatment with multiple IV antibiotics and was hospitalized for multiple days before being able to be discharged home.

48. The experience of one other patient who came to me through the Abortion Pill Reversal Network highlights the dangers of women not being seen in person before these drugs are dispensed. She was pregnant with an unplanned, but not unwanted, child. Her boyfriend, however,

wanted her to get an abortion and she felt threatened by him if she did not go through with it. She ordered the drugs online, thinking that while she waited for them to arrive she could convince him to support her in continuing her pregnancy. However, when the drugs arrived in the mail, her boyfriend continued to insist that she have an abortion. Fearing that he would hurt her if she did not go through with it, she took the mifepristone. Shortly after taking it, she went into the bathroom and forced herself to vomit, hoping that would rid her of the drug meant to end the life of her child. She called the Abortion Pill Reversal Network after not being confident that that had occurred and that is how I spoke with her. She told me how much she wanted her baby and desired to try to halt the effects of mifepristone—which she had only taken because of her boyfriend forcing her to. I administered progesterone treatment, and the baby survived.

49. As an OB/GYN who has seen many women with unplanned pregnancies early in their pregnancies, I have had patients tell me that they wanted information about abortion. My standard first question in this situation, as it would be in any situation in which a patient is requesting a certain intervention, is "Can you tell my why you feel that is the best option for you?" Not only does this give me insight into where she is at and what she is experiencing, but it also helps screen for pressure or coercion. It is not uncommon for a patient's response to be that her parents, boyfriend, or someone else is pressuring or forcing her to consider abortion. This kind of screening and personal interaction, with ensured privacy, is not happening with online dispensing.

VII. Reporting abortion-drug complications

50. I am aware of FDA's actions that require prescribers to report only deaths and no other complications associated with chemical abortion. However, non-fatal complications still have a significant impact on my patients as well as our healthcare system. FDA should require reporting of these complications again. This is the only way for physicians to accurately assess public health impact as well as have accurate information to inform patient choices. The current reporting system is cumbersome for busy physicians to report these complications: it takes a significant amount of time and does not collect all of the pertinent information.

51. To report complications to the abortion-drug manufacturer, a form must be printed, filled out by hand, and then either mailed or scanned and emailed back. Much of the information required by this form is impossible to obtain by the physician seeing the patient if they were not the one who dispensed the chemical abortion drugs (such as lot number and dosage), forcing me to leave several fields blank. I have never received confirmation from the manufacturer that the complications I reported were recorded or reported to FDA.

52. In addition to reporting to the manufacturer, the process of reporting to the FDA Adverse Event Reporting System (FAERS) is also cumbersome. The actual form to be filled out is hard to find online, requiring several steps to access it. It once took me two hours to get the website to accept submission of the form, taking me away from the care of my other patients. The minimum amount of time I have spent reporting a mifepristone complication to FAERS is thirty minutes—valuable time that should be spent in patient care.

53. Due to inadequate adverse event reporting, the true rates of risks associated with chemical abortion drugs remain unknown and undercounted. This lack of information impedes informed consent for women, and it should have raised serious questions for FDA before it approved sending mifepristone through the mail or other remote means.

I declare under 28 U.S.C. § 1746 and under penalty of perjury that this declaration is true and correct based on my personal knowledge.

Executed December 12, 2025.

Christina Francis, M.D.

EXHIBIT 22

Declaration of Michael J. New, Ph.D
(Dec. 15, 2025)

UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF LOUISIANA
LAFAYETTE DIVISION

THE STATE OF LOUISIANA, by and through its Attorney General, LIZ MURRILL, and ROSALIE MARKEZICH, *Plaintiffs*, v. U.S. FOOD AND DRUG ADMINISTRATION, *et al.*, *Defendants*.	Case No.: 6:25-cv-01491-DCJ-DJA Judge David C. Joseph Magistrate Judge David J. Ayo

DECLARATION OF MICHAEL J. NEW, PH.D.

I, Michael J. New, Ph.D., a citizen of the United States of America, declare as follows:

STATEMENT OF OPINIONS AND THE BASES FOR THEM

I have been hired as an expert witness in the case *Louisiana et al. v FDA et al.* Case No 6:25-cv-01494 W.D Louisiana. This case involves the 2023 Risk Evaluation and Mitigation Strategy for the Abortion Drug Mifepristone.

In this declaration, I show that the state of Louisiana has a compelling interest in eliminating mail-order abortion drugs so it can enforce its pro-life laws and prevent economic harm. This is for several reasons. *First*, mail-order abortions increase the incidence of abortion in Louisiana. *Second*, women on Medicaid are more likely to obtain abortions. *Third*, Louisiana's state Medicaid program will incur costs treating Louisiana women who obtain mail-order abortions. *Fourth*, in the absence of mail-order abortion drugs, Louisiana women who are carrying pregnancies to term can obtain pregnancy assistance from a range of public and private sources. *Fifth*, an increase in the incidence of abortion in Louisiana is detrimental to Louisiana's economic and fiscal health.

1) Mail-order Abortions Increase the Incidence of Abortion.

The Supreme Court's June 2022 *Dobbs* decision allowed states to place legal limits on abortion. Many states have done this in the aftermath of the decision. Louisiana has been enforcing a law that largely bans all elective abortions since July 29, 2022 (Hilburn 2022).

The best data on the impact of recent pro-life laws comes from Texas. Texas was able to enforce a Heartbeat Act, on September 1, 2021. Data from the Texas Department of State Health Services found that immediately after the Heartbeat Act took effect the number of abortions performed on Texas residents fell by nearly 2,500 a month (Texas Health and Human Services Commission 2025).[1]

Meanwhile, the study by White et al. (2025) found that out-of-state abortions among Texas women increased by about 1,160 per month. Three separate studies of the Texas birthrate indicate that in the months after the Heartbeat Act took effect, the number of children born in Texas increased by approximately 1,000 per month (New 2022; Bell et al, 2023; The University of Houston Institute for Research on Women, Gender, and Sexuality 2024).

Since Texas' in-state abortion decline was not completely offset by combined increases in births and increases in out-of-state abortions, it seems very likely that hundreds of Texas women were obtaining mail-order abortions.

A research letter that appeared in the *Journal of the American Medical Association* on October 21, 2025 obtained data from Aid Access to analyze the mailing of 118,388 abortion pill packs between July 1, 2023 and September 30, 2024. They found that states with a near-total ban on abortion, which includes

[1] In the 8 months before the enforcement of the Texas Heartbeat Act (January 2021 to August 2021) 41,147 abortions were performed on Texas residents. In the 8 months after the enforcement of the Texas Heartbeat Act (September 2021 to April 2022) there were 21,173 abortions performed on Texas residents. Data obtained from Texas Health and Human Services Commission. Calculations by author.

Louisiana, had a county-level provision rate that was more than seven times higher than states with permissive abortion policies. The map that accompanies the article indicates that nearly all Louisiana counties had an above-average provision of mail-order abortions (Aiken et al. 2025).

The Society of Family Planning's #WeCount project finds that between July 2023 and June 2025, 15,420 mail-order abortions occurred in Louisiana. In calendar year 2024, the #WeCount project estimates 7,530 mail-order abortions took place in Louisiana (Society of Family Planning 2025).

Data from the Centers for Disease Control (CDC) indicates that in both 2020 and 2021, the two full years prior to the *Dobbs* decision, about 7,400 abortions were performed in Louisiana (Kortsmit et al. 2023; Ramer et al. 2024). The Guttmacher Institute estimates that in 2020, 7,610 abortions were performed on Louisiana residents (Jones et al. 2022). As such, because the number of abortions before Louisiana's abortion ban took effect are similar to the number of abortions after it took effect, it's clear that a very large percentage of women who would have obtained chemical or surgical abortions in Louisiana are obtaining mail-order abortions.

Recent data from the Society of Family Planning's #WeCount project indicates that 5,410 abortions were performed via mail-order in Louisiana in the first 6 months of 2025. According to the Society of Family Planning's Data, 100 percent of the abortions obtained in Louisiana in 2025 were done via mail-order. (Society of Family Planning 2025).

In the absence of mail-order abortions, it is impossible to say how many additional Louisiana women would carry pregnancies to term. However, a substantial body of political science, economics, and public health research shows that the incidence of abortion is sensitive to its effective cost (Cook et al. 1999; Hansen 1980; Haas Wilson 1993, 1996, 1997; Meier and McFarlane 1994; Blank 1996; Meier et al. 1996; Korenbrot, Brindis, and Priddy 1990; Levine, Trainor, and Zimmerman 1996; Lundberg and Plotnick 1990; Matthews, Ribar, and Wilhelm 1997; Medoff 1999, 2007; Morgan and Parnell 2002; Trussell et al. 1980). As such, eliminating mail-order abortions would reduce the incidence of abortion, resulting in more Louisiana births, and an increase in Louisiana's fertility rate.

2) Women on Medicaid Are More Likely to Obtain Abortions.

Women on Medicaid are more likely to obtain abortions compared to women who are not enrolled in Medicaid. As such, access to mail-order abortions means that Louisiana's Medicaid program will have to pay for any physical health complications or mental health complications caused by mail-order abortions.

At the outset, it is important to note, a body of research shows that low-income women are more likely to obtain abortions than high-income women. Since Medicaid is a program that typically provides health insurance for low-income earners, it is unsurprising that women enrolled in Medicaid would have a higher incidence of abortion than women not enrolled in Medicaid.

Data from the Guttmacher Institute's 2021-2022 abortion patient survey found that 41.4% of all women seeking abortions had incomes that were less than 100% of the federal poverty level (Jones 2024).

Guttmacher also conducted an abortion patient survey in 2014. That year, women whose incomes were less than 100% of the federal poverty level had an abortion rate of 36.6 per thousand women of childbearing age (15-44). Conversely, in 2014 women whose incomes were between 100% and 199% of

the federal poverty level had an abortion rate of 19.1 per thousand women of childbearing age (15-44), and women whose incomes where above 200% of the federal poverty level had an abortion rate of 6.0 per thousand women of childbearing age (15-44) (Jones and Jerman 2017).

The results from Guttmacher's 2008 abortion patient survey are similar. This survey found that women whose incomes were less than 100% of the federal poverty level had an abortion rate of 49.5 per thousand women of childbearing age (15-44). Conversely, in 2008 women whose incomes were between 100% and 199% of the federal poverty level had an abortion rate of 28.0 per thousand women of childbearing age (15-44) and women whose incomes were above 200% of the federal poverty level had an abortion rate of 9.5 per thousand women of childbearing age (15-44) (Jones and Jerman 2017).

A 2024 study in *Health Services Research* analyzed lifetime abortion incidence among women in Alabama, Delaware, Maryland, Iowa, Ohio, and South Carolina. They used 2016-2019 pre-*Dobbs* data from the Survey of Women studies and obtained data from 8,972 women aged 18-44 residing in the study areas. The authors obtained data on the incidence of abortion using a double list experiment which may improve reporting on sensitive behaviors (Jackson and Rendall 2024).

Among the states whose Medicaid programs did not cover elective abortion (Alabama, Delaware, Iowa, Ohio, and South Carolina) women on Medicaid had a 6.0 percent greater probability of having had an abortion in their lifetimes compared with women with another insurance status. This finding reaches conventional standards of statistical significance (Jackson and Rendall 2024).

The results from these states provide an apt comparison to Louisiana since Louisiana's Medicaid program does not cover abortion. As such, it is very likely that women on Medicaid in Louisiana are more likely to obtain abortions than women in Louisiana who are not on Medicaid.

3) Women who obtain abortions, particularly chemical abortions, frequently need subsequent medical assistance.

The FDA's medication guide for Mifeprex indicates that anywhere from 2.9 percent of women to 4.6 percent of women using mifepristone will visit an emergency room (U.S. Food and Drug Administration, 2025).

A 2025 study authored by Ethics and Public Policy Center analyzed 865,727 prescribed mifepristone abortions from 2017 to 2023. They found 10.93 percent of women experienced a serious adverse event (Hall and Anderson 2025).

A study analyzing over 54,000 abortions that were covered by California's Medicaid program in 2009 and 2010 found that chemical abortions have a complication rate that is four times higher than first trimester surgical abortions (Upadhyay et al. 2015).

A study of over 4,900 induced abortions in Skaraborg Hospital in Sweden between 2008 and 2015 also found that surgical abortions had a higher complication rate than first-trimester surgical abortions. This difference achieved conventional levels of statistical significance.[2] The study also found that the complication rate for chemical abortions increased from 4.2% in 2008 to 8.2% in 2015 (Carlsson, Breding, and Larsson 2018).

[2] A Wald Independent Samples Proportion Test was also performed by the author using SPSS 30.0.

A 2021 study in the journal *Contraception* analyzed over 1,100 women who obtained mail-order abortions during the pandemic. They found that 6 percent reported an emergency room or an urgent care visit related to the abortion (Chong et al. 2021). This is a higher emergency room visit rate than the U.S. Food and Drug Administration reports for women who obtain chemical abortions (U.S. Food and Drug Administration, 2025).

A recent study in the *International Journal of Women's Health Care* analyzed the mental health of women between the ages of 41 and 45. Of women who had obtained abortions (20 years previously on average), 24.1 percent reported high levels of post- abortion distress (Sullins 2025).

A 2025 study in the *Journal of Psychiatric Research* analyzed over 28,000 Canadian women who obtained abortions and over 1.2 million Canadian women who gave birth between 2006 and 2022. The authors found that the rate of mental health hospitalization was more than double following induced abortions than other pregnancies. The study also found that abortion was associated with higher rates of hospitalization for psychiatric disorders and suicide attempts (Auger et al. 2025).

Issues of Law and Medicine published an analysis of the abortion breast cancer link in 2014. Of the 72 studies they considered, 45 studies found a positive correlation between abortion and the incidence of breast cancer. In 19 of these studies the correlation was both positive and statistically significant. This 2014 article also considered three meta analyses of the abortion and breast cancer link. Two of the three meta-analyses found that the correlation between abortion and breast cancer was both positive and statistically significant (Lanfranchi and Fagan, 2014).

4) Assistance is Available to Pregnant Women in Louisiana.

Research shows there is a substantial amount of assistance available to pregnant women in Louisiana. Women who are unable to obtain mail-order abortions can receive both public and private assistance if they carry their pregnancy to term.

Louisiana's Medicaid Program provides coverage for pregnant women whose income is equal to or less than 138 percent FPIG (Federal Poverty Income Guidelines) (Louisiana Department of Health, 2025a). As of April 1, 2022 pregnant Medicaid beneficiaries are provided coverage for 12 months postpartum (Louisiana Department of Health, 2025b).

The Charlotte Lozier Institute obtained survey data from 19 pro-life pregnancy help centers in Louisiana. These centers were located in diverse locations throughout the state including Alexandria, Baton Rouge, Bogalusa, Hammond, Houma, Lafayette, Lake Charles, Leesville, Mamou, Natchitoches, New Orleans, Opelousas, Ruston, Shreveport, and Thibodeaux.

In 2024, these 19 centers served 7,025 clients, performed 5,355 pregnancy tests, performed 3,589 ultrasounds, and performed 1,543 STI tests. They had 2,355 clients attending parenting and prenatal education classes, had 67 clients receiving post-abortion support, and gave Sexual Risk Avoidance and Education presentations to 705 students.

These pregnancy centers gave out 9,605 packs of diapers, 10,107 packs of baby wipes, 408 new car seats, 20,666 clothing outfits, 138 strollers, 226 cribs, and 2,255 cans of infant formula.

Overall, these 19 pro-life pregnancy centers in Louisiana provided $2,303,127.52 worth of goods and services to women, children and families in 2024.

The Charlotte Lozier Institute was not able to obtain data from all of the pro-life pregnancy help centers in Louisiana. According to Heartbeat International, there are 37 stand-alone pro-life pregnancy centers in Louisiana. If the figures from the 19 pregnancy help centers for which Lozier has data are extrapolated to a total of 37 pregnancy help centers, that would mean that pro-life pregnancy centers in Louisiana assisted over 13,680 clients and provided over $4.4 million of goods and services to women, children, and families.[3]

5) Increases in Abortion and Reductions in Fertility Will Hurt Louisiana's Economic and Fiscal Health.

In *Alliance for Hippocratic Medicine v. FDA*, the government argued that "eliminating access to medication abortion" would increase health care costs and therefore "increase the costs imposed on taxpayers." Case No. 2:22-cv-00223-Z, ECF 28-2, Declaration of Jason Lindo. But the impact on taxpayers and the public fiscal health is exactly the opposite. Indeed, although the birth of a child may result in public assistance and safety-net costs, the eventual economic (and tax) contribution of that child will quickly exceed those costs.[4]

A 2022 report from the Republicans on the U.S. Senate Joint Economic Committee analyzed the cost of the 629,989 legal abortions reported by the Centers for Disease Control (CDC) in 2019. To calculate the cost of abortion, they use a value of a statistical life (VSL). This estimate observes the amount of wealth an individual must be provided in return for accepting an increased risk of mortality. For example, if the average individual is willing to accept $10,000 to incur a 1 in 1,000 chance of death, the corresponding VSL would be $10 million.[5]

Using estimates from academic journals, the U.S. Department of Transportation uses a value of a statistical life estimate of $10.9 million. Multiplying the 629,898 lives lost to abortion by the $10.9 million value of statistical life estimate, the Joint Economic Committee found that the economic cost of abortion to society was nearly $6.9 trillion. (Joint Economic Committee Republicans 2022).

Economists Danielle Sandler and Nichole Szembrot estimate that for the average mother, earnings fall by a total of approximately $26,000 over the first six years of the first baby's life (Sandler and Szembrot 2019). However, the $6.9 trillion economic cost to society of aborting unborn children greatly exceeds any estimated earning loss experienced by women in the first six years after giving birth (Joint Economic Committee Republicans 2022).

Also, the authors of the Joint Economic Committee report noted that "abortion imposes additional costs not reflected in the estimate." Specifically, they add that "In the long run, abortion shrinks the labor

[3] Calculation by author.

[4] Not to mention the fact that the presence of a child may lead to an increased sense of responsibility, thus increasing economic productivity. Rebecca Glauber, *Trends in the Motherhood Wage Penalty and Fatherhood Wage Premium for Low, Middle, and High Earners*, 55 Demography 1663 (2018), https://read.dukeupress.edu/demography/article/55/5/1663/167918/Trends-in-the-Motherhood-Wage-Penalty-and.

[5] $10,000*1,000= $10,000,000

force, stunts innovation, and limits economic growth. It also weakens the solvency of social insurance programs like Social Security and Medicare that rely on workers to support a growing elderly population." (Joint Economic Committee Republicans 2022).

The most recent data from #WeCount indicates that approximately 7,530 mail-order abortions are performed annually in Louisiana. Using the $10.9 million value of a statistical life estimate that was utilized by the Joint Economic Committee, this means the annual cost to society of aborting unborn children in Louisiana is approximately $82,077,000,000. In fact, the government's argument in *AHM v. FDA* on the impact to taxpayers is not only wrong but also too narrow. Mail-order abortions also have a negative impact on Louisiana's income, sales, and property tax revenue (Felix and Watkins 2013; Governor's Office of State Budgeting and Planning 2022; Pew Charitable Trusts 2022; Brighton et al. 2021).

In addition to leading to a possible decline in tax revenue, fertility rate reductions could reduce states' federal funding. Several federal programs—including Children's Health Insurance Program, and Head Start—allocate money to states according to formulas that incorporate population counts (Pew Charitable Trusts 2022). A reduction in Louisiana's fertility rate would reduce the amount of federal funds that Louisiana receives for these programs.

STATISTICAL WORK

Excel spreadsheet version 2108 was used for various calculations that were used in this analysis.

A Wald Independent Samples Proportion Test to compare chemical abortion complication rates to surgical abortion complication rates in a study conducted in Sweden was done using SPSS 30.0.

FACTS OR DATA SUPPORTING MY OPINIONS

The opinions in this declaration are my expert opinions, based on my education, training, and research in both Political Science and Statistics. All of the opinions provided in this report are based on my personal knowledge and are provided to a reasonable degree of certainty.

EXHIBITS USED TO SUMMARIZE OR SUPPORT MY OPINIONS

None.

LIST OF CASES WHERE I HAVE SERVED AS AN EXPERT

Served as an expert witness in *The People of the State of California vs. Heartbeat International Inc. and RealOptions Inc.* in the Superior Court of the State of California County of Alameda (Testimony submitted September 9, 2025).

Served as an Expert Witness in *Planned Parenthood Great Northwest, Hawai'i, Alaska, Indiana, Kentucky et al. v. State of Alaska, et al.* in the Superior Court for the State of Alaska Third Judicial District at Anchorage (Testimony submitted August 1, 2022).

Served as an Expert Witness in *Planned Parenthood of Wisconsin, et al. v. Joshua Kaul, et al.* in the United States District Court for the Western District of Wisconsin (Testimony submitted February 28, 2020).

Served as an Expert Witness in *Yashica Robinson M.D., et al. v. Steven Marshall* in the United States District Court for the Middle District of Alabama Northern Division (Testimony submitted August 29, 2019).

Served as an Expert Witness in *Planned Parenthood Federation of America, et al. v. Center for Medical Progress, et al.* in the United States District Court Northern District of California San Francisco Division (Testimony submitted April 15, 2019).

Served as an Expert Witness in *Whole Women's Health, et al., v. Ken Paxton, et al.,* Case No. A-17-CV-690-LY. In the United States District Court for the Western Division of Texas Austin Division.

Served as an Expert Witness in *Springfield Right to Life et al., v. Felicia Norwood*, Director of the Department of Health Care and Family Services, et al., Case No. 2017-MR-1032 in the Circuit Court for the Seventh Judicial Circuit Court Sangamon County.

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QUALIFICATIONS AND PUBLICATIONS

I provide these facts and opinions as someone as an expert in the field of Political Science with an extensive background in Statistics. I hold a Ph.D. in Political Science and a M.S. in Statistics both from Stanford University. After I completed my Ph.D., I completed a two year post-doctoral fellowship at the Harvard-MIT Data Center. I have had full time, academic positions at the University of Alabama, the University of Michigan – Dearborn, and Ave Maria University. I am currently an Assistant Professor of Practice of Social Research at The Catholic University of America.

My areas of expertise include fiscal policy and direct democracy. I have a specific interest in the issue of abortion – specifically the impact of both abortion regulations and contraception programs on the incidence of abortion. For more than 20 years, I have conducted research on these topics and published my findings in policy papers and peer reviewed political science journals. I have also presented my findings at numerous professional and academic conferences. In 2012, I testified in front of a Congressional Subcommittee on the Child Interstate Abortion Notification Act (CIANA). In 2017, I was hired by the State of Texas to serve as an expert witness during litigation over Texas Senate Bill 8, which prohibits dilation and evacuation abortions. I have also been hired as an expert witness by the state of Wisconsin, the state of Alaska, and the state of Alabama in cases involving litigation over abortion regulations and restrictions. I have also been hired as an expert witness in a California case involving the legality of abortion pill reversal.

Four of my papers on the impact of anti-abortion legislation have appeared in peer reviewed journals. Two of these papers have been published in *State Politics and Policy Quarterly*, which is considered to be the best state politics journal in the country. In 2007, I was one of only four junior (untenured) faculty members asked to serve on the editorial board of *State Politics and Policy Quarterly.* I served as a section chair at the 2008 meeting of the Midwest Political Science Association, which is typically the second largest political science conference in the country. During my academic career, I have been asked to review manuscripts for 14 different academic journals.

COMPENSATION

I will be compensated at the rate of $300.00 an hour for my work in this case.

I declare under 28 U.S.C. § 1746 and under penalty of perjury that this declaration is true and correct based on my personal knowledge.

Executed December 15, 2025

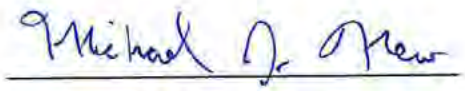

EXHIBIT A

Curriculum Vitae of Michael J. New, Ph.D.

Michael J. New

The Catholic University of America
The Busch School of Business
620 Michigan Ave. NE
Washington, DC 20064
newm@cua.edu

Employment

The Catholic University of America
Assistant Professor of Practice, August 2022 - present
Research Associate, August 2020 – August 2022
Visiting Assistant Professor, July 2018 – August 2020

Ave Maria University
Associate Professor, July 2017 – July 2018
Visiting Associate Professor, July 2015 – July 2017

University of Michigan – Dearborn
Assistant Professor, August 2011 – June 2015

University of Alabama
Assistant Professor, August 2004 – August 2011

Harvard-MIT Data Center
Post-Doctoral Research Fellow, August 2002-August 2004

Education

Stanford University
Ph.D. Political Science, June 2002
Dissertation: *A Comparison of Fiscal Discipline Measures Passed Through The Citizen Initiative To Fiscal Discipline Measures Enacted Through Other Means.*
Reading Committee: Morris Fiorina, Simon Jackman, John Cogan
Fields: American Politics, Political Organizations, Political Economy (GSB sequence)

Stanford University
M.S. Statistics, January 2002

Dartmouth College
B.A. with High Honors, Government, June 1997
B.A. Economics Modified with Mathematics, June 1997
Magna Cum Laude, Phi Beta Kappa Society

Selected Courses Taught

Undergraduate Courses
"Social Research 101: Foundations of Economic Thought I." The Catholic University of America, Fall 2019, Fall 2020, Fall 2021, Fall 2022, Fall 2023, Fall 2024

"Social Research 260: Game Theory and Strategic Thinking." The Catholic University of America, Spring 2019, Spring 2020, Spring 2021, Spring 2022, Spring 2023, Spring 2024, Spring 2025

"Social Research 325: Public Policy and Federal Budgets." The Catholic University of America, Spring 2019, Fall 2020, Fall 2021, Fall 2022, Fall 2023, Fall 2024

Teaching Interests

Economics
Microeconomics, Macroeconomics, Game Theory, Fiscal Policy
American Politics
Introduction to American Politics, State and Local Government,
Statistical Methods
Introductory Statistics, Intermediate Statistics

Research Interests

Economics
Economics of the Family, Morality Policy, Public Finance, Fiscal Constitutions, Health Policy
American Politics
State and Local Politics, Budgetary Politics, Direct Democracy

Published Academic Papers

"Analyzing the Impact of State Level Contraception Mandates on Public Health Outcomes." *Ave Maria Law Review*. Summer 2015.

"Analyzing the Effect of State Level Anti-Abortion Legislation in the Post *Casey* Era: A Re-Assessment." *State Politics and Policy Quarterly*. September 2014.

"Analyzing the Effect of State Level Anti-Abortion Legislation in the Post *Casey* Era." *State Politics and Policy Quarterly*. March 2011.

"State Education Investments and Economic Growth in America: A Path Analysis with Cross-National Controls" with Norman Baldwin and Stephen Borrelli. *Social Science Quarterly.* March 2011.

"U.S. Tax and Expenditure Limitations: A Comparative Political Analysis." *State Politics and Policy Quarterly.* Spring 2010.

"Direct Democracy, Public Opinion, and Public Policy." *PS: Political Science and Politics*, October 2009.

"Starve the Beast: A Further Examination." *Cato Journal.* Fall 2009.

"Using Natural Experiments to Analyze the Impact of State Legislation on the Incidence of Abortion." *Catholic Social Science Review*. Fall 2009.

"Analyzing The Welfare Caseload Decline from 1996-2002." *Cato Journal*. Fall 2008.

"Analyzing the Effect of Anti-Abortion Legislation on the Incidence of Abortion Among Minors." *Catholic Social Science Review*. Fall 2007.

"The Effect of State Regulations on State Health Insurance Premiums." *ICFAI Journal of Insurance Law*. May 2006.

Academic Book Reviews

Review of David Primo's *Rules and Restraint*. *Public Choice*. July 2009.

Academic Letters to the Editor

"Preventing Unintended Pregnancies by Providing No-Cost Contraception." With David Paton. *Obstetrics and Gynecology*. April 2013

Papers in Preparation For Review at Academic Journals

"Analyzing the Effect of Anti-Abortion Parental Involvement Laws" (Previously Received a Revise and Resubmit at *Social Science Quarterly*)

"The Citizen Initiative, Public Opinion, and State Fiscal Outcomes" (Previously Received a Revise and Resubmit at *Social Science Quarterly*)

Selected Papers Presented at Academic Conferences

"Using Birth Data From Texas to Analyze the Impact of the Texas Heartbeat Act." Presented at the Annual Meeting of the American Political Science Association. September 2024, Philadelphia, PA and at annual State Politics and Policy Conference, May 2025, Boston, MA

"Using Birth Data to Analyze the Impact of Anti-Abortion Laws." Presented at the Annual Meeting of the American Political Science Association. September 2024, Philadelphia, PA.

Selected Professional Consulting

Hired by the State of Florida to testify and assist with the drafting of the Financial Impact Statement on Amendment 4. (Oral testimony presented July 1st and July 8th. Written testimony submitted the week of July 1st and July 8th)

Served as an Expert Witness in *Planned Parenthood Great Northwest, Hawai'i, Alaska, Indiana, Kentucky et al. v. State of Alaska, et al.* in the Superior Court for the State of Alaska Third Judicial District at Anchorage (Testimony submitted August 1, 2022)

Served as an Expert Witness in *Planned Parenthood of Wisconsin, et al. v. Joshua Kaul, et al.* in the United States District Court for the Western District of Wisconsin (Testimony submitted February 28, 2020)

Served as an Expert Witness in *Yashica Robinson M.D., et al. v. Steven Marshall* in the United States District Court for the Middle District of Alabama Northern Division (Testimony submitted August 29, 2019)

Served as an Expert Witness in *Planned Parenthood Federation of America, et al. v. Center for Medical Progress, et al.* in the United States District Court Northern District of California San Francisco Division (Testimony submitted April 15, 2019)

Served as an Expert Witness in *Whole Women's Health, et al. vs. Ken Paxton, et al.* in the United States District Court for the Western District of Texas Austin Division (Testimony submitted October 4, 2017)

Compensated Expert on a Department of Health and Human Services (HHS) Project on the Sexual Health of Adolescents and Young Adults. Assisted with the Development of Models of Sexual Risk Avoidance and Sexual Risk Cessation (2018-2020)

Amicus Brief

Brief: On Writ of Certariori in *Zubik v. Burwell* in Support of Petitioners (U.S. Supreme Court argued March 23, 2016; Filed January 11, 2016)

Selected Editorials

"Gann, not Gavin, Is Responsible for Tax Relief in California" *Washington Examiner,* May 25, 2021

"The Trump Administration's Protect Life Rule in a Win for Women" *Washington Examiner*, August 27, 2019

Selected Presentations

"Public Opinion and the Pro-Life Brand." Presentation given at Notre Dame's Vita Institute in 2025, South Bend, IN.

"Pro-Life Success in the States: Strategies for the *Dobbs* Era." Presentation Given at annual convention of the National Right to Life Committee in Arlington, VA on June 29, 2024. Similar presentations given at the 2023 Convention of the National Right to Life Committee, Harvard University (2025), University of New Hampshire (2023), and other university campuses.

"Abortion Access and the Flourishing of Women: A Discussion of the Turnaway Study" Presentation given at Notre Dame's Vita Institute in 2024, South Bend, IN.

"Domestic Politics and Political Messaging on Abortion?" Presentation given at Notre Dame's Vita Institute in 2023, South Bend, IN.

"Analyzing the Effect of State Level Anti-Abortion Legislation in the Post *Casey* Era." Presentation given at Notre Dame's Vita Institute annually from 2011 to 2017, South Bend, IN.

"An Analysis of State Level Contraception Mandates." Presentation given at "The Future of the Families and Family Law." Brigham Young University Law School, October 10, 2014, Provo, UT.

"Taming Leviathan: Do Tax and Expenditure Limits Work?" American Enterprise Institute Policy Forum. June 12, 2013, Washington, DC.

Comments on John Lott's *Freedomnomics*. Cato Institute Book Forum. August 14, 2007, Washington, DC.

"Process and Institutions: Approaches to Responsible Budgeting." Goldwater Institute Fiscal Policy Conference, February 3rd, 2005. Phoenix, AZ.

"Tax Limitation after California's Prop 13." Cato Institute Policy Forum. June 19, 2003, Washington, DC.

Research Grants

$10,000 from the Charlotte Lozier Institute to Analyze State Level Contraception Mandates. Spring 2014

Fellowships

Witherspoon Institute, Bradley Fellow 2008-2009 academic year

American Political Science Association, Centennial Center Visiting Scholar, Summer 2009

Hoover Institution on War, Revolution, and Peace, Academic Fellowship, May 2007

Weaver Fellow, Intercollegiate Studies Institute, 2001-2002

Honors and Awards

Society of St. Sebastian Person of the Year Award, 2023

Society of St. Sebastian's Person of the Year Award, Honorable Mention, 2020

George Mason University Foundation Award, 2005

Intercollegiate Studies Institute's Director's Award, 2000

Disciplinary Service

Chair, Public Administration Section, Annual Conference of the Midwest Political Science Association, Spring 2008. Chicago IL

Editorial Board Member, *State Politics and Policy Quarterly* (2007-2011)

Invited by the General Social Survey (GSS) to write a memo suggesting topics for updated survey questions on various sanctity of life issues

Referee, *American Journal of Political Science*

Referee, *Journal of Politics*

Referee, *Political Research Quarterly*

Referee, *American Politics Review*

Referee, *Eastern Economic Journal*

Referee, *Public Budgeting and Finance*

Referee, *Publius*

Referee, *State Politics and Policy Quarterly*

Referee, *State and Local Government Review*

Referee, *Journal of Policy Analysis and Management*

Referee, *Journal of Women, Politics, and Policy*

Referee, *Social Forces*

Referee, *The Review of Black Political Economy*

Referee, *National Tax Journal*

Discussant, Midwest Political Science Association Meetings, 2022, 2019, 2014, 2013, 2008, 2006, 2003

Discussant, American Political Science Association Meetings, 2005

Discussant Southern Political Science Association Meetings, 2005

University and Departmental Service

The Catholic University of America
Faculty Advisor, Catholic University of America College Republicans, 2019-2020, 2020-2021, 2021-2022, 2022-2023, 2023-2024, and 2024-2025 Academic Years

Faculty Advisor, Catholic University of America Young Americans for Freedom (YAF), 2019-2020, 2020-2021, 2021-2022, 2022-2023, 2023-2024, and 2024-2025 Academic Years

Failed Grades Committee (Busch School of Business), Spring Semester 2023 (partial), 2023-2024 academic year

Ave Maria University
Program Director, Political Economy and Government, 2016-2017 and 2017-2018 Academic Year

Member, Honor Council, 2015-2016, 2016-2017, and 2017-2018 Academic Years

Search Committee for Faculty Member in Economics, 2017-2018 Academic Year

Member, Sophomore Success Committee, 2016-2017 Academic Year

Search Committee for Faculty Member in Business, 2016-2017 Academic Year

Member, Institutional Review Board, Spring Semester 2016

University of Michigan -- Dearborn
Co-Director, University of Michigan Dearborn's Social Science Research Colloquium Fall 2011-Fall 2014

Member, CASL Curriculum Committee, Winter Semester 2014 and Winter Semester 2015

Member, Social and Behavioral Analysis Learning Outcomes Subcommittee, 2013-2014 Academic Year

Graduate Integrity Board, 2013-2014 Academic Year

Search Committee for Assistant Professor in Environmental Politics and Policy, 2012-2013 Academic Year

The University of Alabama
Director, University of Alabama's Washington Experience Summer Internship Program, 2005 – 2011

Vice-President, Phi Beta Kappa Society, 2009-2010 Academic Year

Acting Director, University of Alabama's Masters in Public Administration (MPA) Program, Spring 2006

Dissertation Committee, Sam Clovis. "Federalism, Homeland Security, and National Preparedness: A Case Study in the Development of Public Policy."

Dissertation Committee, Justice Kali. "Innovation Diffusion and the Reinvention of Domestic Violence Policy Within State Welfare Programs: Influences of Adoption of the Family Violence Option and Domestic Violence Policy."

EXHIBIT 23

Declaration of Angela Parise, M.D.
(Dec. 11, 2025)

UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF LOUISIANA
LAFAYETTE DIVISION

THE STATE OF LOUISIANA, by and through its Attorney General, LIZ MURRILL, and ROSALIE MARKEZICH, *Plaintiffs*, v. U.S. FOOD AND DRUG ADMINISTRATION, *et al.*, *Defendants*.	Case No.: 6:25-cv-01491-DCJ-DJA Judge David C. Joseph Magistrate Judge David J. Ayo

DECLARATION OF DR. ANGELA PARISE

I, Angela Parise, M.D., a citizen of the United States of America and a resident of Louisiana, declare under penalty of perjury under 28 U.S.C. § 1746 that the following is true and correct to the best of my knowledge.

1. I am over eighteen years old and make this declaration on personal knowledge. I am fully competent to make this declaration. If called to testify, I could and would testify competently to these facts.
2. I am a board-certified obstetrician and gynecologist with more than 20 years of experience.
3. I am a fellow in the American College of Obstetrics and Gynecology.
4. I received my medical degree from State University of New York Downstate Health Sciences University in 2001 and completed my residency at Ochsner Medical Center (New Orleans) in 2005. I have practiced in Louisiana ever since.
5. I am a practicing obstetrician and gynecologist in private practice and on call at a major health center network in New Orleans, Louisiana. Our health centers are part of the leading nonprofit healthcare provider in the Gulf South. Our facilities provide

labor and delivery, emergency OB/GYN interventions, newborn care, women's health, and maternal-fetal medicine for high-risk pregnancies.

6. I provide general OB/GYN care. I also specialize in minimally invasive procedures and robotic surgery with an interest in routine obstetric care, adolescent gynecology, and advanced gynecologic surgery such as hysteroscopic endometrial ablation, total laparoscopic hysterectomy, and uterine fibroid surgery.

7. I provide emergency care to patients seeking OB/GYN care.

8. I have witnessed firsthand how the abortion drug mifepristone has hurt women in Louisiana.

9. Since 2022, I have personally treated and cared for approximately fourteen patients who suffered complications after taking mifepristone.

10. These fourteen women were Louisiana residents.

11. Of those fourteen patients, I treated approximately eleven patients for an incomplete abortion and three patients for infection. The incomplete abortions required emergency medical intervention by me, including dilation and curettage (D&C) for eight patients and supportive management, ultrasounds, and antibiotics for the other three patients.

12. At least 80% of the patients I have personally treated for mifepristone complications received the drugs through the mail.

13. In a recent two-month span, my team—including the junior partners and nurse practitioners I oversee—treated at least 30 women who suffered mifepristone complications. These complications included hemorrhaging, blood transfusions, the need for D&C, and hospital stays, just from April through May 2025. Among the colleagues in my network, I am aware of women seeking treatment for mifepristone complications every day.

14. Approximately half of the patients my team or I have treated for mifepristone complications were on Medicaid. That means Louisiana Medicaid likely paid for that treatment.

15. In 2024, a patient came to me with what she initially labeled a miscarriage. She was bleeding and septic. I performed a suction D&C. I later discovered that this patient had taken mifepristone that she received in the mail. She took the mifepristone at approximately 19 weeks gestation.

16. In 2025, I managed the treatment plan for a patient suffering mifepristone complications. She ordered mifepristone from Abuzz, who mailed the drugs to her Louisiana home. She took the drugs in Louisiana. After she took the drugs, she bled for three weeks and came to the hospital after she started experiencing lightheadedness at the end of that three-week period. She was at approximately 7 or 8 weeks gestation when she came to the hospital. My partner performed a suction D&C and a blood transfusion. In the operating room, the patient started hemorrhaging. She was on Medicaid.

17. Patients often hide the fact that they took mifepristone.

18. In the last six months, I have personally treated four patients for post-abortion care after they took mail-order mifepristone.

19. Every day, women contact my team because they have abnormal bleeding, cramping, pain, nausea, and fever from mifepristone, and they often do not know the gestational age of their unborn children.

20. The number of Louisiana women whom we treat for mifepristone complications has dramatically increased since January 2023. If the FDA had not formally authorized a national mail-order abortion-drug regime, few, if any, women in Louisiana would be harmed by mifepristone. Based on my experience, the number of women harmed under this regime will continue to increase unless the FDA reverses course or the courts hold the FDA accountable for its reckless actions.

Executed this 11th day of December, 2025.

By _____
Angela Parise, M.D.

EXHIBIT 24

Declaration of Lindsey Sikes
(Dec. 15, 2025)

UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF LOUISIANA
LAFAYETTE DIVISION

THE STATE OF LOUISIANA by and through its Attorney General, Liz Murrill, and Rosalie Markezich, *Plaintiffs*, v. U.S. FOOD AND DRUG ADMINISTRATION, *et al.*, *Defendants.*	Case No.: 6:25-cv-01491-DCJ-DJA Judge David C. Joseph Magistrate Judge David J. Ayo

DECLARATION OF LYNDSEY SIKES

I, Lyndsey Sikes, a citizen of the United States of America and a resident of the State of Louisiana, declare under penalty of perjury under 28 U.S.C. § 1746 that the following is true and correct to the best of my knowledge.

1. I am over eighteen years old and make this declaration on personal knowledge. I am fully competent to make this declaration. If called to testify, I could and would testify competently to these facts.
2. I am the executive director of Life Choices Pregnancy Resource Center in Monroe, Louisiana. I have witnessed how the abortion drug mifepristone has hurt women in Louisiana. Life Choices encounters women considering abortion and women who have had an abortion—including by mifepristone.
3. Before mid-2022, Life Choices rarely encountered women who had ordered or taken abortion drugs. Now the center encounters women who have ordered or taken abortion drugs on a daily basis.
4. These women are Louisiana residents.
5. Most of Life Choices' clients who ordered or took abortion drugs ordered the drugs through Aid Access.

6. One Life Choices client received her drugs through Aid Access from Dr. Margaret Carpenter.

7. Approximately one out of seven Life Choices clients bring their abortion drugs with them to the center.

8. Life Choices encounters two or three women suffering from mifepristone complications every month. These complications include hemorrhaging, cramping, bleeding, fever, and incomplete abortions that require ultrasounds by our nurse practitioner on-site and referrals to the emergency room.

Executed this 15th day of Dec, 2025.

By_____
Lyndsey Sikes

UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF LOUISIANA
LAFAYETTE DIVISION

THE STATE OF LOUISIANA, by and through its Attorney General, LIZ MURRILL, and ROSALIE MARKEZICH, *Plaintiffs*, v. U.S. FOOD AND DRUG ADMINISTRATION, *et al.*, *Defendants.*	Case No.: 6:25-cv-01491-DCJ-DJA Judge David C. Joseph Magistrate Judge David J. Ayo

PLAINTIFFS STATE OF LOUISIANA AND ROSALIE MARKEZICH'S MEMORANDUM OF LAW IN SUPPORT OF THEIR MOTION FOR PRELIMINARY RELIEF UNDER 5 U.S.C. § 705

TABLE OF CONTENTS

Table of Authorities iii

Introduction 1

Background 3

Legal Standard 8

Argument 9

I. The Stay Factors Are Easily Satisfied, as the Fifth Circuit Already Has Held. 9

A. Plaintiffs Are Likely to Succeed on the Merits. 9

1. The 2023 REMS is arbitrary and capricious (Count I). 9

2. The 2023 REMS violates the Comstock Act (Count II). 13

B. The Remaining Stay Factors Favor Plaintiffs. 14

C. A Universal § 705 Stay Is the Proper Preliminary Remedy. 16

II. Plaintiffs Have Article III Standing. 17

A. The 2023 REMS Causes Plaintiffs' Current and Future Injuries in Fact. 18

1. The 2023 REMS causes sovereign harm by facilitating illegal abortions in Louisiana. 19

2. The 2023 REMS causes pocketbook harm by directly increasing Louisiana's Medicaid costs 21

B. These Injuries Are Redressable by a Favorable Decision 24

Conclusion 25

TABLE OF AUTHORITIES

Cases

Alliance for Hippocratic Medicine v. FDA,
2023 WL 2913725 (5th Cir. Apr. 12, 2023) ..... *passim*

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78 F.4th 210 (5th Cir. 2023) ..... *passim*

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591 U.S. 979 (2020) 15

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98 F.4th 220 (5th Cir. 2024) 17

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74 F.4th 627 (5th Cir. 2023) 8–9

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597 U.S. 215 (2022) 1, 15

FCC v. Next Wave Personal Communications, Inc.,
537 U.S. 293 (2003) 14

FCC v. Prometheus Radio Project,
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602 U.S. 367 (2024) 2, 18

GenBioPro, Inc. v. Raynes,
144 F.4th 258 (4th Cir. 2025) 21

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705 F. Supp. 3d 643 (W.D. La. 2024) 15, 17, 19, 21

Louisiana v. EEOC,
784 F. Supp. 3d 886 (W.D. La. 2025) ..... *passim*

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90 F.4th 461 (5th Cir. 2024) 9, 10

Medina v. Planned Parenthood South Atlantic,
606 U.S. 357 (2025) 21–22

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No. 22-cv-223, 2025 WL 2825980 (N.D. Tex. Sep. 30, 2025) 8

Monsanto Co. v. Geertson Seed Farms,
561 U.S. 139 (2010) 16

Rideau v. Keller Independent School District,
819 F.3d 155 (5th Cir. 2016) 24

Texas Corn Producers v. EPA,
141 F.4th 687 (5th Cir. 2025) 21

Texas v. United States,
126 F.4th 392 (5th Cir. 2025) 21, 24

Texas v. United States,
50 F.4th 498 (5th Cir. 2022) 20, 21, 23

TransUnion LLC v. Ramirez,
594 U.S. 413 (2021) 21

Trump v. CASA, Inc.,
606 U.S. 831 (2025) 17

Wages & White Lion Investments, LLC v. FDA,
16 F.4th 1130 (5th Cir. 2021) 9, 10, 15

Statutes

5 U.S.C. § 705 8

5 U.S.C. § 706 ..... 9, 14

18 U.S.C. § 1461 14

18 U.S.C. § 1462 ..... 9, 14

21 U.S.C. § 355 12

42 U.S.C. § 1396a 22

42 U.S.C. § 1396d 21, 22

La. R.S. 14:87.7 3

La. R.S. 14:87.8.1 3

La. R.S. 14:87.9 3

La. R.S. 40:1061 3

La. R.S. 40:1061.1 ..... 3, 19, 20

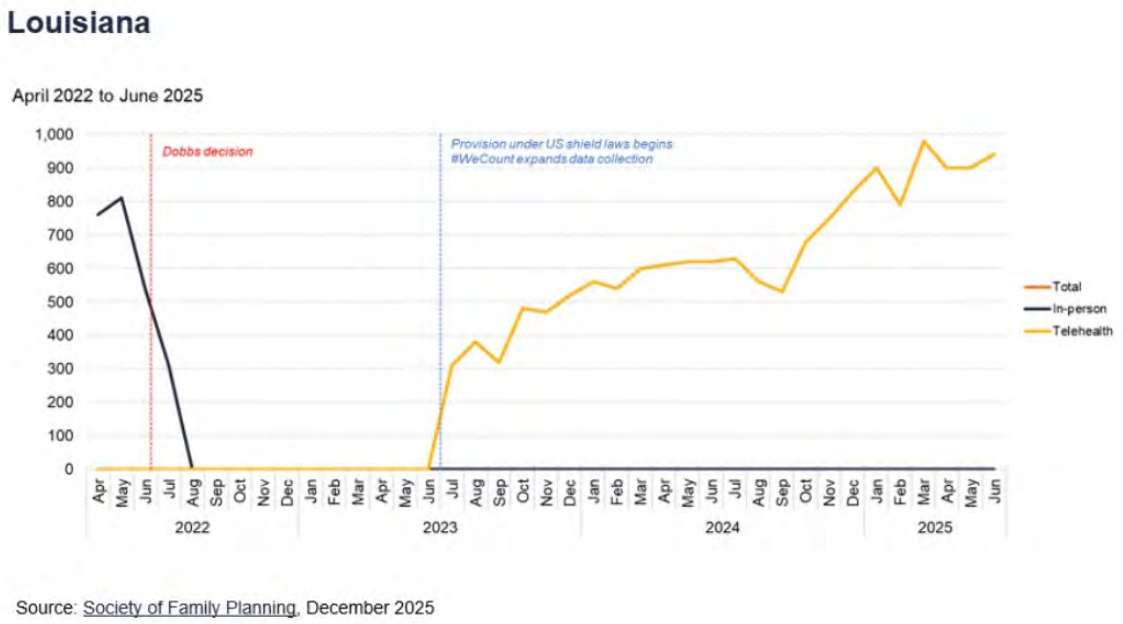
Rules

Fed. R. Civ. P. 65 8

INTRODUCTION

This case presents one of the most profoundly important issues threatening Louisiana's sovereignty, its values, and its people. In *Dobbs v. Jackson Women's Health Organization*, 597 U.S. 215 (2022), the Supreme Court "expressly returned the issue [of abortion] to the States." *Louisiana v. EEOC*, 784 F. Supp. 3d 886, 905 (W.D. La. 2025). States, like Louisiana, had laws on the books that sprang into effect broadly prohibiting abortion unless necessary to save the mother's life. President Biden knew this. So he ordered his administration to end-run *Dobbs* by finding every possible means to facilitate abortion in pro-life states. Relevant here, his Food and Drug Administration (FDA) carried out that directive by promulgating a Risk Evaluation and Mitigation Strategy for the abortion drug mifepristone (the 2023 REMS). The 2023 REMS removed a longstanding in-person dispensing requirement. Why? So doctors in states like New York and California could prescribe and mail FDA-approved mifepristone into pro-life states, causing abortions that otherwise would not occur.

The results are sobering. Hundreds of mifepristone-induced abortions are occurring in Louisiana *every month*. Until now, available data suggested that 800 abortions in December 2024 were a high watermark. ECF 1-2 at PowerPoint slide 35. But that number was a floor. As of about a week ago, new data show that the monthly number often crested 900, and reached nearly 1,000, in 2025:



Ex. 1, #WeCount Report April 2022 to June 2025 (Dec. 9, 2025), perma.cc/AYJ2-FYJ2; Ex. 2, #WeCount Report Summary Slides with National and 51 State-Level Findings April 2022 to June 2025 (Dec. 9, 2025), perma.cc/83U9-TC79; Ex. 3, Abigail R. A. Aiken et al., Research Letter, *Provision of Abortion Medications Using Online Asynchronous Telemedicine Under Shield Laws in the US*, 334(15) JAMA 1388 (Oct. 21, 2025), https://doi.org//10.1001/jama.2025.11420; Ex. 22, New Decl. at 1–2.

That is why this case is so important. Plaintiffs are the State of Louisiana and Rosalie Markezich, a Louisiana resident whose ex-boyfriend ordered mifepristone from a California doctor, received it by mail, and coerced Rosalie to take it, ending her baby's life. This lawsuit challenges the 2023 REMS as unlawful under the Administrative Procedure Act (APA) and seeks to vacate the 2023 REMS to restore the in-person dispensing requirement. There is no serious question that the 2023 REMS is unlawful. Secretary Robert F. Kennedy, Jr., and FDA Commissioner Martin A. Makary both admit that there was a "lack of adequate consideration" of the safety risks "underlying the prior REMS approvals," including the decision to "remov[e] the in-person dispensing requirement." ECF 1-110 at 2. And in fact, two Fifth Circuit panels have addressed this problem, holding—in suits filed by doctors and medical associations—that the 2023 REMS is likely unlawful. *See All. for Hippocratic Med. v. FDA*, No. 23-10362, 2023 WL 2913725, at *17–18 (5th Cir. Apr. 12, 2023) (*Alliance I); All. for Hippocratic Med. v. FDA*, 78 F.4th 210, 249–51 (5th Cir. 2023) (*Alliance II*), *rev'd and remanded on other grounds*, 602 U.S. 367 (2024) (*Alliance*). The Supreme Court later reversed, solely on the ground that those plaintiffs lacked Article III standing—but the Court thought it was "not clear that no one else would have standing." *Alliance*, 602 U.S. at 396.

The only real question in this case, therefore, is whether Plaintiffs have standing to challenge the 2023 REMS, which the Fifth Circuit already determined is likely unlawful. They unquestionably do. Most notably, this is a smoking-gun case where the public record reflects the Biden Administration's avowed intent to "interfere[ ] with [pro-life] States' abilities to enforce their laws and implement the chosen public policies of their citizens"—by unlawfully removing the in-person dispensing requirement for the sole purpose of allowing out-of-state doctors to facilitate illegal mail-order abortions in pro-life states like Louisiana. *Louisiana*, 784 F. Supp. 3d at 897 (citation modified).

It is difficult to imagine a federal action that is more "destructive of state sovereignty," *id.* at 901 (citation modified), particularly one that ends the lives of hundreds of unborn Louisiana children, like Rosalie's, every month. On top of that, Louisiana has suffered, and continues to suffer, a classic pocketbook injury from the 2023 REMS in the form of hundreds of thousands of dollars in increased Medicaid costs attributable to mifepristone-induced abortions that have required emergency care—costs that would not be incurred but for the 2023 REMS.

This case is hard to swallow because of its egregious facts—but it is easy to resolve on the merits and standing. As the Fifth Circuit previously directed, the proper route is to enter a preliminary stay of the 2023 REMS under 5 U.S.C. § 705 and ensure that the "in-person dispensing requirements, and FDA's obligation to enforce them, will continue to apply." *Alliance II*, 78 F.4th at 254.

BACKGROUND

A. "The Louisiana Legislature has expressly set forth the State's policy with respect to abortion." *Louisiana*, 784 F. Supp. 3d at 895 n.10. The State's policy is "that every unborn child is a human being from the moment of conception"—and accordingly, the Legislature has "declare[d] that the longstanding policy of this state [is] to protect the right to life of every unborn child from conception." *Id.* (quoting La. R.S. 40:1061.1). Following *Dobbs*, Louisiana law "prohibits all abortions except those that are determined to be medically necessary to prevent the death or substantial risk of death of the mother," with other narrow exceptions. *Louisiana*, 784 F. Supp. 3d at 895 n.10 (citing La. R.S. 40:1061, 14:87.7, 14:87.8.1). Relevant here, that includes a prohibition on abortion "by means of an abortion-inducing drug." La. R.S. 14:87.9.

Stunningly, however, hundreds of abortions occur every month in Louisiana. That is the direct and intended consequence of a drug war authorized by President Biden's FDA. The same day the Supreme Court decided *Dobbs*, President Biden announced a whole-of-government attack on states that choose to ban or otherwise restrict abortion. In particular, he identified "threats from state officials saying they will try to ban or severely restrict access to medication for reproductive health care." ECF 1-47 at 3. He followed that up with Executive Order No. 14,076 of July 8, 2022, Protecting

Access to Reproductive Health Care Services, 87 Fed. Reg. 42053 (July 13, 2022), which promised "abortion care, including medication abortion"—"especially for those who live in States that are banning or severely restricting abortion care." ECF 1-44 at 2; *see* ECF 1-45 (Executive Order No. 14,079 of Aug. 3, 2022, Securing Access to Reproductive and Other Healthcare Services, 87 Fed. Reg. 49505 (Aug. 11, 2022), challenging "the continued advancement of restrictive abortion laws in States across the country" and announcing a policy to protect "medication abortions").

Abortion "medication" is code for the FDA-approved abortion drug mifepristone. President Biden "directed the Secretary of Health and Human Services" (and thus FDA) "to identify all ways to ensure that mifepristone is as widely accessible as possible ... *including when prescribed through telehealth and sent by mail*." ECF 1-47 at 3 (emphasis added); ECF 1-60 at 2–3 (President Biden's fact sheet claiming that "states may not ban mifepristone" and promising "to allow mifepristone to continue to be prescribed by telehealth and sent by mail"). That directive was significant because, until the COVID-19 pandemic, FDA required mifepristone to be dispensed in person; in 2021, the Biden FDA cited its enforcement discretion to temporarily "not enforce the in-person dispensing requirement" and thereby facilitate "the dispensing of mifepristone through the mail" (the 2021 Non-Enforcement Decision). *See Alliance II*, 78 F.4th at 222, 226 (citation modified). In the wake of *Dobbs*, that temporary position gave way to the Biden Administration's vow that it would "ensure every American has access to ... medication abortion." ECF 1-48 at 2. "[W]e will double down," then-Secretary Becerra said, "and use every lever we have to protect access to abortion care." *Id.*; *see also* ECF 1-49 at 2, 4; ECF 1-61 at 4, 7; *accord* ECF 1-59 at 2 ("Since *Dobbs*, HHS has worked to protect and expand access to reproductive care amidst unprecedented efforts by Republican officials at the national and state level to restrict access to abortion[.]"). Fulfilling that promise, the Biden FDA issued the 2023 REMS in January 2023, ECF 1-3 at 2; ECF 1-50 at 9, 16, which permanently "formalize[d] the removal of the in-person dispensing requirement," "allow[ing] mifepristone to be prescribed remotely and sent via mail." *Alliance II*, 78 F.4th at 226; *accord Alliance I*, 2023 WL 2913725, at *2; Ex. 21, Francis Decl. ¶ 19.

B. That targeted assault on pro-life states worked as intended. While in-person abortions virtually vanished from Louisiana, mifepristone-induced abortions—authorized by out-of-state

doctors mailing FDA-approved mifepristone—skyrocketed. Said one mifepristone mailer: "We really don't change things unless we're legally required to." ECF 1-106 at 2. "We're confident people in … every state … will still be able to get abortion pills by mail," said another. *Id.* at 3.

To carry out this plan, organizations like AidAccess.org have blanketed the Internet with order forms for FDA-approved mifepristone, ECF 1-71, extolling the ease with which New York and California doctors may inject pills into locales from Baton Rouge to Lafayette:

Get Abortion Pill Online in Louisiana · Order Here

You can buy an abortion pill online and get it by mail in Louisiana. The FDA has approved abortion pills by mail. Aid Acces works with U.S. based abortion providers in so called shield law states (this means that the states will protect the providers against legal action). Therefor Aid Access can provide abortion services to all 50 U.S. states including Louisiana.

Aid Access will help you order abortion pills and have them delivered to your home in New Orleans, Baton Rouge, Shreveport, Metairie, Lafayette, or anywhere else in Louisiana.

Louisiana abortion pill online orders:

- Louisiana abortion pill online orders costs $150 USD
- Reliable abortion pill shipping to Louisiana in 1-5 days
- Tracking numbers provided when the pills are mailed
- Help desk support available in 16 languages

When Louisiana filed this suit, the available data showed a monthly abortion rate that fluctuated between 300 and 600, with an apparent high watermark of just over 800 abortions in December 2024 alone. ECF 1-2 at 36. Last week, however, new data revealed that 800 mifepristone-induced abortions per month was *the minimum* in Louisiana in 2025; more frequently, that monthly number was approximately 900, and nearly 1,000 in March 2025. Ex. 2, #WeCount Report Summary Slides, *supra* pp. 1–2; Ex. 22, New Decl. at 1–2.

There are real women and real-world harms behind those numbers. *See, e.g.*, Ex. 23, Parise Decl. ¶¶ 8–13, 15–16, 17–20; Ex. 18, Voltz Decl. ¶¶ 8–12; Ex. 19, Richard Decl. ¶¶ 2–9; Ex. 24, Sikes Decl. ¶¶ 2–8 (testifying to dozens of women who took or received mifepristone from out-of-state prescribers). Just take Plaintiff Rosalie Markezich, who did not want an abortion. ECF 1-92 at ¶ 16. She told her then-boyfriend that she wanted to raise their unborn baby. *Id.* ¶¶ 5, 11. Yet he went online

in late 2023, filled out a form with her information, gave her money to pay a California doctor through Venmo, and had the drug mailed to her Louisiana home. *Id.* ¶¶ 7, 8, 9. She pleaded, "Don't make me do this." *Id.* ¶ 11. But he grew angry and volatile, and Rosalie was so terrified that she thought taking the drugs was her only route to safety. *Id.* ¶¶ 12, 13. She ended up on a bathroom floor for an hour, and then a garage floor, as she began bleeding—an unspeakable experience that continued "for about a week" and "still haunts [her]." *Id.* ¶¶ 14, 15, 18. She mourns her child. *Id.* ¶ 17.

Rosalie is not alone. Consider the well-known story of Margaret Carpenter, a New York doctor who mailed mifepristone to a Louisiana woman who forced the drug on her pregnant teenage daughter. ECF 1-4, 1-83 to 1-86. The teen faced a medical emergency alone at home, called 911, and was rushed to the hospital in an ambulance after delivering a dead fetus. ECF 1-86. Or, consider data from the Louisiana Department of Health showing that over $92,000 in Medicaid dollars were paid for emergency room care and hospitalization resulting from just *two* mifepristone-induced abortions in 2025. Ex. 20, Willis Decl. ¶¶ 11–12. And these instances are just two examples of many women believed to have suffered similar adverse events requiring emergency medical care at Louisiana hospitals, paid for by Louisiana Medicaid. *Id.* ¶ 13.

These stories are not just disturbing but entirely predictable. That is because, as the Fifth Circuit previously held, the federal government's "own documents" show that "emergency room care is statistically certain" in mifepristone cases. *Alliance I*, 2023 WL 2913725, at *10. For example, FDA's own mifepristone label warns that roughly 1 in 25 (or 4% of) women who take mifepristone *as directed* will end up in the emergency room. ECF 1-9 at 8–9, 16; Ex. 21, Francis Decl. ¶¶ 30–31. And this was *before* the Biden Administration removed the requirement for an initial in-person visit—the only opportunity to screen for dangerous conditions like ectopic pregnancy, to accurately assess gestational age, to screen for coercion and trafficking, and to ensure informed consent. Ex. 21, Francis Decl. ¶¶ 22–28, 41, 49. The label also features a black box warning that mifepristone can cause "[s]erious and sometimes fatal infections and bleeding," and mifepristone can cause other problems warranting emergency attention. ECF 1-9 at 2; Ex. 21, Francis Decl. ¶¶ 31–32, 38, 42–48. What's more, there is good reason to believe that the emergency-room-visit and hospitalization rate is at least as high as

11%, Ex. 21, Francis Decl. ¶ 34—and FDA's own data demonstrates that dispensing mifepristone by mail exacerbates that rate. *See* ECF 1-13 at 2; Ex. 4, Robin Wallace et al, *P040 - Expanding Access to Abortion with Mifepristone and Misoprostol Through 84 Days Estimated Gestational Duration*, 151 Contraception 111117 (Nov. 2025), perma.cc/KXC7-9TFA; *see also* ECF 1-50 at 75; ECF 1-10 at 34–35. It is thus unsurprising that the flood of mifepristone into Louisiana under the 2023 REMS is directly resulting in life-threatening harm to Louisiana women and babies, as well as identifiable sovereign and monetary harms to Louisiana itself.

C. Because of the seriousness of this issue, Louisiana has expended substantial time and resources attempting to stop the mailing of mifepristone into the State. Among Louisiana's efforts are outstanding arrest warrants for Dr. Carpenter and the California doctor Rosalie's ex-boyfriend engaged, Dr. Remy Coeytaux. ECF 1-84; ECF 1 at 46, ¶ 159. But, as predicted, governors in states like New York and California have pursued every avenue available to thwart pro-life states from stopping the mifepristone flood. New York Governor Kathy Hochul, for example, refused to extradite Dr. Carpenter: "Let me be clear: we will never comply with Louisiana's extradition request. Not now, not ever." ECF 1-90. New York and other states have also passed aggressive "shield" laws that, among other things, permit doctors and clinics to omit identifying information from pill bottles—so that a pill bottle with mifepristone can arrive in Louisiana without indicating who sent it. *See, e.g.*, Ex. 5, *Governor Newsom Signs New Landmark Laws to Protect Reproductive Freedom, Patient Privacy Amid Trump's War on Women*, Gov. Gavin Newsom (Sep. 26, 2025), perma.cc/SB5E-V4QB (California law giving doctors "the option to prescribe abortion care medication to patients anonymously"). The stated intent: to prevent pro-life states from stopping the importation of abortion drugs.

Because of those difficulties, Louisiana and Rosalie tried a different tack on September 19, 2025, when they filed a motion to intervene in the still-pending *Alliance* litigation. *See* Rosalie Markezich and the State of Louisiana's Motion for Leave to Intervene and Memorandum in Support, *Missouri v. FDA*, No. 22-cv-223 (N.D. Tex. Sep. 19, 2025), ECF 264, 265. Following the Supreme Court's decision in *Alliance*, the states of Kansas, Idaho, and Missouri moved to intervene in the *Alliance* district court to continue the litigation—and Louisiana and Rosalie sought to join that fight.

On September 30, 2025, however, the *Alliance* district court transferred the case to the Eastern District of Missouri and denied Louisiana and Rosalie's intervention motion as moot. *Missouri v. FDA*, No. 22-cv-223, 2025 WL 2825980, at *1 (N.D. Tex. Sep. 30, 2025). Four business days later, Louisiana and Rosalie filed their Complaint in this Court. ECF 1. They seek a stay of the unlawful 2023 REMS that causes irreparable harm to Louisiana and its citizens every day.

The importance of a preliminary stay of the 2023 REMS has become blindingly clear in recent days. Under pressure from pro-life states and advocates, Secretary Kennedy announced on September 19, 2025, that, "through the FDA, HHS will conduct a study of the safety of the current REMS, in order to determine whether modifications are necessary." ECF 1-110 at 2. Yet on December 8, 2025, it was publicly reported that FDA Commissioner Marty Makary "has told agency officials to delay [a] safety review [of mifepristone] until after the midterm elections." Ex. 6, *US FDA Has Delayed Abortion Pill Safety Study, Bloomberg News Reports*, Reuters (Dec. 8, 2025, at 14:23 PT), perma.cc/DH8S-89TM. He later admitted that study data has not yet been acquired. Ex. 7, Elizabeth Troutman Mitchell, *EXCLUSIVE: Makary Responds to Report Saying He Slow-Walked Abortion Pill Safety Review*, Daily Signal (Dec. 9, 2025), perma.cc/AXP5-XTYS. In other words, FDA will not consider taking action on the 2023 REMS until 2027 at the earliest. And if FDA attempts to rescind or modify the 2023 REMS, the governing statutory framework imposes a timeline of nearly a year before that action could take effect. *See* 21 U.S.C. ¶ 355-1. So absent preliminary relief in this case, Louisiana and its citizens face the prospect of unbounded and illegal mifepristone-induced abortions for at least two more years if not longer. That is untenable. Preliminary relief is essential.

LEGAL STANDARD

Under the APA, Plaintiffs request a stay of the 2023 REMS or, alternatively, a preliminary injunction against Defendants' enforcement of the 2023 REMS. 5 U.S.C. § 705 (a court may stay an agency action "to the extent necessary to prevent irreparable injury"); Fed. R. Civ. P. 65. Plaintiffs are entitled to relief pending review if they show "(1) a substantial likelihood of success on the merits, (2) a substantial threat of irreparable harm if the injunction does not issue, (3) that the threatened

injury outweighs any harm that will result if the injunction is granted, and (4) that granting the injunction is in the public interest." *Clarke v. Commodity Futures Trading Comm'n*, 74 F.4th 627, 640–41 (5th Cir. 2023); *see Wages & White Lion Invs., LLC v. FDA*, 16 F.4th 1130, 1143–44 (5th Cir. 2021) (applying these factors to relief under the APA's Section 705).

ARGUMENT

I. The Stay Factors Are Easily Satisfied, as the Fifth Circuit Already Has Held.

A. Plaintiffs Are Likely to Succeed on the Merits.

Start with the merits—which two Fifth Circuit panels already have assessed and decided in Plaintiffs' favor. *See Alliance I*, 2023 WL 2913725, at *17–18; *Alliance II*, 78 F.4th at 249–51.[1] That is because the 2023 REMS is plainly unlawful for two reasons. *First*, as both panels held, the 2023 REMS is likely arbitrary and capricious and amounted to an abuse of discretion because it has no reasonable or reasoned scientific basis. 5 U.S.C. § 706(2)(A). *Second*, as Judge Ho explained in *Alliance II*, the 2023 REMS is "not in accordance with law" because it authorizes the mailing of abortion drugs, which is prohibited by federal law. 78 F.4th at 267 (Ho, J. concurring in part and dissenting in part) (quoting 5 U.S.C. § 706(2)(A); citing 18 U.S.C. § 1462(c)). For either or both of these reasons, Plaintiffs here—like the plaintiffs in the *Alliance* litigation—are likely to succeed on the merits.

1. The 2023 REMS is arbitrary and capricious (Count I).

Arbitrary-and-capricious review "has serious bite." *Louisiana v. Dep't of Energy*, 90 F.4th 461, 470 (5th Cir. 2024) (citation modified). It "requires that agency action be reasonable and reasonably explained," meaning that the agency "has reasonably considered the relevant issues and reasonably explained the decision." *Wages & White Lion*, 16 F.4th at 1136 (citation modified). "[B]are

[1] As the Complaint explains, ECF 1 at 48 n.200, the Fifth Circuit in *Alliance II* technically considered the 2021 Non-Enforcement Decision, not the 2023 REMS. But, as Chief Judge Elrod explained, the 2023 REMS "formaliz[ed]" the 2021 Non-Enforcement Decision and, in fact, that formalization kept the case alive since "[t]he decision that FDA made in 2021 … remains in force" through the 2023 REMS. 78 F.4th at 248. Because "the effect" of both the 2021 Non-Enforcement Decision and the 2023 REMS "is the same," the Fifth Circuit's analyses in *Alliance I* and *Alliance II* directly govern the 2023 REMS. *Id.*; *see supra* p. 4.

acknowledgement" of concerns and "conclusory statements" are "no substitute for reasoned consideration." *Louisiana*, 90 F.4th at 473. And when an agency changes its position, the agency must "recognize[ ] the change, reason[ ] through it without factual or legal error, and balance[ ] all relevant interests affected by the change," *id.* at 469, including reliance interests on the longstanding prior policy. *Wages & White Lion*, 16 F.4th at 1139.

In the 2023 REMS, FDA removed the in-person dispensing requirement with no legitimate justification for doing so. *Alliance I*, 2023 WL 2913725, at *17–18; *Alliance II*, 78 F.4th at 249–51. FDA's decision was based on two things: (a) an allegedly small number of adverse event reports in FDA's Adverse Event Reporting System (FAERS) database and from the drug sponsors; and (b) a review of the scientific literature. ECF 1-10 at 23. As discussed further below, all this was nonsense, not least because FDA elsewhere admitted that FAERS data is not reliable for purposes of evaluating safety and the scientific literature was inadequate. Indeed, Secretary Kennedy and Commissioner Makary have admitted that there was a "lack of adequate consideration" of the safety risks "underlying the prior REMS approvals," including the decision to "remov[e] the in-person dispensing requirement." ECF 1-110 at 2; *see* ECF 1-108 ("The Biden administration removed mifepristone's in-person dispensing rule without studying the safety risks."); Ex. 8, Ian Lopez, *RFK Jr. Says Biden 'Twisted the Data' on Abortion Pill Safety,* BL (Sep. 4, 2025, at 12:45 ET), perma.cc/ST5H-94H6 ("We know that during the Biden administration, they actually twisted the data, to bury one of the safety signals, a very high safety signal, around 11%, so we're going to make sure that that doesn't happen anymore."); Ex. 9, U.S. Senator Bill Cassidy, M.D. (@SenBillCassidy), X (Dec. 12, 2025, at 13:05 PT), perma.cc/LR7T-9UZT (archived Dec. 13, 2025). That admission, combined with the *Alliance I* and *Alliance II* decisions, makes for an easy merits determination in Plaintiffs' favor.

a. FAERS Data. Start with the FAERS data from 2020 and 2021 that FDA invoked. ECF 1-10 at 25. This is difficult to recount with a straight face. *Alliance I*, 2023 WL 2913725, at *17. FDA had already told the public that FAERS data was not a reliable source for the number of adverse events. That is, in part, because the "[r]ates of occurrence [for an adverse event] cannot be established with [FAERS] reports." ECF 1-52 at 5. Because reporting is voluntary, "FDA does not receive reports for

every adverse event ... that occurs." ECF 1-52 at 5. FDA even cautions on its website that (i) "[t]he number of suspected reactions in FAERS should not be used to determine the likelihood of a side effect occurring"; and (ii) "FAERS data cannot be used to calculate the incidence of an adverse event or medication error in the U.S. population." *Id.* at 3. Summarizing the utility (or lack thereof) of the data, FDA has said that "the FAERS data by themselves are not an indicator of the safety profile of the drug." *Id.* at 5. Just last week, Commissioner Makary dismissed the quality of this mifepristone data, saying, "There are studies that are done using adverse events, self-reported data. But that data's not very good.... When you do a study based on self-reported data, you're not capturing a lot of the data that you wanna know in a study." Ex. 10, Video posted by Elizabeth Mitchell Troutman (@TheElizMitchell), X, at 02:02–2:19 (Dec. 9, 2025, at 14:56 PT), perma.cc/Q9CV-8FDN.

This defect alone drives a stake through the 2023 REMS. As the Fifth Circuit reasoned, because FAERS does not accurately reflect the number of adverse events and does not indicate mifepristone's safety profile, FDA's reliance on it was plainly arbitrary and an abuse of discretion. *Alliance II*, 78 F.4th at 250. Indeed, "FDA's decision to rely so heavily on data from FAERS 'runs counter to' the critical limitations associated with that data." *Id.*

But there is more: The deficiencies in the FAERS data *are of FDA's own making*. FDA had removed the requirement that abortion prescribers report serious adverse events other than death to FDA—this stripped the FAERS database of actual reporting of non-fatal adverse events. ECF 1-11 at 5–10, 28. Faced with that fact, the Fifth Circuit expressed disbelief that, "[a]fter eliminating th[e] adverse-event reporting requirement [in 2016], FDA turned around in 2021 and declared the absence of non-fatal adverse-event reports means mifepristone is 'safe.'" *Alliance I*, 2023 WL 2913725, at *17. "This ostrich's-head-in-the-sand approach is deeply troubling," it said, "especially on a record that, according to [FDA's] own documents, necessitates a REMS program, a 'Patient Agreement Form,' and a 'Black Box' warning." *Id.* "And it suggests FDA's actions are well outside the zone of reasonableness." *Id.* (citation modified). For those reasons, the Fifth Circuit emphasized that "[i]t's unreasonable for an agency to eliminate a reporting requirement for a thing and then use the resulting

absence of data to support its decision"—and thus "it [is] unlikely that plaintiffs' arbitrary-and-capricious challenges will fail on the merits." *Id.* at *17–18; *accord Alliance II*, 78 F.4th at 249–50.

Perhaps sensing this problem, FDA also considered adverse event data submitted by the drug manufacturers. But that data "was exactly the same as the data FDA obtained from FAERS," *Alliance II*, 78 F.4th at 250, suffered from the same flaws, and thus provided no independent justification for removing the in-person dispensing requirement. *See* ECF 1-10 at 28. And that was damning: "If anything, the fact that [mifepristone's manufacturer] submitted identical data tends to confirm the assertion that FDA lacked sufficient information[.]" *Alliance II*, 78 F.4th at 250.

As this straightforward analysis shows, Secretary Kennedy and Commissioner Makary were exactly right to admit that there was a "lack of adequate consideration" of the safety risks surrounding the decision to "remov[e] the in-person dispensing requirement." ECF 1-110 at 2. On the FAERS ground alone, Plaintiffs are all but certain to succeed on their challenge to the 2023 REMS—just as *Alliance I* and *Alliance II* held.

b. Scientific Literature. To add "extra icing on a cake already frosted," *Yates v. United States*, 574 U.S. 528, 557 (2015) (Kagan, J., dissenting), the 2023 REMS is independently arbitrary and capricious because no scientific literature actually "supported" removing the in-person dispensing requirement. *Alliance I*, 2023 WL 2913725, at *17; *see Alliance II*, 78 F.4th at 250 ("The second defect ...is that it relied on various literature relating to remote prescription of mifepristone—despite FDA's admission that the literature did not affirmatively support its position.").

FDA admitted that the studies it considered were "not adequate on their own to establish the safety of ...dispensing mifepristone by mail." ECF 1-10 at 36; *cf.* 21 U.S.C. § 355(d)(1) (directing FDA to reject drug applications that "do not include adequate tests"). The most FDA could say was that "the literature was only 'not inconsistent with [its] conclusion.'" *Alliance II*, 78 F.4th at 250; ECF 1-10

at 29. FDA thus conceded that "the studies neither confirmed nor rejected the idea that mifepristone would be safe if the in-person dispensing requirement were removed." *Alliance II*, 78 F.4th at 250.[2]

That makes this an extraordinarily easy arbitrary-and-capricious case: "Especially in light of the unreliability of the adverse-event data, it was not reasonable for FDA to depend on the published literature to support its decision." *Id.* "Courts must set aside agency action," the Fifth Circuit summed up, "where there are shortcomings in the agency's explanations or where no record evidence affirmatively makes' the agency's case." *Id.* (citation modified). "That is the case here":

> In the face of concededly limited data, and lacking more probative information from prescribers, FDA fell back on studies that were merely 'not inconsistent' with its intended conclusion. It did not refer to any literature that affirmatively supported the notion that mifepristone would remain safe and effective even without the in-person dispensing requirement.

Id. at 250–51. Accordingly, Plaintiffs "are likely to succeed in showing that [the 2023 REMS] violated the APA." *Id.*

2. The 2023 REMS violates the Comstock Act (Count II).

Although the Court need not proceed further, Judge Ho identified in *Alliance II* a separate reason why the 2023 REMS is unlawful—namely, that the 2023 REMS violates the Comstock Act and thus is not in accordance with law. *See Alliance II*, 78 F.4th at 267–70 (Ho, J., concurring in part and dissenting in part); *id.* at 251 n.8 (maj. op.) (declining to consider this issue); *see also Alliance I*, 2023 WL

[2] Two aspects of those studies warrant additional emphasis. *First*, it is not hard to see why FDA carefully qualified its statements about them—as the Fifth Circuit explained, "FDA recognized many significant limitations" in the studies, including that they could not be "generalize[d]" to the general United States population. *Alliance II*, 78 F.4th at 250. *Second*, if anything, the studies actually showed *increased* risk of harm from removing the in-person dispensing requirement. FDA admitted that "the literature suggests there may be more frequent ED/urgent care visits related to the use of mifepristone when dispensed by mail from the clinic." ECF 1-10 at 35. And in fact, the studies showed that as many as 1 in 8 women would need unplanned medical care if the in-person dispensing requirement were eliminated. *Id.* at 33–34. FDA's only response to these alarming figures was a nonanswer: that "there are no apparent increases in *other* significant adverse events related to mifepristone use." *Id.* at 36 (emphasis added). FDA never explained why the high rates of emergency-room visits were not themselves red flags. Nor did it identify what other serious adverse events it had in mind. Those defects, too, mean the 2023 REMS is well "outside the zone of reasonableness." *FCC v. Prometheus Radio Project*, 592 U.S. 414, 428 (2021).

2913725, at *20–21 (all but agreeing on the violation of the Comstock Act yet determining that the panel "need not definitively interpret the Comstock Act to resolve this stay application").

Through the Comstock Act, Congress prohibited the use of the mail or "any express company or other common carrier or interactive computer service" for "any drug, medicine, article, or thing designed, adapted, or intended for producing abortion." 18 U.S.C. §§ 1461–62. And FDA cannot authorize conduct that violates federal law. "The Administrative Procedure Act requires federal courts to set aside federal agency action that is 'not in accordance with law,' 5 U.S.C. § 706(2)(A)—which means, of course, *any* law, and not merely those laws that the agency itself is charged with administering." *FCC v. Next Wave Pers. Commc'ns, Inc.*, 537 U.S. 293, 300 (2003). Thus, under the plain terms of the Act, "the mailing of abortifacient drugs" is illegal, as is "us[ing] the internet to ship or receive abortifacients." *Alliance II*, 78 F.4th at 267 (concurring in part and dissenting in part). The 2023 REMS thus "violates the Comstock Act" because it "authorizes the dispensing of mifepristone 'through the mail ... or through a mail-order pharmacy.'" *Id.*

To date, FDA's sole defense has been to "argue that the Comstock Act does not mean what it says." *Alliance I*, 2023 WL 2913725, at *21. Yet as Judge Ho explained, the 2023 REMS is "precisely what the Comstock Act prohibits." *Alliance II*, 78 F.4th at 268 (concurring in part and dissenting in part). Indeed, whereas the 2021 Non-Enforcement Decision was only temporary, the 2023 REMS "doubles down on this violation by permanently eliminating the in-person dispensing requirement" and thus permitting doctors and others to "ship mifepristone to its users." *Id.* That is a direct violation of federal law. And thus, there can be no question that the 2023 REMS violates the APA.

B. The Remaining Stay Factors Favor Plaintiffs.

As the *Alliance II* panel determined, the remaining stay factors also favor a stay of the 2023 REMS. "[N]either FDA nor the public has any interest in enforcing a regulation that violates federal law"—and there is no dispute that the 2023 REMS violates federal law. *Id.* at 251 (maj. op.). "In this regard, the government/public-interest analysis collapses with the merits." *Id.* And because Plaintiffs "are likely to succeed on their claims as to" the 2023 REMS, "[i]t follows that FDA and the public will not be injured by an order staying th[at] likely unlawful action[ ]." *Id.* at 251–52. Indeed, that is

especially so because "the public interest is disserved by a drug that does not afford adequate protections to its users," which is the case here since FDA promulgated the 2023 REMS "without sufficient consideration of the effects those changes would have on patients." *Id.* at 253.

With nothing on FDA's side of the ledger, the mountain of irreparable harm to Plaintiffs carries the day. That includes hundreds of thousands of dollars in Medicaid costs that Plaintiff Louisiana is currently incurring due to the influx of mifepristone-induced abortions resulting in emergency room visits. *See infra* Section II.A(2). Those "[m]onetary harm[s] cannot be remedied where, as here, the defendant[s] [are] entitled to sovereign immunity." *Alliance II*, 78 F.4th at 251 (citing *Wages & White Lion*, 16 F.4th at 1142). Those "economic injuries" are thus, by definition, "irreparable." *Id.*; *accord Louisiana v. EEOC*, 705 F. Supp. 3d 643, 653 (W.D. La. 2024) (collecting cases). But "more fundamental" is irreparable harm in the form of the 2023 REMS's "interfere[nce] with [Louisiana's] ability to enforce [its] laws and implement the chosen public policies of [its] citizens." *Louisiana*, 705 F. Supp. 3d at 653. As discussed above and below, *see infra* Section II.A, the avowed purpose of the 2023 REMS was to override pro-life states' chosen public policies—to facilitate the mailing of FDA-approved mifepristone into those states so that abortion may persist with impunity. Louisiana suffers irreparable sovereign harm from that gambit every time an unborn Louisiana child loses her life through an illegal, mifepristone-induced abortion. "Because the principles of federalism afford the states a sovereign interest in creating and enforcing their own laws and public policy, [Louisiana] clearly" faces ongoing, irreparable harm from the 2023 REMS. *Louisiana*, 705 F. Supp. 3d at 654; *id.* at 663 (finding Article III standing and irreparable harm "[f]or the same reasons").

On top of this, the current and future harm for the unborn lives at stake is obvious. A life hanging in the balance presents perhaps "the most irreparable of harms." *Barr v. Lee*, 591 U.S. 979, 986 (2020) (Sotomayor, J., dissenting from vacatur of stay). Because Louisiana has a "legitimate interest[ ]" in the "preservation of prenatal life," *Dobbs*, 597 U.S. at 301—and because Louisiana law expressly protects "every unborn child [as] a human being from the moment of conception," *Louisiana*, 784 F. Supp. 3d at 895 n.10—there can be no question that the public interest favors staying the 2023 REMS and preventing the termination of these lives. The same goes for women like Rosalie who find

themselves in unspeakable situations where they are forced to end their babies' lives—and for women who willingly take the drug but wind up in an emergency room fighting for their own lives. These tragedies are possible only because the 2023 REMS authorizes the mailing of FDA-approved mifepristone into Louisiana. Thus, again, there can be no question that a stay is in the public interest.

C. A Universal § 705 Stay Is the Proper Preliminary Remedy.

1. Because the preliminary-relief factors are satisfied, the only remaining question is the proper form of preliminary relief. The Fifth Circuit spoke to that issue, too, in *Alliance II*, holding that a universal stay under 5 U.S.C. § 705 was warranted. The Fifth Circuit reached that conclusion by focusing on vacatur—the default relief in an APA action, which "effectively rescinds the unlawful agency action." *Alliance II*, 78 F.4th at 254. The Fifth Circuit explained that, "[i]n the same way that a preliminary injunction is the temporary form of a permanent injunction, a stay is the temporary form of vacatur." *Id.* Vacatur is a "'less drastic remedy'" than an injunction "because vacatur does not order the defendant to do anything; it only removes the source of the defendant's authority." *Id.* (quoting *Monsanto Co. v. Geertson Seed Farms*, 561 U.S. 139, 165 (2010); *accord Louisiana*, 784 F. Supp. 3d at 910 (an injunction "is neither required nor permitted" if vacatur is "sufficient to address the injury" (citation modified)). And "[k]eeping with the preliminary-permanent injunction analogy," a stay (rather than a preliminary injunction) is the least drastic temporary remedy because it simply "temporarily voids the challenged authority." *Alliance II*, 78 F.4th at 254.

Applying these principles, the *Alliance II* court held that the "appropriate form of relief" was a universal § 705 stay. *Id.* "Practically speaking," that meant FDA-approved mifepristone and its generic equivalent would be distributed "under the conditions that were in effect before" the challenged agency action. *Id.* FDA actions in 2016 also were at issue in *Alliance II*, and so the stay there returned FDA to pre-2016 conditions. *Id.* That meant "[t]he in-person dispensing requirements, and FDA's obligation to enforce them"—which existed before the stayed 2021 Non-Enforcement Decision and 2023 REMS—"will continue to apply." *Id.* The Fifth Circuit also made clear that this universal stay was preferable to a preliminary injunction because "a stay does not actively prohibit conduct, and so does not carry the same threat of contempt." *Id.*

The same route is appropriate here. A universal § 705 stay of the 2023 REMS is the least drastic remedy. Granting such relief would simply mean that the in-person dispensing requirement that existed for well over a decade before the 2021 Non-Enforcement Decision and 2023 REMS "will continue to apply." *Id.* The Court need only cite *Alliance II* to say as much.

2. The Supreme Court's recent decision on universal *injunctions* in *Trump v. CASA, Inc.*, 606 U.S. 831 (2025), has no bearing here. That is because the injunctions at issue in *CASA* were for strictly *equitable* relief—so a federal court's authority to issue universal injunctions was necessarily bounded by inherent and historical limitations on the courts' "equitable authority" "under the Judiciary Act of 1789." *Id.* at 841 & n.4; *see id.* (emphasizing that *CASA* "rests solely" on that specific statutory authority). By contrast, a § 705 remedy under the APA is *legal* relief authorized by Congress to temporarily address invalid agency actions. *See, e.g.*, *Griffin v. HM Fla.-ORL, LLC*, 144 S. Ct. 1, 2 n.1 (2023) (Kavanaugh, J., statement respecting the denial of application) (The APA "empower[s] the judiciary to act directly against the challenged agency action."). Thus, even after *CASA*, "[u]niversal remedies under the APA ... remain within Article III limits because they are legal, not equitable, remedies created by Congress." Ex. 11, T. Elliot Gaiser et al., *The Truth of Erasure: Universal Remedies for Universal Agency Actions*, U. Chi. L. Rev. Online (Aug. 28, 2024), at *11, perma.cc/Y4C6-G7ZX.

That is especially so because, as this Court has recognized, "[i]t is [ ] clear that the scope of ultimate relief under Section 706 is not party-restricted, but rather directs federal courts to wholly 'set aside' unlawful agency action." *Louisiana*, 784 F. Supp. 3d at 910 (citing *Career Colls. & Schs. of Tex. v. U.S. Dep't of Educ.*, 98 F.4th 220, 255 (5th Cir. 2024)). Because a § 705 stay is "the temporary form of vacatur," *Alliance II*, 78 F.4th at 254, a § 705 stay likewise is not party-restricted. Accordingly, the Court need only enter the same universal § 705 stay of the 2023 REMS that the *Alliance II* Court entered to resolve the case at this preliminary stage.

II. Plaintiffs Have Article III Standing.

The only remaining question is whether Plaintiffs here, unlike the *Alliance* plaintiffs, have Article III standing to challenge the 2023 REMS. "For the same reasons" they have established irreparable harm, they have Article III standing. *Louisiana*, 705 F. Supp. 3d at 663. A plaintiff has

standing when she shows "(i) that she has suffered or likely will suffer an injury in fact, (ii) that the injury likely was caused or will be caused by the defendant, and (iii) that the injury likely would be redressed by the requested judicial relief." *Alliance*, 602 U.S. at 380. Plaintiffs have suffered sovereign, pocketbook, and bodily harms from the 2023 REMS's authorization of mail-order abortions occurring in Louisiana. Those injuries are directly traceable to—and indeed are the intended consequence of—FDA's removal of the in-person dispensing requirement. And those injuries are redressable by a decision vacating the 2023 REMS. This easily satisfies Article III standing.

A. The 2023 REMS Causes Plaintiffs' Current and Future Injuries in Fact.

Start with injury-in-fact and causation, which, in this case, go hand-in-hand. In *Diamond Alternative Energy, LLC v. EPA*, 606 U.S. 100 (2025), the Supreme Court addressed a suit where "regulated third parties not before the court" would "likely react to the government regulation ... in predictable ways that will likely cause ... the plaintiff's injury." *Id.* at 112 (citation modified). In such suits, the plaintiff, though technically not a regulated entity, nonetheless "might be considered an object of the [ ] regulation[ ]"—and thus, the plaintiff's Article III standing is obvious. *Id.* at 114–15. That is especially so where the plaintiff's injuries are, in fact, "the whole point of the regulation[ ]." *Id.*

That is the case here. Following *Dobbs*, President Biden knew that pro-life states like Louisiana would prohibit abortion with narrow exceptions. So, through the 2023 REMS, his FDA eliminated the in-person dispensing requirement for mifepristone in an avowed effort to generate mail-order abortions in pro-life states. The direct "objects" of that agency action include mifepristone-prescribing doctors in states like New York and California—"regulated parties not before the court" who are acting "in predictable ways" by prescribing and mailing mifepristone into pro-life states to cause illegal abortions. *Id.* That is not just the predictable consequence of the 2023 REMS but "the whole point" of it: to override the sovereign prerogatives of pro-life states by "ensur[ing] that mifepristone is as widely accessible as possible," "including when prescribed through telehealth and sent by mail." ECF 1-47 at 3. And thus, pro-life states like Louisiana are the "object of the regulation[ ]." *Diamond*, 606 U.S. at 115. Indeed they are the true "targets." *Id.* at 120.

Given this, there is no question that Plaintiffs have suffered Article III injuries caused by the 2023 REMS. Two injuries are most obvious. First, Louisiana has suffered and will continue to suffer quintessential sovereign harms. Second, the State has endured and will continue to endure classic monetary harm. For these reasons, Plaintiffs satisfy the injury-in-fact and traceability requirements.

1. The 2023 REMS causes sovereign harm by facilitating illegal abortions in Louisiana.

It is difficult to imagine a federal action that is more "destructive of state sovereignty" than the 2023 REMS. *Louisiana*, 784 F. Supp. 3d at 901 (citation modified). "Generally, states have an interest in 'the exercise of sovereign power over individuals and entities within the relevant jurisdiction—this involves the power to create and enforce a legal code, both civil and criminal.'" *Louisiana*, 705 F. Supp. 3d at 653. Central among the sorts of "federal intrusions" sufficient to give a state standing is "federal interference with the enforcement of state law." *Id.* (citation modified). "Because a state alone has the right to create and enforce its legal code, only the state has the kind of direct stake necessary to satisfy standing in defending the standards embodied in that code." *Id.* (citation modified).

So it is here. As this Court recently recounted, the people of Louisiana, "through the democratic process, have unambiguously expressed their opposition to purely elective abortions by passing laws prohibiting the same." *Id.*; *accord Louisiana*, 784 F. Supp. 3d at 901. That policy is "expressly set forth" in Louisiana law. *Louisiana*, 784 F. Supp. 3d at 895 n.10. And that law protects "every unborn child ... from the moment of conception" as "a legal person." La. R.S. 40:1061.1(A)(1). Abortion is prohibited except if "determined to be medically necessary to prevent the death or substantial risk of death of the mother," with other narrow exceptions. *Louisiana*, 784 F. Supp. 3d at 895 n.10.

This case presents extreme "federal interference" with Louisiana's enforcement of that policy. President Biden's—and his FDA's—avowed purpose in promulgating the 2023 REMS was to override that policy in all pro-life states that sought to "ban or severely restrict access to medication for reproductive health care" after *Dobbs*. ECF 1-47 at 3; ECF 1-59 at 2; *see supra* pp. 3–4 (cataloguing

statements from the Biden Administration). "[S]tates may not ban mifepristone," President Biden threatened before promising "to allow mifepristone to continue to be prescribed by telehealth and sent by mail." ECF 1-60 at 2–3. Nobody pretended otherwise, including Senator Elizabeth Warren and her Democrat colleagues who demanded the 2023 REMS. The 2023 REMS was a direct response to pro-life states' "new restrictions" and a belief that "it is more important than ever [to] take immediate steps to expand access to medication abortion ... *across the nation*." Ex. 12, Letter from Elizabeth Warren et al. to FDA (Nov. 18, 2022), perma.cc/Y6RB-XDPT (emphasis added).

It is no wonder then that the 2023 REMS has functionally overridden Louisiana's pro-life laws, just as the Biden Administration intended. Freed from the in-person dispensing requirement, faceless doctors from states like New York and California are prescribing and mailing mifepristone into Louisiana with impunity—to the tune of 800, 900, and now 1,000 abortions a month. *See supra* pp. 1–2, 4–5. Each abortion is an independent violation of Louisiana law. *Supra* p.3 (collecting statutes). Each life lost is an independent abrogation of Louisiana's legislative policy to protect "every unborn child ... from the moment of conception." La. R.S. 40:1061.1(A)(1). Again, it is difficult to imagine a scheme that is more destructive of Louisiana's sovereignty—and that is a quintessential injury-in-fact. And Louisiana's defense of its sovereignty has itself resulted in monetary harm and depletion of resources, including through investigations of and warrants for Dr. Carpenter and Dr. Coeytaux regarding their violations of Louisiana's law.

Though Defendants themselves are not directly mailing mifepristone into Louisiana, the 2023 REMS makes this assault on pro-life states possible. But for the 2023 REMS, out-of-state doctors could not—without violating federal law—mail FDA-approved brands of mifepristone into Louisiana. That was "the entire purpose" of the 2023 REMS, *Diamond*, 606 U.S. at 112: to remove the in-person dispensing requirement so that it may be "sent by mail." ECF 1-47 at 3. Nor is it an answer to say that the 2023 REMS "is not the sole cause of the State's injury." *Texas v. United States*, 50 F.4th 498, 519 (5th Cir. 2022). Article III does not impose a "sole cause" standard. There is no question that the 2023 REMS "has exacerbated" Louisiana's injury, and "[t]hat is sufficient" for standing. *Id.* The 2023 REMS is why a flood of mifepristone-induced abortions are occurring in a state that bans

them—and indeed, that is why the Biden Administration "target[ed]," *Diamond*, 606 U.S. at 120, pro-life states in this way. That is a clear example of "federal interference with the enforcement of state law." *Louisiana*, 705 F. Supp. 3d at 653.[3]

2. The 2023 REMS causes pocketbook harm by directly increasing Louisiana's Medicaid costs.

Louisiana also suffers basic pocketbook injuries from the 2023 REMS: the loss of hundreds of thousands of dollars paid through Louisiana Medicaid for care related to FDA-approved mifepristone. Economic losses are "obvious" harms, *TransUnion LLC v. Ramirez*, 594 U.S. 413, 425 (2021), because "[m]onetary costs are of course an injury," *United States v. Texas*, 599 U.S. 670, 676 (2023). Even "one dollar's worth of harm" counts. *Id.* at 688 (Gorsuch, J., concurring); *accord Tex. Corn Producers v. EPA*, 141 F.4th 687, 696–97 (5th Cir. 2025) (same). As the Fifth Circuit has repeatedly held, increased Medicaid costs due to a federal agency action are plainly "a pocketbook-injury." *E.g.*, *Texas v. United States*, 126 F.4th 392, 408, 413 n.26, 414–15 (5th Cir. 2025) (citing *Texas*, 50 F.4th 498); *accord id.* at 411 n.22 (collecting cases). In one case, the Fifth Circuit explained that because Texas had to provide Medicaid services to illegal aliens covered by the challenged Deferred Action for Childhood Arrivals (DACA) program, that program increased the Medicaid costs that Texas had to cover. *Texas*, 126 F.4th at 408 (citation modified); *Texas*, 50 F.4th at 517–18. Those increased costs constituted "an 'injury in fact.'" *Id.* (quoting *Texas*, 50 F.4th at 519).[4]

All the same here. Under the Medicaid statute, Louisiana is required to cover medical assistance for eligible pregnant women, including inpatient and outpatient hospital services. *See* 42 U.S.C. § 1396d(a)(viii); *id.* § 1396d(a)(1), (2); *see also Medina v. Planned Parenthood S. Atl.*, 606 U.S. 357, 363 (2025) (citation modified) ("Congress created Medicaid in 1965 to subsidize state efforts to

[3] The Biden Administration said that the 2023 REMS preempts Louisiana's laws on abortion. *See* ECF 1, ¶¶ 116–19; ECF 1-61 at 8. That view is dead wrong. *See GenBioPro, Inc. v. Raynes*, 144 F.4th 258 (4th Cir. 2025). But any purported preemption would independently give Louisiana standing. *Louisiana*, 705 F. Supp. 3d at 653 (citing federal preemption of state law as a basis for a state's standing).

[4] In the *Texas* litigation, the Fifth Circuit emphasized that this standing analysis holds regardless of whether Texas was entitled to "special solicitude" in the standing analysis. 126 F.4th at 414. Here, as there, Plaintiff Louisiana does not need "special solicitude" to establish standing.

provide healthcare to families and individuals whose income and resources are insufficient to meet the costs of medical services."). Louisiana "must" pay at least some of the total Medicaid costs, *id.* § 1396a(a)(2), while the federal government will pay between 50% and 83%, *id.* § 1396d(b).

The 2023 REMS is undoubtedly imposing a Medicaid burden on Louisiana. *First*, President Biden's FDA believed that "state actions" restricting abortion would "be felt most acutely by underserved communities, including those with low incomes"—thus, FDA envisioned that the 2023 REMS would particularly benefit low-income individuals. ECF 1-61 at 7–8. *Second*, as the Fifth Circuit previously held, the federal government's "own documents" show that "emergency room care is statistically certain" in mifepristone cases. *Alliance I*, 2023 WL 2913725, at *10. In fact, the FDA label states that roughly 1 in 25 (or 4% of) women who receive an in-person visit with a medical provider and take mifepristone *as directed* will end up in the emergency room. ECF 1-9 at 8–9, 16. The label even features a black box warning that mifepristone can cause "[s]erious and sometimes fatal infections and bleeding" requiring ER care. *Id.* at 2. Real-world data suggest that the emergency-room-visit and hospitalization rate may be as high as 11%—plus dispensing mifepristone by mail could raise that rate even higher. *See* ECF 1-13 at 2; Ex. 4, Wallace et al., *supra*, at 111117; ECF 1-10 at 34–35; *see also* ECF 1-50 at 75 ("[T]he literature suggests there may be more frequent ED/urgent care visits related to the use of mifepristone when dispensed by mail from the clinic[.]"). And that was *before* the Biden Administration ended the in-person requirement—removing the sole opportunity to screen women for an ectopic pregnancy and verify gestational age. *See* Ex. 21, Francis Decl. ¶¶ 22–23, 41.

These basic facts demonstrate the increased Medicaid costs imposed on Louisiana by the 2023 REMS. Take March 2025, for example, when roughly 1,000 mail-order abortions occurred in Louisiana. *Supra* pp. 1, 5. FDA's own label concedes that at least 40 (4%) of those abortions resulted in emergency room visits—and the actual number of emergency room visits and hospitalizations may be as high 110 (11%). Further, according to the federal government, the women involved most likely have low incomes and thus are almost certainly are on Medicaid. *See* Ex. 22, New Decl. at 2–3. So in March 2025 alone, Louisiana faced increased Medicaid costs for many—if not most—of the 40 to 110 mifepristone-induced abortions that required emergency-room visits and hospitalizations.

This is not hypothetical—this is real world "commonsense economic[s]." *Diamond*, 606 U.S. at 116. As a supporting declaration shows, the Louisiana Department of Health has identified over $92,000 in Medicaid costs incurred for emergency room care and hospitalization required because of just two mifepristone-induced abortions in 2025. Ex. 20, Willis Decl. ¶¶ 11–12. And those costs are just the tip of the iceberg, underscoring that the hundreds of mifepristone-induced abortions that are occurring every month in Louisiana are leading directly to increased Medicaid costs for Louisiana. *See id.* ¶¶ 10, 13–15*; see also, e.g.*, Ex. 23, Parise Decl. ¶¶ 14–16; Ex. 19, Richard Decl. ¶¶ 7–8 (attesting that Louisiana women on Medicaid have been rushed to emergency rooms due to adverse events caused by mifepristone); *see also* ECF 1-14 at 4 (Medicaid-specific study finding significantly higher ER-visit acuity following chemical abortion). As of January 1, 2023 (the most recent data of its kind available), 534,294 women from ages 15 to 44 were enrolled in Louisiana Medicaid and 538,139 women from ages 15 to 44 were recipients of Louisiana Medicaid. Ex. 20, Willis Decl. ¶ 6. And women on Medicaid are more likely to get abortions than women who are not enrolled. Ex. 22, New Decl. 2–3.

To be sure, it is difficult to quantify *the full extent* of this monetary harm. The data Louisiana receives is almost certainly an underrepresentation of the actual state costs incurred due to the illegal importation of mifepristone. *See* Ex. 20, Willis Decl. ¶¶ 14–15. Women may not admit that they took the drug, and they may present at the emergency room with an apparent miscarriage (which Louisiana Medicaid covers) after they have ingested mifepristone. *See, e.g.*, Ex. 23, Parise Decl. ¶¶ 15–17; Ex. 21, Francis Decl. ¶ 37; Ex. 20, Willis Decl. ¶ 14. But whether Louisiana's harm is tens of thousands of dollars or millions of dollars, nobody can dispute that Louisiana's financial harm is more than zero. *Cf. Texas*, 50 F.4th at 517–18 ("The record does not indicate precisely what portion of all costs for illegal aliens is spent on DACA recipients, but no one disputes that some are."). That is all that is necessary to "demonstrat[e] injury in fact" directly caused by the 2023 REMS. *Id.* at 517.[5]

[5] For this Court to have jurisdiction, only Louisiana needs standing. *See Town of Chester v. Laroe Ests., Inc.*, 581 U.S. 433, 438–41 (2017). But Rosalie also has standing because FDA turned a blind eye to women like her. If FDA had never authorized mail-order abortion drugs, Rosalie's then-boyfriend could not have ordered FDA-approved abortion drugs and coerced her to take the drugs against her

B. These Injuries Are Redressable by a Favorable Decision.

For the same reasons, a decision from this Court vacating the 2023 REMS would redress these injuries. As the Fifth Circuit explained, vacating the 2023 REMS means that "[t]he in-person dispensing requirements, and FDA's obligation to enforce them, will continue to apply." *Alliance II*, 78 F.4th at 254. With the in-person dispensing requirement restored, FDA would not authorize doctors in States like New York and California to prescribe and mail mifepristone into pro-life states like Louisiana—and without that flood of mifepristone, Louisiana's monthly average of nearly 1,000 abortions per month will come crashing down.[6] That, in turn, would redress the harms above.

As to the monetary harms from increased Medicaid costs, common sense dictates that as the number of mifepristone-induced abortions decreases, so too will the number of Medicaid-implicated emergency room visits caused by such abortions. *See* Ex. 20, Willis Decl. ¶ 15. As a result, Louisiana's increased Medicaid burden will be alleviated. That was precisely the Fifth Circuit's reasoning embraced in *Texas*, when it said that Texas's increased Medicaid costs "would be partially alleviated if DACA were enjoined." 126 F.4th at 413.

Likewise, as to Louisiana's sovereign harms, it is obvious that, if mailing mifepristone into Louisiana becomes no longer authorized by FDA again (as before the 2023 REMS), the number of

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will. ECF 1-92 at ¶¶ 5–16. The doctor who sent the drugs could prescribe them because FDA had authorized it. *See* Ex. 13, Aria Bendix, *Why Abortions Rose After* Roe *Was Overturned*, NBC News (Nov. 26, 2:00 PT), perma.cc/QP3F-U82N (describing how Dr. Remy Coeytaux partners with A Safe Choice to dispense FDA-approved mifepristone); Ex. 14, Complaint, *Rodriguez v. Coeytaux*, No. 3:25-cv-00225, (S.D. Tex. July 20, 2025), ECF 1 to 1-2 (describing how Dr. Remy Coeytaux partners with Aid Access to dispense FDA-approved mifepristone); Ex. 15, Notice of Cease and Desist from Ken Paxton, Att'y Gen. of Tex., to Remy Coeytaux (Aug. 14, 2025), perma.cc/P7NE-7RTH (same). Rosalie's bodily injury, pain and suffering, mental anguish, and her lost child are thus injuries-in-fact for standing. *Rideau v. Keller Indep. Sch. Dist.*, 819 F.3d 155, 163 (5th Cir. 2016). Rosalie should never be subject to mail-order abortion-drug coercion again—and she is entitled to relief to protect herself and her future children.

[6] Under the pre-2023 REMS, sponsors of mifepristone were required to "[e]nsure that their mifepristone [wa]s available to be dispensed to patients only in clinics, medical offices and hospitals," Ex. 16, FDA, REMS Single Shared System for Mifepristone 200MG (May 2021), perma.cc/W522-9F7G, or they risked severe "enforcement action[s] such as product seizure, injunction or civil money penalties," Ex. 17, *REMS Compliance Program*, FDA (Sep. 22, 2022), perma.cc/KE9P-UKGU. Noncompliant prescribers would face decertification and lose access to mifepristone. *Id.*

mifepristone-induced abortions in Louisiana will dramatically decrease. So too the number of independent violations of Louisiana law, thereby mitigating the ongoing destruction of Louisiana's sovereignty.

It is no answer to say that, even if the in-person dispensing requirement were restored, rebellious doctors could choose to violate federal law and continue mailing mifepristone into Louisiana. *Diamond* squarely forecloses that reasoning. As the Court recognized, "the fact that a regulation was designed to produce a particular effect on the market ordinarily means that the likely result of vacating the regulation would be to reduce that effect on the market." 606 U.S. at 117. The same principle applies here: The 2023 REMS was designed to facilitate mail-order abortions in pro-life states. Accordingly, vacating the REMS would have "the likely result of ... reduc[ing] that effect," if not eliminating it entirely, in pro-life states. *Id.*

One final note underscores the strength of Plaintiffs' redressability argument here: The emergence of shield laws designed to permit anonymous mailing of mifepristone into pro-life states is unquestionably a problem for pro-life states attempting to enforce their policies and laws. But those shield laws are meaningless unless such mailing is FDA-approved to begin with. Staying the 2023 REMS, and thereby restoring the in-person dispensing requirement, would ensure that such mailing is unauthorized and unlawful, leaving no role for shield laws. In that way, staying this concededly unlawful agency action is perhaps the most important step toward restoring Louisiana's and all other pro-life states' sovereignty. In a world where the prevailing sentiment among pro-abortion advocates is to thumb their noses at pro-life laws—"'We really don't change things unless we're legally required to,'" ECF 1-106 at 2—a stay (and then vacatur) of the 2023 REMS is necessary.

CONCLUSION

The Court should stay the 2023 REMS under 5 U.S.C. § 705 and direct that "[t]he in-person dispensing requirement[ ], and FDA's obligation to enforce [it], will continue to apply." *Alliance II*, 78 F.4th at 254. In the alternative, Plaintiffs request a preliminary injunction under 5 U.S.C. § 705 against FDA's enforcement of the 2023 REMS.

Respectfully submitted this 17th day of December, 2025.

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IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF LOUISIANA
LAFAYETTE DIVISION

THE STATE OF LOUISIANA, *et al.*, *Plaintiffs*, v. U.S. FOOD AND DRUG ADMINISTRATION, *et al.*, *Defendants.*	No. 6:25-cv-01491-DCJ-DJA

DEFENDANTS' MOTION TO STAY THE CASE

Defendants respectfully move that this Court stay all proceedings in this matter pursuant to its inherent authority while the U.S. Food and Drug Administration reviews the mifepristone Risk Evaluation and Mitigation Strategy. The grounds for this motion are fully set forth in the accompanying memorandum of law. If the Court grants this motion, Defendants will file a status report within 14 days of any decision concerning whether modifications to the REMS are necessary.

January 27, 2026

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CERTIFICATE OF CONFERENCE

I hereby certify that, pursuant to Local Rule 7.4.1, counsel conferred in good faith regarding the relief sought in this motion. Plaintiffs oppose this motion. One of the parties that has given notice of intent to intervene, Danco Laboratories, reports through counsel that "Danco will respond to the Federal Defendants' motion to stay as part of its own forthcoming motion to intervene, after Danco has had an opportunity to review Federal Defendants' filing." The other party that has given notice of intent to intervene, GenBioPro, likewise has advised through counsel "that it will need to review the Government's motion to determine what position, if any, it takes on the requested stay, and will address that issue in its upcoming motion to intervene."

/s/ Noah T. Katzen
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IN THE UNITED STATES DISTRICT COURT
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DEFENDANTS' MEMORANDUM IN SUPPORT OF MOTION TO STAY THE CASE AND IN RESPONSE TO PLAINTIFFS' MOTION FOR PRELIMINARY RELIEF

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TABLE OF CONTENTS

Introduction 1

Background 5

Standard of Review 8

Argument 9

I. The Court Should Stay This Case And Deny Plaintiffs' Motion Pending FDA's Review of The Mifepristone REMS. 9

II. Plaintiffs Would Not Be Prejudiced By A Stay Pending FDA's Review of The Mifepristone REMS Because They Are Not Suffering Ongoing Harm. 13

A. Louisiana lacks standing 13

1. The 2023 REMS Modification does not cause "sovereign harm" 14

2. Medicaid-based economic harm is too attenuated to establish standing 16

3. Louisiana cannot sue the Federal Government as *parens patriae* 18

B. Ms. Markezich lacks standing 19

Conclusion 20

TABLE OF AUTHORITIES

Cases

Ali v. Quarterman,
607 F.3d 1046 (5th Cir. 2010) 8, 10

All. for Hippocratic Med. v. FDA,
78 F.4th 210 (5th Cir. 2023) 1,11

Am. Coll. of Obstetricians & Gynecologists v. FDA,
472 F. Supp. 3d 183 (D. Md. 2020) 6

Amid, Inc. v. Medic Alert Found. U.S., Inc.,
241 F. Supp. 3d 788 (S.D. Tex. 2017) 12

Chelius v. Becerra,
No. 1:17-cv-493-JAO-RT (D. Haw. May 7, 2021) 12, 13

City of Dallas v. Delta Air Lines, Inc.,
847 F.3d 279 (5th Cir. 2017) 11

City of L.A. v. Lyons,
461 U.S. 96 (1983) 19

Clinton v. Jones,
520 U.S. 681 (1997) 8

DaimlerChrysler Corp. v. Cuno,
547 U.S. 332 (2006) 9

Dennis Melancon, Inc. v. City of New Orleans,
703 F.3d 262 (5th Cir. 2012) 9

Diamond Alternative Energy, LLC v. EPA,
606 U.S. 100 (2025) 16

Dobbs v. Jackson Women's Health Org.,
597 U.S. 215 (2022) 5, 14

FDA v. All. for Hippocratic Med.,
No. 22A902, 143 S. Ct. 1075 (Apr. 21, 2023) (mem.) 12

FDA v. All. for Hippocratic Med.,
602 U.S. 367 (2024) ..... *passim*

FDA v. Am. Coll. of Obstetricians & Gynecologists,
141 S. Ct. 578 (2021) 6

GenBioPro, Inc. v. Raynes,
144 F.4th 258 (4th Cir. 2025) 14

Haaland v. Brackeen,
599 U.S. 255 (2023) 18

Landis v. N. Am. Co.,
299 U.S. 248 (1936) 8, 9

Louisiana v. EEOC,
784 F. Supp. 3d 886 (W.D. La. 2025) 15

Missouri v. FDA,
Case No. 2:22-cv-223-Z, 2025 WL 2825980 (N.D. Tex. Sept. 30, 2025) 8

Murthy v. Missouri,
603 U.S. 43 (2024) 13, 18

Niz-Chavez v. Garland,
593 U.S. 155 (2021) 11

Nken v. Holder,
556 U.S. 418 (2009) 9

Parker v. Dacres,
130 U.S. 43 (1889) 12

Peak v. Dist. of Columbia,
No. 06-cv-0373, 2006 WL 8445985 (D.D.C. Mar. 20, 2006) 10

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Civ. No. 17-00493 JAO-RT, 2025 WL 3101785 (D. Haw. Oct. 30, 2025) 2, 7

Renne v. Geary,
501 U.S. 312 (1991) 9

Ricci v. Chi. Mercantile Exch.,
409 U.S. 289 (1973) 9

Ridgely v. FEMA,
512 F.3d 727 (5th Cir. 2008) 9

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939 F.3d 649 (5th Cir. 2019) 10

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979 F.3d 319 (5th Cir. 2020) 9

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No. 13-1253-P, 2014 WL 6455794 (W.D. La. Nov. 17, 2014) 12

Texas v. U.S. Dep't of Health & Hum. Servs.,
770 F. Supp. 3d 940 (E.D. Tex. 2025) 9

Texas v. United States,
50 F.4th 498 (5th Cir. 2022) 17

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United States v. Texas,
599 U.S. 670 (2023) 15

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108 F.4th 1163 (9th Cir. 2024) 15, 17, 18, 19

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668 F. Supp. 3d 1125 (E.D. Wash. 2023) 4

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No. 1:23-cv-3026-TOR, 2025 WL 1888794 (E.D. Wash. 2025) 2

Statutes

5 U.S.C. § 705 ..... 9, 11, 12

21 U.S.C. § 355-1(g)(4)(B) 6

21 U.S.C. § 355(a) 5

Regulations

21 C.F.R. § 314.520 5

73 Fed. Reg. 16313 (Mar. 27, 2008) 6

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Webster's New International Dictionary (1928) 11

INTRODUCTION

Protecting the health and safety of pregnant women is of paramount importance. To that end, on September 19, 2025, the Secretary of Health and Human Services and the Commissioner of Food and Drugs announced that the Food and Drug Administration (FDA) is reviewing the Risk Evaluation and Mitigation Strategy (REMS) for mifepristone, a drug approved for medical abortion. ECF No. 1-110 (Letter to State Attorneys General (Sept. 19, 2025)). The Secretary and the Commissioner explained that this review—which will include a study undertaken by FDA itself—is "informed by the lack of adequate consideration underlying prior REMS approvals," including a 2023 modification to the mifepristone REMS that approved the removal of an in-person dispensing requirement. *Id.* at 1. FDA's review is rooted in the agency's commitment "to protecting the health and safety of pregnant women" and "ensur[ing] . . . decisions are grounded in Gold Standard Science and rigorous, transparent, and objective evidence." *Id.* at 2.

FDA's decision to review the REMS for mifepristone is consistent with the concerns about removing the in-person dispensing requirement foreshadowed by the Fifth Circuit in *Alliance for Hippocratic Medicine v. FDA*. *See* 78 F.4th 210, 249-51 (5th Cir. 2023), *rev'd on other grounds*, 602 U.S. 367 (2024). Although ultimately reversed on jurisdictional grounds, the Fifth Circuit held that, in calling for the removal of the in-person dispensing requirement in December 2021, FDA erroneously "gave dispositive weight to adverse-event data in [the FDA Adverse Event Reporting System]," despite limitations of that data—including the fact that, as a result of action FDA took in 2016,

the REMS no longer requires prescribers to report non-fatal serious adverse events. *Id.* at 249. The court also faulted FDA's reliance on studies that had "significant limitations" and "did not affirmatively support" eliminating the in-person dispensing requirement. *Id.* at 250.

In deciding to review the REMS for mifepristone, the FDA recognized that the validity of FDA's restrictions on mifepristone is a hotly contested legal and scientific issue that has been the subject of litigation for many years. Louisiana and Ms. Markezich are not the only plaintiffs to have challenged the current requirements for dispensing mifepristone. Indeed, five other states are challenging either the approval of mifepristone or subsequent actions easing restrictions. *See Missouri v. FDA*, No. 4:25-cv-1580-CMS (E.D. Mo.) (Missouri, Idaho, and Kansas challenging actions easing REMS restrictions); *Florida v. FDA*, No. 7:25-cv-126-O (N.D. Tex.) (Florida and Texas challenging approval of mifepristone and actions easing REMS restrictions). Still other plaintiffs have challenged FDA's restrictions as too burdensome. *Purcell v. Kennedy*, Civ. No. 17-00493 JAO-RT, 2025 WL 3101785, at *28 (D. Haw. Oct. 30, 2025) (plaintiffs challenged REMS as too restrictive); *Washington v. FDA*, No. 1:23-cv-3026-TOR, 2025 WL 1888794 (E.D. Wash. 2025) (same); *Whole Woman's Health All. v. FDA*, No. 3:23-cv-00019 (W.D. Va.) (same). And aside from litigation, before the FDA are numerous citizen petitions—citing voluminous material and seeking mutually inconsistent relief, such as suspending approval of the drug, restoring previous REMS requirements, or eliminating the REMS entirely. *See infra* n.3.

Given this widespread debate over the safety of mifepristone, FDA has concluded that the best path forward is for the agency to reconsider the restrictions on mifepristone based on all the evidence before the agency. As noted above, that evidence will include FDA's own study. FDA has emphasized that it "is taking care to do this study properly and in the right way." FDA, Questions and Answers on Mifepristone for Medical Termination of Pregnancy Through Ten Weeks Gestation.[1] At this time, "FDA continues to work on the collection of the robust and timely data that is necessary for a well-controlled study with adequate statistical power." *Id.* Although studies like these "often take approximately a year or more to conduct," FDA's current plan is to complete the study "sooner than that timeframe." *Id.* And once FDA has analyzed the data from that study (as well as all other evidence before the agency), it will decide whether "substantive changes to the REMS" are necessary. *Id.*

Plaintiffs now threaten to short circuit the agency's orderly review and study of the safety risks of mifepristone by asking this Court for an immediate stay of the 2023 REMS Modification approved three years ago. They would have this Court set aside the 2023 REMS Modification—all without the benefit of FDA's expertise, and even as the agency is already reconsidering the matter in its review. And Plaintiffs' requested relief may prove as unnecessary as it is disruptive, if FDA ultimately decides that the in-person dispensing requirement must be restored.

[1] https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/questions-and-answers-mifepristone-medical-termination-pregnancy-through-ten-weeks-gestation (item No. 37) (accessed Jan. 27, 2026).

Moreover, awarding preliminary relief to these Plaintiffs could easily prompt other plaintiffs to seek a conflicting injunction that would sow administrative and judicial chaos. If this Court were to grant Plaintiffs' motion, the plaintiffs in *Whole Woman's Health Alliance* could promptly seek conflicting relief, which would only add to FDA's burden and complicate any future modification efforts. The prospect of conflicting injunctions is hardly far-fetched. In 2023, literally minutes after the Northern District of Texas in *Alliance for Hippocratic Medicine* stayed FDA's approval of mifepristone, the Eastern District of Washington prohibited FDA from altering the status quo in certain States. *Washington v. FDA*, 668 F. Supp. 3d 1125, 1144 (E.D. Wash. 2023), *vacated*, No. 1:23-cv-3026-TOR, 2025 WL 1888794 (E.D. Wash. 2025).

To prevent that disruption, the Court should exercise its inherent authority to stay this litigation pending the outcome of FDA's review of the mifepristone REMS. FDA's review will necessarily result in a new agency decision that could supersede the 2023 REMS Modification, obviating any need to consider the merits of Plaintiffs' arguments challenging the validity of the 2023 REMS Modification. Any party adversely affected by the new agency decision on mifepristone may seek judicial review at that time. And in the event of a further REMS modification, adherence to FDA's normal process will create far less disruption than the abrupt, judicially imposed change sought by Plaintiffs.

Deferring judicial review until FDA's review is complete will not prejudice Plaintiffs. Louisiana waited nearly three years to challenge the 2023 REMS Modification, and Rosalie Markezich does not identify any ongoing or imminent injury from which

she needs relief. Indeed, although Plaintiffs have alleged the 2023 REMS Modification causes serious harms to women, Plaintiffs lack standing to challenge that modification. Louisiana suffers no sovereign injury because it remains free to make and enforce its pro-life policies after *Dobbs v. Jackson Women's Health Org.*, 597 U.S. 215 (2022). Nor are Defendants standing in the way of Louisiana enforcing its abortion laws against out-of-state prescribers of mifepristone. The State's allegations about Medicaid costs and "quasi-sovereign" interests also do not create any case or controversy between Louisiana and FDA. And the tragic injury that Ms. Markezich alleges she suffered in the past due to the independent actions of her former boyfriend is neither traceable to FDA nor redressable by the prospective relief Plaintiffs seek. For all those reasons, the Court should stay this case until after FDA completes its review of the mifepristone REMS and deny Plaintiffs' motion without prejudice.

BACKGROUND

The Federal Food, Drug, and Cosmetic Act generally prohibits introducing a "new drug" into interstate commerce without FDA approval. 21 U.S.C. § 355(a). In 2000, FDA approved mifepristone for medical abortion, subject to certain restrictions to assure safe use. *See All. for Hippocratic Med.*, 602 U.S. at 376; 21 C.F.R. § 314.520.[2] Since 2008, those restrictions have been part of a REMS. *See* Identification of Drug and Biological Products Deemed to Have Risk Evaluation and Mitigation Strategies for

[2] FDA has separately approved another manufacturer's mifepristone product, Korlym, for the treatment of Cushing's syndrome. Plaintiffs do not challenge FDA's actions regarding Korlym, and all references to mifepristone throughout this brief refer to the drug approved for medical abortion (Mifeprex and the approved generic equivalents).

Purposes of the Food and Drug Administration Amendments Act of 2007, 73 Fed. Reg. 16313, 16314 (Mar. 27, 2008).

For most of the drug's history, mifepristone's restrictions included an "in-person dispensing requirement," ensuring that the drug could be dispensed only in "clinics, medical offices, and hospitals, by or under the supervision of a certified prescriber." *See, e.g.*, ECF No. 20-16 (REMS Single Shared System for Mifepristone 200MG (May 2021)) at 2. In July 2020, a district court preliminarily enjoined enforcement of the in-person dispensing requirement during the COVID-19 pandemic. *Am. Coll. of Obstetricians & Gynecologists v. FDA*, 472 F. Supp. 3d 183, 233 (D. Md. 2020). The Supreme Court stayed that injunction pending appeal in January 2021. *FDA v. Am. Coll. of Obstetricians & Gynecologists*, 141 S. Ct. 578 (2021) (mem.). ECF No. 1 (Compl.) ¶¶ 49-50. But in April 2021, FDA announced that it would not enforce the in-person dispensing requirement during the COVID-19 public health emergency, and the following month it announced it would conduct a review of the REMS. *See* ECF No. 1-10 (2021 FDA Letter to AAPLOG, *et al*.) at 5 & 6 n.10.

On December 16, 2021, the agency directed the sponsors of the drug to submit supplemental applications proposing to remove the in-person dispensing requirement. *See* Compl. ¶ 56; 21 U.S.C. § 355-1(g)(4)(B) (authorizing FDA to direct the sponsors of a drug to propose REMS modifications to "ensure the benefits of the drug outweigh the risks of the drug" and "minimize the burden on the health care delivery system of complying with [the REMS]"). The sponsors submitted those applications on June 22, 2022, and FDA approved them on January 3, 2023, in the 2023 REMS Modification.

Today, the agency is once again reviewing the mifepristone REMS. As the Secretary and the Commissioner told state attorneys general on September 19, 2025, FDA's "review of the evidence . . . will contribute to the understanding of the drug's safety profile." ECF No. 1-110, at 1. "[T]o determine whether modifications [to the REMS] are necessary," FDA will consider evidence relating to "real-world outcomes" and conduct "a study of the safety of the current REMS." *Id.* FDA will also consider aspects of the 2023 REMS Modification that a court has ordered the agency to reassess, *see Purcell*, 2025 WL 3101785, at *28, as well as numerous citizen petitions that cite voluminous materials and seek competing outcomes.[3]

On the same day the Secretary and the Commissioner issued their letter regarding the REMS review, Plaintiffs sought to intervene in *Missouri v. FDA*, No. 2:22-cv-223-Z, ECF No. 264 (N.D. Tex. filed Sept. 19, 2025). That case began in late 2022 styled as *Alliance for Hippocratic Medicine v. FDA* and wound its way to the Supreme Court. *See All. for Hippocratic Med.*, 602 U.S. at 376-77 (discussing procedural history).

[3] The petitions include, but are not limited to, the following (all accessed January 27, 2026): https://www.regulations.gov/document/FDA-2025-P-0377-0001 (American College of Obstetricians and Gynecologists, et al.); https://www.regulations.gov/document/FDA-2025-P-1242-0001 (James D. Brinkruff, MD); https://www.regulations.gov/document/FDA-2025-P-1576-0001 (Andrew Joy Campbell, Attorney General of Massachusetts and the Attorneys General for 3 other states); https://www.regulations.gov/document/FDA-2025-P-2162-0001 (GenBioPro, Inc.); https://www.regulations.gov/document/FDA-2025-P-3287-0001 (Nick Brown, Attorney General of Washington and the Attorneys General for 18 other states); https://www.regulations.gov/document/FDA-2025-P-5434-0001 (Students for Life of America); https://www.regulations.gov/document/FDA-2025-P-5436-0001 (Students for Life of America); and https://www.regulations.gov/document/FDA-2025-P-5437-0001 (Students for Life of America).

There, the Supreme Court determined that, despite the original plaintiffs' "sincere legal, moral, ideological, and policy objections to elective abortion and to FDA's relaxed regulation of mifepristone," they "failed to demonstrate that FDA's relaxed regulatory requirements likely would cause them to suffer an injury in fact." *Id.* at 396.

Plaintiffs' attempted intervention was unsuccessful. At the end of September 2025, the Northern District of Texas transferred *Missouri* to the Eastern District of Missouri and denied Plaintiffs' motion to intervene. *Missouri v. FDA*, No. 2:22-cv-223-Z, 2025 WL 2825980, at *13 (N.D. Tex. Sept. 30, 2025).

On October 6, 2025, Plaintiffs filed this suit. Then, Plaintiffs filed a motion for preliminary relief on December 17, ECF No. 20 (Pl. Mot.)—nearly three years after the agency action that they challenge took effect.

STANDARD OF REVIEW

"[T]he power to stay proceedings is incidental to the power inherent in every court to control the disposition of the causes on its docket with economy of time and effort for itself, for counsel, and for litigants." *Landis v. N. Am. Co.*, 299 U.S. 248, 254 (1936). In exercising its "broad discretion to stay proceedings," *Clinton v. Jones*, 520 U.S. 681, 706 (1997), a court "must weigh competing interests and maintain an even balance," *Landis*, 299 U.S. at 254-55. In particular, a court must balance "the harm of moving forward" against "the harm of holding back" when determining whether to grant a stay of proceedings. *Ali v. Quarterman*, 607 F.3d 1046, 1049 (5th Cir. 2010).

To obtain a preliminary injunction or a stay of agency action under the Administrative Procedure Act, Plaintiffs must show "(1) a substantial likelihood of

prevailing on the merits; (2) a substantial threat of irreparable injury if the injunction is not granted; (3) the threatened injury outweighs any harm that will result to [a] non-movant if the injunction is granted; and (4) the injunction will not disserve the public interest." *Ridgely v. FEMA*, 512 F.3d 727, 734 (5th Cir. 2008); *see also Nken v. Holder*, 556 U.S. 418, 435 (2009); *Texas v. U.S. Dep't of Health & Hum. Servs.*, 770 F. Supp. 3d 940, 947 (E.D. Tex. 2025) ("Courts grant relief under [5 U.S.C.] § 705 based on the traditional four equitable factors for injunctive relief . . . ."). Preliminary relief "should not be granted unless the party seeking it has clearly carried the burden of persuasion on all four requirements." *Dennis Melancon, Inc. v. City of New Orleans*, 703 F.3d 262, 268 (5th Cir. 2012) (quotation marks and citation omitted).

"A preliminary injunction . . . cannot be requested by a plaintiff who lacks standing to sue." *Speech First, Inc. v. Fenves*, 979 F.3d 319, 329 (5th Cir. 2020). "[T]he party asserting federal jurisdiction when it is challenged has the burden of establishing it." *DaimlerChrysler Corp. v. Cuno*, 547 U.S. 332, 342 n.3 (2006). And courts presume that they "lack jurisdiction unless the contrary appears affirmatively from the record." *Renne v. Geary*, 501 U.S. 312, 316 (1991) (quotation marks omitted).

ARGUMENT

I. The Court Should Stay This Case And Deny Plaintiffs' Motion Pending FDA's Review of The Mifepristone REMS.

The Court should stay further litigation until after FDA's mifepristone REMS review is complete and deny Plaintiffs' motion without prejudice. *Landis*, 299 U.S. at 254-55; *see also Ricci v. Chi. Mercantile Exch.*, 409 U.S. 289, 305 (1973) (upholding stay of

judicial proceedings pending completion of agency proceedings). The rationale for deferring judicial review is simple: the "harm of moving forward" with judicial review of the 2023 REMS Modification outweighs the "harm of holding back." *Ali*, 607 F.3d at 1049. And the same calculus confirms that granting preliminary relief would not be equitable at this time because it would disrupt FDA's ongoing review.

The harms of judicial review before the ongoing agency review is complete are manifold. Plaintiffs ask the Court to make the very sort of difficult scientific judgment about the 2023 REMS Modification that Congress entrusted to FDA while the agency itself is considering the same issues. *See Sierra Club v. EPA*, 939 F.3d 649, 680 (5th Cir. 2019). Such parallel reviews would waste judicial resources because FDA's own review may eliminate any need for the Court's. Moreover, if the Court vacates or stays the 2023 REMS Modification before FDA's review is complete, it could prompt the sponsors of mifepristone to file supplemental applications seeking modifications to the REMS. This, in turn, would add to the burdens on the agency as it seeks to conduct its own study, review all the evidence before it, comply with the *Purcell* remand, and weigh competing views presented in numerous pending citizen petitions. *See supra* pp. 2-3, 7. And on top of all that, granting Plaintiffs interim relief could lead to conflicting injunctions, further complicating FDA's efforts. *See supra* p. 4.

These disruptive effects on FDA's ongoing review also confirm that the balance of the equities and the public interest weigh against Plaintiffs' request. *See Peak v. Dist. of Columbia*, No. 06-cv-0373, 2006 WL 8445985, at *6 (D.D.C. Mar. 20, 2006) ("[I]t is not in the public interest to interrupt the administrative process."). The purpose of

preliminary relief is "to preserve" the existing positions of the parties and thereby "prevent irreparable harm" before the merits are determined. *City of Dallas v. Delta Air Lines, Inc.*, 847 F.3d 279, 285 (5th Cir. 2017) (citation omitted). Far from preserving existing positions, preliminary relief would upend the status quo as well as the agency's administrative process.

Indeed, the text of 5 U.S.C. § 705 only underscores why the Court should decline to award preliminary relief. It authorizes the Court "to postpone the effective date of an agency action or to preserve status or rights pending conclusion of the review proceedings." 5 U.S.C. § 705. The effective date of the 2023 REMS Modification cannot be "postpone[d]" because it occurred three years ago. *Postpone*, Webster's New International Dictionary 1682 (1928) (def. 1) (defining "postpone" to mean "to defer to a future or later time; to put off; delay"); *Postpone*, Black's Law Dictionary 1389 (3d ed. 1933) ("To put off; defer; delay"); *see also Niz-Chavez v. Garland*, 593 U.S. 155, 160 (2021) (affording "the law's terms their ordinary meaning at the time Congress adopted them"). And none of the relevant definitions of "preserve" suggests relief that would upend a status quo that has existed for three years. *Preserve*, Webster's New International Dictionary 1699 (def. 1 & 3) (defining "preserve" as "[t]o keep or save from injury or destruction," "to guard or defend from evil," "to protect," "to maintain" or "to retain").[4]

[4] Although a Fifth Circuit panel "strongly doubt[ed] that § 705 should be read to impose the limit urged by FDA" here, the court did not reach "a definitive answer on this question." *All. for Hippocratic Med.*, 78 F.4th at 256. In any event, that opinion was later reversed on jurisdictional grounds. The question therefore remains open.

Finally, Plaintiffs' three-year delay in challenging the 2023 REMS Modification weighs against disrupting the status quo at this time. *Parker v. Dacres*, 130 U.S. 43, 50 (1889) (applying "the principle upon which courts of equity uniformly proceed, independently of any statute of limitations, of refusing relief to those who unreasonably delay to invoke their aid"); *see, e.g.*, *Tate v. LeBlanc*, No. 13-1253-P, 2014 WL 6455794, at *2 (W.D. La. Nov. 17, 2014) (finding a delay of "more than one year" sufficient to deny relief). Despite being aware of the 2023 REMS Modification and its alleged consequences since its inception, *see* Amicus Curiae Br. of Mississippi, et al., *Alliance for Hippocratic Medicine v. FDA*, No. 2:22-cv-00223-Z, ECF No. 55-1, at 3 (N.D. Tex. filed Feb. 10, 2023), the State has waited until this past October to seek relief of its own.[5] That there is "no apparent urgency" to Louisiana's request for preliminary relief further indicates that there is little harm in the Court holding back. *Amid, Inc. v. Medic Alert Found. U.S., Inc.*, 241 F. Supp. 3d 788, 821 (S.D. Tex. 2017).

Granting a stay while an agency reviews the matter under litigation is par for the course. *Purcell* is a case in point. There, the plaintiffs originally challenged the REMS that existed before the 2023 REMS modification. After FDA announced a REMS review in May 2021, the *Purcell* court stayed the litigation. *See Chelius v. Becerra*, No. 1:17-cv-

[5] Louisiana cannot excuse its delay based on the district court having granted universal relief in *Alliance for Hippocratic Medicine*. The relief granted in that case never took effect because the Supreme Court stayed it, *FDA v. All. for Hippocratic Med.*, No. 22A902, 143 S. Ct. 1075 (Apr. 21, 2023) (mem.), and ultimately held that the plaintiffs lacked standing, 602 U.S. 367. Even if it were justifiable for Louisiana to refrain from seeking relief until the Supreme Court's ultimate disposition, that does not explain why the State then waited a year and a half to seek preliminary relief.

493-JAO-RT, ECF No. 149 (D. Haw. May 7, 2021) (staying and administratively closing case).[6] The case remained stayed until after the 2023 REMS Modification. *Id.*, ECF No. 158 (D. Haw. Feb. 28, 2023) (reopening case). The Court should take a similar course here to allow FDA to complete its review of the mifepristone REMS.

II. Plaintiffs Would Not Be Prejudiced By A Stay Pending FDA's Review of The Mifepristone REMS Because They Are Not Suffering Ongoing Harm.

Plaintiffs would not be prejudiced by a stay pending FDA's review of the mifepristone REMS because they are experiencing no ongoing harm—much less irreparable harm—caused by FDA's 2023 REMS Modification. In any event, because Plaintiffs lack Article III standing, the Court should deny Plaintiffs' motion for preliminary relief.

The federal "judicial Power" is limited to "Cases" and "Controversies." U.S. Const. art. III. "A proper case or controversy exists only when at least one plaintiff establishes that she has standing to sue." *Murthy v. Missouri*, 603 U.S. 43, 57 (2024) (alterations and quotation marks omitted). To have standing, "a plaintiff must demonstrate (i) that she has suffered or likely will suffer an injury in fact, (ii) that the injury likely was caused or will be caused by the defendant, and (iii) that the injury likely would be redressed by the requested judicial relief." *All. for Hippocratic Med.*, 602 U.S. at 380. Neither Louisiana nor Ms. Markezich satisfies this test.

[6] *Chelius* was later renamed *Purcell v. Kennedy*.

A. Louisiana lacks standing

Like the plaintiffs in *Alliance for Hippocratic Medicine* that lacked standing, Louisiana "do[es] not prescribe or use mifepristone." *Id.* at 385. Nor does the 2023 REMS Modification "require[] [Louisiana] to do anything or to refrain from doing anything." *Id.* The State therefore faces an uphill battle to establish standing: in addition to showing a cognizable and redressable Article III injury, it must also show that the indirect causal chain between the 2023 REMS Modification and the State's alleged injury is neither "speculative" nor "attenuated." *Id.* at 383. Louisiana has not done so.

1. The 2023 REMS Modification does not cause "sovereign harm"

Contrary to Louisiana's contention, the 2023 REMS Modification does not implicate the State's sovereign "power to create and enforce a legal code." Compl. ¶ 111; Pl. Mot. 19. The Fourth Circuit has held that the mifepristone REMS establishes "a regulatory floor, not a ceiling," *GenBioPro, Inc. v. Raynes*, 144 F.4th 258, 274 (4th Cir. 2025), and the federal government has not taken any position that would leave Louisiana unable to "regulate abortion for legitimate reasons," including through legislation that furthers a "respect for and preservation of prenatal life at all stages of development," *Dobbs*, 597 U.S. at 300-01.

Recognizing this,[7] Louisiana argues instead that the 2023 REMS Modification has "functionally overridden" state laws by "making it possible" for *others*, especially out-

[7] Louisiana agrees that the REMS does not preempt its laws but contends that the Executive Branch previously suggested otherwise. Pl. Mot. 21 n.3. That is incorrect. The public statements Plaintiffs identify claimed only that states could not ban mifepristone

of-state actors, to violate them. Pl. Mot. 20. However, as the Ninth Circuit recognized, "even if the availability of retail and mail-order dispensing does make mifepristone more difficult to police," that "logistical burden on law enforcement" does not "constitute[] a cognizable Article III injury." *Washington v. FDA*, 108 F.4th 1163, 1177 (9th Cir. 2024).

Furthermore, the Supreme Court rejected a similar makes-state-crime-possible theory in *United States v. Texas*, 599 U.S. 670 (2023). There, a district court found standing in part based on a State's assertion that a federal policy led to individuals "committing[] more crimes" within that State. *Texas v United States*, 606 F. Supp. 3d 437, 467 (S.D. Tex. 2022). The Supreme Court reversed, concluding that "none of the various theories of standing asserted by the States . . . overcomes the fundamental Article III problem with this lawsuit." 599 U.S. at 680 n.3.

Accepting Louisiana's theory "would greatly expand state standing to challenge any federal action that allegedly increases crime or disorder, or imposes indirect compliance costs for state law enforcement." *Washington*, 108 F.4th at 1177. States could challenge the loosening of federal regulations relating to firearms, the environment, banking, or anything else—all on the hypothesis that removing a *federal* restriction on certain activity "mak[es] it possible" for persons to violate *state* law restricting that same activity.

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based on "disagreement" with FDA's "scientific judgment" about "safety and efficacy." ECF Nos. 1-60, 1-61. In any event, the Executive Branch now concurs with the Fourth Circuit's view that the mifepristone REMS establishes a regulatory floor, not a ceiling.

Louisiana's primary authority, *Louisiana v. EEOC*, 784 F. Supp. 3d 886 (W.D. La. 2025), does not support this limitless theory of state standing. That case involved a challenge to a rule that "directly regulated" the State by "mandat[ing]" that it "provide (and fund) accommodations for elective abortions that directly conflict with the States' own laws and policies." *Id.* at 900-01 (citation omitted). Unlike the abortion-accommodation "mandate," the 2023 REMS Modification does not require or forbid Louisiana to do anything. So the "direct[] conflict" that was present in *Louisiana* is absent here. *Id.* at 901 (citation omitted)

Diamond Alternative Energy, LLC v. EPA, 606 U.S. 100 (2025), is even further afield. There, the Court found standing where "government regulation of a business" caused economic injuries "to other linked businesses" in a "chain." 606 U.S. at 117; *see also All. for Hippocratic Med.*, 602 U.S. at 384 ("[W]hen the government regulates (or under-regulates) a business, the regulation (or lack thereof) may cause downstream or upstream economic injuries to *others in the chain*, such as certain manufacturers, retailers, suppliers, competitors, or customers." (emphasis added)). There is no similar "link[]" or "chain" between Louisiana and those regulated by the REMS, *i.e.*, drug manufacturers, prescribers, and pharmacies located throughout the country. Thus, unlike *Diamond Alternative Energy*, Louisiana's causal theory is far too "attenuated" to satisfy Article III. *See id.* at 383.

2. Medicaid-based economic harm is too attenuated to establish standing

Louisiana argues next that it has standing as a Medicaid payor. Pl. Mot. 21-23. As with the sovereign harm theory, the only court to have considered whether a State has

standing to challenge the 2023 REMS Modification based on Medicaid costs rejected that theory as too attenuated. *Washington*, 108 F.4th at 1175-76. This Court should do the same.

Indeed, the reasoning of *Alliance for Hippocratic Medicine* compels that conclusion. There, the Court rejected as too attenuated a theory that doctors can "challenge the government's loosening of general public safety requirements simply because more individuals might then show up at emergency rooms or in doctors' offices with follow-on injuries." 602 U.S. at 391. Louisiana extends that debunked theory a step further. Louisiana argues that it has standing because the very doctors who lack standing under *Alliance for Hippocratic Medicine* can pass their costs on to the State through Medicaid. That is illogical. If the chain of causation between the challenged agency action and the doctors' alleged injury is already too attenuated, adding a link (doctors cause Medicaid to incur costs) only weakens it more.

Plaintiffs' version of Medicaid-payor standing is also just as limitless as doctor standing. So long as the Louisiana (through Medicaid) foots the bill for at least one patient, the State could challenge *any* federal policy alleged to have caused that visit to the doctor or hospital, including "EPA roll[ing] back emissions standards for power plants," "[a] federal agency increas[ing] a speed limit from 65 to 80 miles per hour," and the federal government "repeal[ing] certain restrictions on guns." *All. for Hippocratic Med.*, 602 U.S. at 391. And the logic of this broad theory would apply to "every entity that provides health insurance or subsidized medical care," not just States or Medicaid payors. *Washington*, 108 F.4th at 1176; *see* Pl. Mot. 21 n.4 (conceding that this theory does

not depend on "special solicitude" for States). Article III's limitations are not so easily eviscerated.

Plaintiffs' alleged authority for its Medicaid-payor theory, *Texas v. United States*, 50 F.4th 498, 517-20 (5th Cir. 2022), relied on a much different—and less attenuated—causal chain. It involved a challenge to a policy alleged to increase a State's Medicaid costs by increasing the total number of people on that State's Medicaid rolls. The State's theory did not rely on any supposition that those additional Medicaid enrollees would engage in a particular activity or suffer a particular type of injury. By contrast, Louisiana alleges that the 2023 REMS Modification leads more women who are already on its Medicaid rolls to use a specific drug, which in turn causes some of them to suffer specific types of adverse events, which in turn causes those women to seek medical care, which in turn generates costs that doctors and hospitals then pass on to the State. That is the sort of theory that *Alliance for Hippocratic Medicine* rejected as too attenuated, and so it fails here, too.

3. Louisiana cannot sue the Federal Government as *parens patriae*

Finally, in its Complaint (though not in its motion for preliminary relief), Louisiana asserts standing based on "quasi sovereign" interests in protecting Louisianans. Compl. ¶¶ 120-131. But the Supreme Court has expressly held that "States do not have standing as *parens patriae* to bring an action against the Federal Government." *Murthy*, 603 U.S at 76 (quotation marks omitted); *see also Haaland v. Brackeen*, 599 U.S. 255, 294-95 & n.11 (2023).

Recognizing this, Louisiana eschews the label "*parens patriae*" and disclaims "asserting the rights of its citizens." Compl. ¶ 131. This is just "'a thinly veiled attempt to circumvent the limits on *parens patriae* standing.'" *Murthy*, 603 U.S. at 76 (quoting *Brackeen*, 599 U.S. at 295 n.11). The Complaint plainly asserts a *parens patriae* theory based on "direct injuries to pregnant Louisiana women" and "fatal injuries to [] unborn babies." Compl. ¶ 129; *see Washington*, 108 F.4th at 1178 ("Idaho alleges that elimination of the in-person dispensing requirement will endanger specific pregnant women who take the drug and 'unborn children' subjected to its effects. These allegations concern the well-being of individual citizens—not a distinct interest of the state as a whole."). Whatever label is applied, this theory remains disapproved by the Supreme Court.

B. Ms. Markezich lacks standing

For her part, Ms. Markezich avers standing because her former boyfriend allegedly forced her to take mifepristone to end a pregnancy. Compl ¶¶ 150-59; Pl. Mot. 23 n.5. That past injury (though of course tragic) is not redressable by the prospective relief she seeks. *See All. for Hippocratic Med.*, 602 U.S. at 381 (explaining that a plaintiff seeking "prospective relief" must establish "a sufficient likelihood of future injury"). Seeking to avoid that problem, Ms. Markezich alleges that she "could be placed in the same position for future pregnancies." Compl. ¶ 155. But such speculation (including about the actions of third parties) is insufficient to satisfy the injury-in-fact requirement. *See, e.g.*, *City of L.A. v. Lyons*, 461 U.S. 96, 108 (1983) (finding no case or controversy where it was "no more than speculation to assert" that the plaintiffs "will be" subject to the allegedly unlawful conduct in the future). Also, her theory of causation—that the

2023 REMS Modification is ultimately responsible for Ms. Markezich's boyfriend obtaining mifepristone from an out-of-state prescriber under false pretenses and then coercing her into taking the drug, *see* Compl. ¶¶ 150-52—is exactly the kind of attenuated theory rejected in *Alliance for Hippocratic Medicine*. *See* 602 U.S. at 385-393.

CONCLUSION

For the foregoing reasons, the Court should stay this case pending FDA's review and deny Plaintiffs' motion without prejudice.

January 27, 2026

Respectfully submitted,

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IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF LOUISIANA
LAFAYETTE DIVISION

THE STATE OF LOUISIANA, *et al.*, *Plaintiffs*, v. U.S. FOOD AND DRUG ADMINISTRATION, *et al.*, *Defendants.*	No. 6:25-cv-01491-DCJ-DJA

[proposed] ORDER GRANTING DEFENDANTS' MOTION TO STAY THE CASE

Before the Court is Defendants' Motion to Stay the Case. Having reviewed the Motion, the Court finds good cause to exercise its inherent authority to stay this matter pending the completion of agency proceedings. Those proceedings may result in an agency decision that will supersede the decision Plaintiffs ask this Court to review. Furthermore, judicial review at this time may disrupt the administrative process. And finally, Plaintiffs will not be prejudiced by deferring review until agency proceedings are completed.

Accordingly, the motion is **GRANTED** and the case is **STAYED** pending further order of the Court. Defendants **SHALL FILE** a status report within fourteen (14) days of determining whether a modification to the mifepristone Risk Evaluation and Mitigation Strategy is necessary.

SO ORDERED.

_____
Date

_____
Hon. David C. Joseph
United States District Court Judge

_____
Hon. David J. Ayo
United States Magistrate Judge

IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF LOUISIANA
LAFAYETTE DIVISION

THE STATE OF LOUISIANA, *et al.*, *Plaintiffs*, v. U.S. FOOD AND DRUG ADMINISTRATION, *et al.*, *Defendants.*	No. 6:25-cv-01491-DCJ-DJA

DEFENDANTS' MEMORANDUM IN SUPPORT OF MOTION TO STAY THE CASE AND IN RESPONSE TO PLAINTIFFS' MOTION FOR PRELIMINARY RELIEF

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TABLE OF CONTENTS

Introduction 1

Background 5

Standard of Review 8

Argument 9

I. The Court Should Stay This Case And Deny Plaintiffs' Motion Pending FDA's Review of The Mifepristone REMS. 9

II. Plaintiffs Would Not Be Prejudiced By A Stay Pending FDA's Review of The Mifepristone REMS Because They Are Not Suffering Ongoing Harm. 13

A. Louisiana lacks standing 13

1. The 2023 REMS Modification does not cause "sovereign harm" 14

2. Medicaid-based economic harm is too attenuated to establish standing 16

3. Louisiana cannot sue the Federal Government as *parens patriae* 18

B. Ms. Markezich lacks standing 19

Conclusion 20

TABLE OF AUTHORITIES

Cases

Ali v. Quarterman,
607 F.3d 1046 (5th Cir. 2010) 8, 10

All. for Hippocratic Med. v. FDA,
78 F.4th 210 (5th Cir. 2023) 1,11

Am. Coll. of Obstetricians & Gynecologists v. FDA,
472 F. Supp. 3d 183 (D. Md. 2020) 6

Amid, Inc. v. Medic Alert Found. U.S., Inc.,
241 F. Supp. 3d 788 (S.D. Tex. 2017) 12

Chelius v. Becerra,
No. 1:17-cv-493-JAO-RT (D. Haw. May 7, 2021) 12, 13

City of Dallas v. Delta Air Lines, Inc.,
847 F.3d 279 (5th Cir. 2017) 11

City of L.A. v. Lyons,
461 U.S. 96 (1983) 19

Clinton v. Jones,
520 U.S. 681 (1997) 8

DaimlerChrysler Corp. v. Cuno,
547 U.S. 332 (2006) 9

Dennis Melancon, Inc. v. City of New Orleans,
703 F.3d 262 (5th Cir. 2012) 9

Diamond Alternative Energy, LLC v. EPA,
606 U.S. 100 (2025) 16

Dobbs v. Jackson Women's Health Org.,
597 U.S. 215 (2022) 5, 14

FDA v. All. for Hippocratic Med.,
No. 22A902, 143 S. Ct. 1075 (Apr. 21, 2023) (mem.) 12

FDA v. All. for Hippocratic Med.,
602 U.S. 367 (2024) ..... *passim*

FDA v. Am. Coll. of Obstetricians & Gynecologists,
141 S. Ct. 578 (2021) 6

GenBioPro, Inc. v. Raynes,
144 F.4th 258 (4th Cir. 2025) 14

Haaland v. Brackeen,
599 U.S. 255 (2023) 18

Landis v. N. Am. Co.,
299 U.S. 248 (1936) 8, 9

Louisiana v. EEOC,
784 F. Supp. 3d 886 (W.D. La. 2025) 15

Missouri v. FDA,
Case No. 2:22-cv-223-Z, 2025 WL 2825980 (N.D. Tex. Sept. 30, 2025) 8

Murthy v. Missouri,
603 U.S. 43 (2024) 13, 18

Niz-Chavez v. Garland,
593 U.S. 155 (2021) 11

Nken v. Holder,
556 U.S. 418 (2009) 9

Parker v. Dacres,
130 U.S. 43 (1889) 12

Peak v. Dist. of Columbia,
No. 06-cv-0373, 2006 WL 8445985 (D.D.C. Mar. 20, 2006) 10

Purcell v. Kennedy,
Civ. No. 17-00493 JAO-RT, 2025 WL 3101785 (D. Haw. Oct. 30, 2025) 2, 7

Renne v. Geary,
501 U.S. 312 (1991) 9

Ricci v. Chi. Mercantile Exch.,
409 U.S. 289 (1973) 9

Ridgely v. FEMA,
512 F.3d 727 (5th Cir. 2008) 9

Sierra Club v. EPA,
939 F.3d 649 (5th Cir. 2019) 10

Speech First, Inc. v. Fenves,
979 F.3d 319 (5th Cir. 2020) 9

Tate v. LeBlanc,
No. 13-1253-P, 2014 WL 6455794 (W.D. La. Nov. 17, 2014) 12

Texas v. U.S. Dep't of Health & Hum. Servs.,
770 F. Supp. 3d 940 (E.D. Tex. 2025) 9

Texas v. United States,
50 F.4th 498 (5th Cir. 2022) 17

Texas v. United States,
606 F. Supp. 3d 437 (S.D. Tex. 2022) 15

United States v. Texas,
599 U.S. 670 (2023) 15

Washington v. FDA,
108 F.4th 1163 (9th Cir. 2024) 15, 17, 18, 19

Washington v. FDA,
668 F. Supp. 3d 1125 (E.D. Wash. 2023) 4

Washington v. FDA,
No. 1:23-cv-3026-TOR, 2025 WL 1888794 (E.D. Wash. 2025) 2

Statutes

5 U.S.C. § 705 ..... 9, 11, 12

21 U.S.C. § 355-1(g)(4)(B) 6

21 U.S.C. § 355(a) 5

Regulations

21 C.F.R. § 314.520 5

73 Fed. Reg. 16313 (Mar. 27, 2008) 6

Other Authorities

Black's Law Dictionary (3d ed. 1933) 11

FDA, Questions and Answers on Mifepristone for Medical Termination of Pregnancy Through Ten Weeks Gestation, (accessed Jan. 27, 2026), https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/questions-and-answers-mifepristone-medical-termination-pregnancy-through-ten-weeks-gestation 3

Webster's New International Dictionary (1928) 11

INTRODUCTION

Protecting the health and safety of pregnant women is of paramount importance. To that end, on September 19, 2025, the Secretary of Health and Human Services and the Commissioner of Food and Drugs announced that the Food and Drug Administration (FDA) is reviewing the Risk Evaluation and Mitigation Strategy (REMS) for mifepristone, a drug approved for medical abortion. ECF No. 1-110 (Letter to State Attorneys General (Sept. 19, 2025)). The Secretary and the Commissioner explained that this review—which will include a study undertaken by FDA itself—is "informed by the lack of adequate consideration underlying prior REMS approvals," including a 2023 modification to the mifepristone REMS that approved the removal of an in-person dispensing requirement. *Id.* at 1. FDA's review is rooted in the agency's commitment "to protecting the health and safety of pregnant women" and "ensur[ing] . . . decisions are grounded in Gold Standard Science and rigorous, transparent, and objective evidence." *Id.* at 2.

FDA's decision to review the REMS for mifepristone is consistent with the concerns about removing the in-person dispensing requirement foreshadowed by the Fifth Circuit in *Alliance for Hippocratic Medicine v. FDA*. *See* 78 F.4th 210, 249-51 (5th Cir. 2023), *rev'd on other grounds*, 602 U.S. 367 (2024). Although ultimately reversed on jurisdictional grounds, the Fifth Circuit held that, in calling for the removal of the in-person dispensing requirement in December 2021, FDA erroneously "gave dispositive weight to adverse-event data in [the FDA Adverse Event Reporting System]," despite limitations of that data—including the fact that, as a result of action FDA took in 2016,

the REMS no longer requires prescribers to report non-fatal serious adverse events. *Id.* at 249. The court also faulted FDA's reliance on studies that had "significant limitations" and "did not affirmatively support" eliminating the in-person dispensing requirement. *Id.* at 250.

In deciding to review the REMS for mifepristone, the FDA recognized that the validity of FDA's restrictions on mifepristone is a hotly contested legal and scientific issue that has been the subject of litigation for many years. Louisiana and Ms. Markezich are not the only plaintiffs to have challenged the current requirements for dispensing mifepristone. Indeed, five other states are challenging either the approval of mifepristone or subsequent actions easing restrictions. *See Missouri v. FDA*, No. 4:25-cv-1580-CMS (E.D. Mo.) (Missouri, Idaho, and Kansas challenging actions easing REMS restrictions); *Florida v. FDA*, No. 7:25-cv-126-O (N.D. Tex.) (Florida and Texas challenging approval of mifepristone and actions easing REMS restrictions). Still other plaintiffs have challenged FDA's restrictions as too burdensome. *Purcell v. Kennedy*, Civ. No. 17-00493 JAO-RT, 2025 WL 3101785, at *28 (D. Haw. Oct. 30, 2025) (plaintiffs challenged REMS as too restrictive); *Washington v. FDA*, No. 1:23-cv-3026-TOR, 2025 WL 1888794 (E.D. Wash. 2025) (same); *Whole Woman's Health All. v. FDA*, No. 3:23-cv-00019 (W.D. Va.) (same). And aside from litigation, before the FDA are numerous citizen petitions—citing voluminous material and seeking mutually inconsistent relief, such as suspending approval of the drug, restoring previous REMS requirements, or eliminating the REMS entirely. *See infra* n.3.

Given this widespread debate over the safety of mifepristone, FDA has concluded that the best path forward is for the agency to reconsider the restrictions on mifepristone based on all the evidence before the agency. As noted above, that evidence will include FDA's own study. FDA has emphasized that it "is taking care to do this study properly and in the right way." FDA, Questions and Answers on Mifepristone for Medical Termination of Pregnancy Through Ten Weeks Gestation.[1] At this time, "FDA continues to work on the collection of the robust and timely data that is necessary for a well-controlled study with adequate statistical power." *Id.* Although studies like these "often take approximately a year or more to conduct," FDA's current plan is to complete the study "sooner than that timeframe." *Id.* And once FDA has analyzed the data from that study (as well as all other evidence before the agency), it will decide whether "substantive changes to the REMS" are necessary. *Id.*

Plaintiffs now threaten to short circuit the agency's orderly review and study of the safety risks of mifepristone by asking this Court for an immediate stay of the 2023 REMS Modification approved three years ago. They would have this Court set aside the 2023 REMS Modification—all without the benefit of FDA's expertise, and even as the agency is already reconsidering the matter in its review. And Plaintiffs' requested relief may prove as unnecessary as it is disruptive, if FDA ultimately decides that the in-person dispensing requirement must be restored.

[1] https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/questions-and-answers-mifepristone-medical-termination-pregnancy-through-ten-weeks-gestation (item No. 37) (accessed Jan. 27, 2026).

Moreover, awarding preliminary relief to these Plaintiffs could easily prompt other plaintiffs to seek a conflicting injunction that would sow administrative and judicial chaos. If this Court were to grant Plaintiffs' motion, the plaintiffs in *Whole Woman's Health Alliance* could promptly seek conflicting relief, which would only add to FDA's burden and complicate any future modification efforts. The prospect of conflicting injunctions is hardly far-fetched. In 2023, literally minutes after the Northern District of Texas in *Alliance for Hippocratic Medicine* stayed FDA's approval of mifepristone, the Eastern District of Washington prohibited FDA from altering the status quo in certain States. *Washington v. FDA*, 668 F. Supp. 3d 1125, 1144 (E.D. Wash. 2023), *vacated*, No. 1:23-cv-3026-TOR, 2025 WL 1888794 (E.D. Wash. 2025).

To prevent that disruption, the Court should exercise its inherent authority to stay this litigation pending the outcome of FDA's review of the mifepristone REMS. FDA's review will necessarily result in a new agency decision that could supersede the 2023 REMS Modification, obviating any need to consider the merits of Plaintiffs' arguments challenging the validity of the 2023 REMS Modification. Any party adversely affected by the new agency decision on mifepristone may seek judicial review at that time. And in the event of a further REMS modification, adherence to FDA's normal process will create far less disruption than the abrupt, judicially imposed change sought by Plaintiffs.

Deferring judicial review until FDA's review is complete will not prejudice Plaintiffs. Louisiana waited nearly three years to challenge the 2023 REMS Modification, and Rosalie Markezich does not identify any ongoing or imminent injury from which

she needs relief. Indeed, although Plaintiffs have alleged the 2023 REMS Modification causes serious harms to women, Plaintiffs lack standing to challenge that modification. Louisiana suffers no sovereign injury because it remains free to make and enforce its pro-life policies after *Dobbs v. Jackson Women's Health Org.*, 597 U.S. 215 (2022). Nor are Defendants standing in the way of Louisiana enforcing its abortion laws against out-of-state prescribers of mifepristone. The State's allegations about Medicaid costs and "quasi-sovereign" interests also do not create any case or controversy between Louisiana and FDA. And the tragic injury that Ms. Markezich alleges she suffered in the past due to the independent actions of her former boyfriend is neither traceable to FDA nor redressable by the prospective relief Plaintiffs seek. For all those reasons, the Court should stay this case until after FDA completes its review of the mifepristone REMS and deny Plaintiffs' motion without prejudice.

BACKGROUND

The Federal Food, Drug, and Cosmetic Act generally prohibits introducing a "new drug" into interstate commerce without FDA approval. 21 U.S.C. § 355(a). In 2000, FDA approved mifepristone for medical abortion, subject to certain restrictions to assure safe use. *See All. for Hippocratic Med.*, 602 U.S. at 376; 21 C.F.R. § 314.520.[2] Since 2008, those restrictions have been part of a REMS. *See* Identification of Drug and Biological Products Deemed to Have Risk Evaluation and Mitigation Strategies for

[2] FDA has separately approved another manufacturer's mifepristone product, Korlym, for the treatment of Cushing's syndrome. Plaintiffs do not challenge FDA's actions regarding Korlym, and all references to mifepristone throughout this brief refer to the drug approved for medical abortion (Mifeprex and the approved generic equivalents).

Purposes of the Food and Drug Administration Amendments Act of 2007, 73 Fed. Reg. 16313, 16314 (Mar. 27, 2008).

For most of the drug's history, mifepristone's restrictions included an "in-person dispensing requirement," ensuring that the drug could be dispensed only in "clinics, medical offices, and hospitals, by or under the supervision of a certified prescriber." *See, e.g.*, ECF No. 20-16 (REMS Single Shared System for Mifepristone 200MG (May 2021)) at 2. In July 2020, a district court preliminarily enjoined enforcement of the in-person dispensing requirement during the COVID-19 pandemic. *Am. Coll. of Obstetricians & Gynecologists v. FDA*, 472 F. Supp. 3d 183, 233 (D. Md. 2020). The Supreme Court stayed that injunction pending appeal in January 2021. *FDA v. Am. Coll. of Obstetricians & Gynecologists*, 141 S. Ct. 578 (2021) (mem.). ECF No. 1 (Compl.) ¶¶ 49-50. But in April 2021, FDA announced that it would not enforce the in-person dispensing requirement during the COVID-19 public health emergency, and the following month it announced it would conduct a review of the REMS. *See* ECF No. 1-10 (2021 FDA Letter to AAPLOG, *et al.*) at 5 & 6 n.10.

On December 16, 2021, the agency directed the sponsors of the drug to submit supplemental applications proposing to remove the in-person dispensing requirement. *See* Compl. ¶ 56; 21 U.S.C. § 355-1(g)(4)(B) (authorizing FDA to direct the sponsors of a drug to propose REMS modifications to "ensure the benefits of the drug outweigh the risks of the drug" and "minimize the burden on the health care delivery system of complying with [the REMS]"). The sponsors submitted those applications on June 22, 2022, and FDA approved them on January 3, 2023, in the 2023 REMS Modification.

Today, the agency is once again reviewing the mifepristone REMS. As the Secretary and the Commissioner told state attorneys general on September 19, 2025, FDA's "review of the evidence . . . will contribute to the understanding of the drug's safety profile." ECF No. 1-110, at 1. "[T]o determine whether modifications [to the REMS] are necessary," FDA will consider evidence relating to "real-world outcomes" and conduct "a study of the safety of the current REMS." *Id.* FDA will also consider aspects of the 2023 REMS Modification that a court has ordered the agency to reassess, *see Purcell*, 2025 WL 3101785, at *28, as well as numerous citizen petitions that cite voluminous materials and seek competing outcomes.[3]

On the same day the Secretary and the Commissioner issued their letter regarding the REMS review, Plaintiffs sought to intervene in *Missouri v. FDA*, No. 2:22-cv-223-Z, ECF No. 264 (N.D. Tex. filed Sept. 19, 2025). That case began in late 2022 styled as *Alliance for Hippocratic Medicine v. FDA* and wound its way to the Supreme Court. *See All. for Hippocratic Med.*, 602 U.S. at 376-77 (discussing procedural history).

[3] The petitions include, but are not limited to, the following (all accessed January 27, 2026): https://www.regulations.gov/document/FDA-2025-P-0377-0001 (American College of Obstetricians and Gynecologists, et al.); https://www.regulations.gov/document/FDA-2025-P-1242-0001 (James D. Brinkruff, MD); https://www.regulations.gov/document/FDA-2025-P-1576-0001 (Andrew Joy Campbell, Attorney General of Massachusetts and the Attorneys General for 3 other states); https://www.regulations.gov/document/FDA-2025-P-2162-0001 (GenBioPro, Inc.); https://www.regulations.gov/document/FDA-2025-P-3287-0001 (Nick Brown, Attorney General of Washington and the Attorneys General for 18 other states); https://www.regulations.gov/document/FDA-2025-P-5434-0001 (Students for Life of America); https://www.regulations.gov/document/FDA-2025-P-5436-0001 (Students for Life of America); and https://www.regulations.gov/document/FDA-2025-P-5437-0001 (Students for Life of America).

There, the Supreme Court determined that, despite the original plaintiffs' "sincere legal, moral, ideological, and policy objections to elective abortion and to FDA's relaxed regulation of mifepristone," they "failed to demonstrate that FDA's relaxed regulatory requirements likely would cause them to suffer an injury in fact." *Id.* at 396.

Plaintiffs' attempted intervention was unsuccessful. At the end of September 2025, the Northern District of Texas transferred *Missouri* to the Eastern District of Missouri and denied Plaintiffs' motion to intervene. *Missouri v. FDA*, No. 2:22-cv-223-Z, 2025 WL 2825980, at *13 (N.D. Tex. Sept. 30, 2025).

On October 6, 2025, Plaintiffs filed this suit. Then, Plaintiffs filed a motion for preliminary relief on December 17, ECF No. 20 (Pl. Mot.)—nearly three years after the agency action that they challenge took effect.

STANDARD OF REVIEW

"[T]he power to stay proceedings is incidental to the power inherent in every court to control the disposition of the causes on its docket with economy of time and effort for itself, for counsel, and for litigants." *Landis v. N. Am. Co.*, 299 U.S. 248, 254 (1936). In exercising its "broad discretion to stay proceedings," *Clinton v. Jones*, 520 U.S. 681, 706 (1997), a court "must weigh competing interests and maintain an even balance," *Landis*, 299 U.S. at 254-55. In particular, a court must balance "the harm of moving forward" against "the harm of holding back" when determining whether to grant a stay of proceedings. *Ali v. Quarterman*, 607 F.3d 1046, 1049 (5th Cir. 2010).

To obtain a preliminary injunction or a stay of agency action under the Administrative Procedure Act, Plaintiffs must show "(1) a substantial likelihood of

prevailing on the merits; (2) a substantial threat of irreparable injury if the injunction is not granted; (3) the threatened injury outweighs any harm that will result to [a] non-movant if the injunction is granted; and (4) the injunction will not disserve the public interest." *Ridgely v. FEMA*, 512 F.3d 727, 734 (5th Cir. 2008); *see also Nken v. Holder*, 556 U.S. 418, 435 (2009); *Texas v. U.S. Dep't of Health & Hum. Servs.*, 770 F. Supp. 3d 940, 947 (E.D. Tex. 2025) ("Courts grant relief under [5 U.S.C.] § 705 based on the traditional four equitable factors for injunctive relief . . . ."). Preliminary relief "should not be granted unless the party seeking it has clearly carried the burden of persuasion on all four requirements." *Dennis Melancon, Inc. v. City of New Orleans*, 703 F.3d 262, 268 (5th Cir. 2012) (quotation marks and citation omitted).

"A preliminary injunction . . . cannot be requested by a plaintiff who lacks standing to sue." *Speech First, Inc. v. Fenves*, 979 F.3d 319, 329 (5th Cir. 2020). "[T]he party asserting federal jurisdiction when it is challenged has the burden of establishing it." *DaimlerChrysler Corp. v. Cuno*, 547 U.S. 332, 342 n.3 (2006). And courts presume that they "lack jurisdiction unless the contrary appears affirmatively from the record." *Renne v. Geary*, 501 U.S. 312, 316 (1991) (quotation marks omitted).

ARGUMENT

I. The Court Should Stay This Case And Deny Plaintiffs' Motion Pending FDA's Review of The Mifepristone REMS.

The Court should stay further litigation until after FDA's mifepristone REMS review is complete and deny Plaintiffs' motion without prejudice. *Landis*, 299 U.S. at 254-55; *see also Ricci v. Chi. Mercantile Exch.*, 409 U.S. 289, 305 (1973) (upholding stay of

judicial proceedings pending completion of agency proceedings). The rationale for deferring judicial review is simple: the "harm of moving forward" with judicial review of the 2023 REMS Modification outweighs the "harm of holding back." *Ali*, 607 F.3d at 1049. And the same calculus confirms that granting preliminary relief would not be equitable at this time because it would disrupt FDA's ongoing review.

The harms of judicial review before the ongoing agency review is complete are manifold. Plaintiffs ask the Court to make the very sort of difficult scientific judgment about the 2023 REMS Modification that Congress entrusted to FDA while the agency itself is considering the same issues. *See Sierra Club v. EPA*, 939 F.3d 649, 680 (5th Cir. 2019). Such parallel reviews would waste judicial resources because FDA's own review may eliminate any need for the Court's. Moreover, if the Court vacates or stays the 2023 REMS Modification before FDA's review is complete, it could prompt the sponsors of mifepristone to file supplemental applications seeking modifications to the REMS. This, in turn, would add to the burdens on the agency as it seeks to conduct its own study, review all the evidence before it, comply with the *Purcell* remand, and weigh competing views presented in numerous pending citizen petitions. *See supra* pp. 2-3, 7. And on top of all that, granting Plaintiffs interim relief could lead to conflicting injunctions, further complicating FDA's efforts. *See supra* p. 4.

These disruptive effects on FDA's ongoing review also confirm that the balance of the equities and the public interest weigh against Plaintiffs' request. *See Peak v. Dist. of Columbia*, No. 06-cv-0373, 2006 WL 8445985, at *6 (D.D.C. Mar. 20, 2006) ("[I]t is not in the public interest to interrupt the administrative process."). The purpose of

preliminary relief is "to preserve" the existing positions of the parties and thereby "prevent irreparable harm" before the merits are determined. *City of Dallas v. Delta Air Lines, Inc.*, 847 F.3d 279, 285 (5th Cir. 2017) (citation omitted). Far from preserving existing positions, preliminary relief would upend the status quo as well as the agency's administrative process.

Indeed, the text of 5 U.S.C. § 705 only underscores why the Court should decline to award preliminary relief. It authorizes the Court "to postpone the effective date of an agency action or to preserve status or rights pending conclusion of the review proceedings." 5 U.S.C. § 705. The effective date of the 2023 REMS Modification cannot be "postpone[d]" because it occurred three years ago. *Postpone*, Webster's New International Dictionary 1682 (1928) (def. 1) (defining "postpone" to mean "to defer to a future or later time; to put off; delay"); *Postpone*, Black's Law Dictionary 1389 (3d ed. 1933) ("To put off; defer; delay"); *see also Niz-Chavez v. Garland*, 593 U.S. 155, 160 (2021) (affording "the law's terms their ordinary meaning at the time Congress adopted them"). And none of the relevant definitions of "preserve" suggests relief that would upend a status quo that has existed for three years. *Preserve*, Webster's New International Dictionary 1699 (def. 1 & 3) (defining "preserve" as "[t]o keep or save from injury or destruction," "to guard or defend from evil," "to protect," "to maintain" or "to retain").[4]

[4] Although a Fifth Circuit panel "strongly doubt[ed] that § 705 should be read to impose the limit urged by FDA" here, the court did not reach "a definitive answer on this question." *All. for Hippocratic Med.*, 78 F.4th at 256. In any event, that opinion was later reversed on jurisdictional grounds. The question therefore remains open.

Finally, Plaintiffs' three-year delay in challenging the 2023 REMS Modification weighs against disrupting the status quo at this time. *Parker v. Dacres*, 130 U.S. 43, 50 (1889) (applying "the principle upon which courts of equity uniformly proceed, independently of any statute of limitations, of refusing relief to those who unreasonably delay to invoke their aid"); *see, e.g.*, *Tate v. LeBlanc*, No. 13-1253-P, 2014 WL 6455794, at *2 (W.D. La. Nov. 17, 2014) (finding a delay of "more than one year" sufficient to deny relief). Despite being aware of the 2023 REMS Modification and its alleged consequences since its inception, *see* Amicus Curiae Br. of Mississippi, et al., *Alliance for Hippocratic Medicine v. FDA*, No. 2:22-cv-00223-Z, ECF No. 55-1, at 3 (N.D. Tex. filed Feb. 10, 2023), the State has waited until this past October to seek relief of its own.[5] That there is "no apparent urgency" to Louisiana's request for preliminary relief further indicates that there is little harm in the Court holding back. *Amid, Inc. v. Medic Alert Found. U.S., Inc.*, 241 F. Supp. 3d 788, 821 (S.D. Tex. 2017).

Granting a stay while an agency reviews the matter under litigation is par for the course. *Purcell* is a case in point. There, the plaintiffs originally challenged the REMS that existed before the 2023 REMS modification. After FDA announced a REMS review in May 2021, the *Purcell* court stayed the litigation. *See Chelius v. Becerra*, No. 1:17-cv-

[5] Louisiana cannot excuse its delay based on the district court having granted universal relief in *Alliance for Hippocratic Medicine*. The relief granted in that case never took effect because the Supreme Court stayed it, *FDA v. All. for Hippocratic Med.*, No. 22A902, 143 S. Ct. 1075 (Apr. 21, 2023) (mem.), and ultimately held that the plaintiffs lacked standing, 602 U.S. 367. Even if it were justifiable for Louisiana to refrain from seeking relief until the Supreme Court's ultimate disposition, that does not explain why the State then waited a year and a half to seek preliminary relief.

493-JAO-RT, ECF No. 149 (D. Haw. May 7, 2021) (staying and administratively closing case).[6] The case remained stayed until after the 2023 REMS Modification. *Id.*, ECF No. 158 (D. Haw. Feb. 28, 2023) (reopening case). The Court should take a similar course here to allow FDA to complete its review of the mifepristone REMS.

II. Plaintiffs Would Not Be Prejudiced By A Stay Pending FDA's Review of The Mifepristone REMS Because They Are Not Suffering Ongoing Harm.

Plaintiffs would not be prejudiced by a stay pending FDA's review of the mifepristone REMS because they are experiencing no ongoing harm—much less irreparable harm—caused by FDA's 2023 REMS Modification. In any event, because Plaintiffs lack Article III standing, the Court should deny Plaintiffs' motion for preliminary relief.

The federal "judicial Power" is limited to "Cases" and "Controversies." U.S. Const. art. III. "A proper case or controversy exists only when at least one plaintiff establishes that she has standing to sue." *Murthy v. Missouri*, 603 U.S. 43, 57 (2024) (alterations and quotation marks omitted). To have standing, "a plaintiff must demonstrate (i) that she has suffered or likely will suffer an injury in fact, (ii) that the injury likely was caused or will be caused by the defendant, and (iii) that the injury likely would be redressed by the requested judicial relief." *All. for Hippocratic Med.*, 602 U.S. at 380. Neither Louisiana nor Ms. Markezich satisfies this test.

[6] *Chelius* was later renamed *Purcell v. Kennedy*.

A. Louisiana lacks standing

Like the plaintiffs in *Alliance for Hippocratic Medicine* that lacked standing, Louisiana "do[es] not prescribe or use mifepristone." *Id.* at 385. Nor does the 2023 REMS Modification "require[] [Louisiana] to do anything or to refrain from doing anything." *Id.* The State therefore faces an uphill battle to establish standing: in addition to showing a cognizable and redressable Article III injury, it must also show that the indirect causal chain between the 2023 REMS Modification and the State's alleged injury is neither "speculative" nor "attenuated." *Id.* at 383. Louisiana has not done so.

1. The 2023 REMS Modification does not cause "sovereign harm"

Contrary to Louisiana's contention, the 2023 REMS Modification does not implicate the State's sovereign "power to create and enforce a legal code." Compl. ¶ 111; Pl. Mot. 19. The Fourth Circuit has held that the mifepristone REMS establishes "a regulatory floor, not a ceiling," *GenBioPro, Inc. v. Raynes*, 144 F.4th 258, 274 (4th Cir. 2025), and the federal government has not taken any position that would leave Louisiana unable to "regulate abortion for legitimate reasons," including through legislation that furthers a "respect for and preservation of prenatal life at all stages of development," *Dobbs*, 597 U.S. at 300-01.

Recognizing this,[7] Louisiana argues instead that the 2023 REMS Modification has "functionally overridden" state laws by "making it possible" for *others*, especially out-

[7] Louisiana agrees that the REMS does not preempt its laws but contends that the Executive Branch previously suggested otherwise. Pl. Mot. 21 n.3. That is incorrect. The public statements Plaintiffs identify claimed only that states could not ban mifepristone

of-state actors, to violate them. Pl. Mot. 20. However, as the Ninth Circuit recognized, "even if the availability of retail and mail-order dispensing does make mifepristone more difficult to police," that "logistical burden on law enforcement" does not "constitute[] a cognizable Article III injury." *Washington v. FDA*, 108 F.4th 1163, 1177 (9th Cir. 2024).

Furthermore, the Supreme Court rejected a similar makes-state-crime-possible theory in *United States v. Texas*, 599 U.S. 670 (2023). There, a district court found standing in part based on a State's assertion that a federal policy led to individuals "committing[] more crimes" within that State. *Texas v United States*, 606 F. Supp. 3d 437, 467 (S.D. Tex. 2022). The Supreme Court reversed, concluding that "none of the various theories of standing asserted by the States . . . overcomes the fundamental Article III problem with this lawsuit." 599 U.S. at 680 n.3.

Accepting Louisiana's theory "would greatly expand state standing to challenge any federal action that allegedly increases crime or disorder, or imposes indirect compliance costs for state law enforcement." *Washington*, 108 F.4th at 1177. States could challenge the loosening of federal regulations relating to firearms, the environment, banking, or anything else—all on the hypothesis that removing a *federal* restriction on certain activity "mak[es] it possible" for persons to violate *state* law restricting that same activity.

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based on "disagreement" with FDA's "scientific judgment" about "safety and efficacy." ECF Nos. 1-60, 1-61. In any event, the Executive Branch now concurs with the Fourth Circuit's view that the mifepristone REMS establishes a regulatory floor, not a ceiling.

Louisiana's primary authority, *Louisiana v. EEOC*, 784 F. Supp. 3d 886 (W.D. La. 2025), does not support this limitless theory of state standing. That case involved a challenge to a rule that "directly regulated" the State by "mandat[ing]" that it "provide (and fund) accommodations for elective abortions that directly conflict with the States' own laws and policies." *Id.* at 900-01 (citation omitted). Unlike the abortion-accommodation "mandate," the 2023 REMS Modification does not require or forbid Louisiana to do anything. So the "direct[] conflict" that was present in *Louisiana* is absent here. *Id.* at 901 (citation omitted)

Diamond Alternative Energy, LLC v. EPA, 606 U.S. 100 (2025), is even further afield. There, the Court found standing where "government regulation of a business" caused economic injuries "to other linked businesses" in a "chain." 606 U.S. at 117; *see also All. for Hippocratic Med.*, 602 U.S. at 384 ("[W]hen the government regulates (or under-regulates) a business, the regulation (or lack thereof) may cause downstream or upstream economic injuries to *others in the chain*, such as certain manufacturers, retailers, suppliers, competitors, or customers." (emphasis added)). There is no similar "link[]" or "chain" between Louisiana and those regulated by the REMS, *i.e.*, drug manufacturers, prescribers, and pharmacies located throughout the country. Thus, unlike *Diamond Alternative Energy*, Louisiana's causal theory is far too "attenuated" to satisfy Article III. *See id.* at 383.

2. Medicaid-based economic harm is too attenuated to establish standing

Louisiana argues next that it has standing as a Medicaid payor. Pl. Mot. 21-23. As with the sovereign harm theory, the only court to have considered whether a State has

standing to challenge the 2023 REMS Modification based on Medicaid costs rejected that theory as too attenuated. *Washington*, 108 F.4th at 1175-76. This Court should do the same.

Indeed, the reasoning of *Alliance for Hippocratic Medicine* compels that conclusion. There, the Court rejected as too attenuated a theory that doctors can "challenge the government's loosening of general public safety requirements simply because more individuals might then show up at emergency rooms or in doctors' offices with follow-on injuries." 602 U.S. at 391. Louisiana extends that debunked theory a step further. Louisiana argues that it has standing because the very doctors who lack standing under *Alliance for Hippocratic Medicine* can pass their costs on to the State through Medicaid. That is illogical. If the chain of causation between the challenged agency action and the doctors' alleged injury is already too attenuated, adding a link (doctors cause Medicaid to incur costs) only weakens it more.

Plaintiffs' version of Medicaid-payor standing is also just as limitless as doctor standing. So long as the Louisiana (through Medicaid) foots the bill for at least one patient, the State could challenge *any* federal policy alleged to have caused that visit to the doctor or hospital, including "EPA roll[ing] back emissions standards for power plants," "[a] federal agency increas[ing] a speed limit from 65 to 80 miles per hour," and the federal government "repeal[ing] certain restrictions on guns." *All. for Hippocratic Med.*, 602 U.S. at 391. And the logic of this broad theory would apply to "every entity that provides health insurance or subsidized medical care," not just States or Medicaid payors. *Washington*, 108 F.4th at 1176; *see* Pl. Mot. 21 n.4 (conceding that this theory does

not depend on "special solicitude" for States). Article III's limitations are not so easily eviscerated.

Plaintiffs' alleged authority for its Medicaid-payor theory, *Texas v. United States*, 50 F.4th 498, 517-20 (5th Cir. 2022), relied on a much different—and less attenuated—causal chain. It involved a challenge to a policy alleged to increase a State's Medicaid costs by increasing the total number of people on that State's Medicaid rolls. The State's theory did not rely on any supposition that those additional Medicaid enrollees would engage in a particular activity or suffer a particular type of injury. By contrast, Louisiana alleges that the 2023 REMS Modification leads more women who are already on its Medicaid rolls to use a specific drug, which in turn causes some of them to suffer specific types of adverse events, which in turn causes those women to seek medical care, which in turn generates costs that doctors and hospitals then pass on to the State. That is the sort of theory that *Alliance for Hippocratic Medicine* rejected as too attenuated, and so it fails here, too.

3. Louisiana cannot sue the Federal Government as *parens patriae*

Finally, in its Complaint (though not in its motion for preliminary relief), Louisiana asserts standing based on "quasi sovereign" interests in protecting Louisianans. Compl. ¶¶ 120-131. But the Supreme Court has expressly held that "States do not have standing as *parens patriae* to bring an action against the Federal Government." *Murthy*, 603 U.S at 76 (quotation marks omitted); *see also Haaland v. Brackeen*, 599 U.S. 255, 294-95 & n.11 (2023).

Recognizing this, Louisiana eschews the label "*parens patriae*" and disclaims "asserting the rights of its citizens." Compl. ¶ 131. This is just "'a thinly veiled attempt to circumvent the limits on *parens patriae* standing.'" *Murthy*, 603 U.S. at 76 (quoting *Brackeen*, 599 U.S. at 295 n.11). The Complaint plainly asserts a *parens patriae* theory based on "direct injuries to pregnant Louisiana women" and "fatal injuries to [] unborn babies." Compl. ¶ 129; *see Washington*, 108 F.4th at 1178 ("Idaho alleges that elimination of the in-person dispensing requirement will endanger specific pregnant women who take the drug and 'unborn children' subjected to its effects. These allegations concern the well-being of individual citizens—not a distinct interest of the state as a whole."). Whatever label is applied, this theory remains disapproved by the Supreme Court.

B. Ms. Markezich lacks standing

For her part, Ms. Markezich avers standing because her former boyfriend allegedly forced her to take mifepristone to end a pregnancy. Compl ¶¶ 150-59; Pl. Mot. 23 n.5. That past injury (though of course tragic) is not redressable by the prospective relief she seeks. *See All. for Hippocratic Med.*, 602 U.S. at 381 (explaining that a plaintiff seeking "prospective relief" must establish "a sufficient likelihood of future injury"). Seeking to avoid that problem, Ms. Markezich alleges that she "could be placed in the same position for future pregnancies." Compl. ¶ 155. But such speculation (including about the actions of third parties) is insufficient to satisfy the injury-in-fact requirement. *See, e.g.*, *City of L.A. v. Lyons*, 461 U.S. 96, 108 (1983) (finding no case or controversy where it was "no more than speculation to assert" that the plaintiffs "will be" subject to the allegedly unlawful conduct in the future). Also, her theory of causation—that the

2023 REMS Modification is ultimately responsible for Ms. Markezich's boyfriend obtaining mifepristone from an out-of-state prescriber under false pretenses and then coercing her into taking the drug, *see* Compl. ¶¶ 150-52—is exactly the kind of attenuated theory rejected in *Alliance for Hippocratic Medicine*. *See* 602 U.S. at 385-393.

CONCLUSION

For the foregoing reasons, the Court should stay this case pending FDA's review and deny Plaintiffs' motion without prejudice.

January 27, 2026

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UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF LOUISIANA
LAFAYETTE DIVISION

THE STATE OF LOUISIANA, by and through its Attorney General, LIZ MURRILL, and ROSALIE MARKEZICH, PLAINTIFFS, v. U.S. FOOD AND DRUG ADMINISTRATION, et al. DEFENDANTS.	Civ. No.: 6:25-cv-01491 Judge: David C. Joseph Mag. Judge: David J. Ayo

STATE OF LOUISIANA AND ROSALIE MARKEZICH'S REPLY MEMORANDUM IN SUPPORT OF THEIR MOTION FOR PRELIMINARY RELIEF AND IN OPPOSITION TO DEFENDANTS' MOTION TO STAY

TABLE OF CONTENTS

TABLE OF AUTHORITIES iii

INTRODUCTION 1

ARGUMENT 2

I. PLAINTIFFS HAVE STANDING 2

A. Louisiana Has Suffered Injuries in Fact. 3

1. Louisiana suffers classic pocketbook injuries. 3

2. Louisiana suffers classic sovereign harms. 5

B. Louisiana's Harms Are Traceable to the 2023 REMS. 7

C. Plaintiffs' Injuries Are Redressable. 12

D. Plaintiffs Fall Within the Relevant Zones of Interest. 13

II. THE COURT SHOULD PRELIMINARILY STAY THE 2023 REMS. 15

A. As FDA Does Not Dispute—and As Two Fifth Circuit Panels Have Held—Plaintiffs Are Likely to Succeed on the Merits. 15

B. The Equities Favor Plaintiffs. 18

C. FDA's "Delay" Argument Is Meritless. 20

D. As the Fifth Circuit Has Held, a Universal Preliminary Stay Is the Appropriate Relief. 22

E. The Manufacturers' Exhaustion Argument Is Meritless. 23

III. THE COURT SHOULD DENY FDA'S REQUEST TO INDEFINITELY STAY THIS CASE. 25

CONCLUSION 28

TABLE OF AUTHORITIES

Cases

Abbott Laboratories v. Gardner,
387 U.S. 136 (1967) 27

Abbott v. Perez,
585 U.S. 579 (2018) 6

ADT, LLC v. Cap. Connect, Inc.,
145 F. Supp. 3d 671 (N.D. Tex. 2015) 20, 21

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458 U.S. 592 (1982) 6

Ali v. Quarterman,
607 F.3d 1046 (5th Cir. 2010) 26

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668 F. Supp. 3d 507 (N.D. Tex. 2023) 15, 24

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No. 23-10362, 2023 WL 2913725 (5th Cir. Apr. 12, 2023) 16, 23, 24, 25

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463 U.S. 60 (1983) 15

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No. 24-568, 2026 WL 96707 (U.S. Jan. 14, 2026) 3, 4

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229 F. 960 (7th Cir. 1915) 15

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No. CV 17-00493 JAO-RT, 2023 WL 5041616 (D. Haw. Aug. 8, 2023) 27

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568 U.S. 398 (2013) 3, 4, 5

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No. 20A34 (U.S. Aug. 26, 2020) 17

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299 U.S. 248 (1936) 27

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456 U.S. 228 (1982) 13

Lexmark Int'l, Inc. v. Static Control Components, Inc.,
572 U.S. 118 (2014) 14

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130 U.S. 43 (1889) 21

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No. CV 06-0373 (JGP), 2006 WL 8445985 (D.D.C. Mar. 20, 2006) 26

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549 F.3d 842 (Fed. Cir. 2008) 25

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No. CIV.A. 13-1253-P, 2014 WL6455794 (W.D. La. Nov. 17, 2014) 21

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141 F.4th 687 (5th Cir. 2025) 8, 11

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623 F. Supp. 3d 696 (N.D. Tex. 2022) 7

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646 F. Supp. 3d 753 (N.D. Tex. 2022) 23

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706 F.2d 541 (5th Cir. 1983) 27

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574 U.S. 528 (2015) 4

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73 F.4th 304 (5th Cir. 2023) 3

Statutes

21 U.S.C. § 331 14

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INTRODUCTION

The Federal Defendants (collectively, "FDA"), Danco, and GenBioPro do not dispute that certified prescribers are mailing FDA-approved mifepristone into Louisiana in violation of Louisiana law and ending the lives of nearly 1,000 babies in the State each month.[1] They also do not dispute that FDA's removal of the in-person dispensing requirement through the 2023 REMS is the indispensable ingredient in those unlawful abortions: Prescribers could not lawfully (under federal law) mail mifepristone without the 2023 REMS. And FDA *concedes* the 2023 REMS was "informed by [a] lack of adequate consideration." ECF 51 at 1. Indeed, FDA has virtually embraced "the concerns about removing the in-person dispensing requirement foreshadowed by the Fifth Circuit." *Id.*

All this makes for an easy case as "some judges" (ECF 52-4 at 17)—Chief Judge Elrod and Judges Ho, Wilson, Engelhardt, and Oldham—already have concluded. The proper route is to preliminarily stay the 2023 REMS.

Perhaps because the route is so easy, FDA and the drug manufacturers try to scuttle the case on standing grounds. But that tactic does not work. That is because they do not seriously dispute that Louisiana is suffering injuries in fact, whether they are sovereign or economic; instead, they dispute only traceability, trying to cast prescribers, pro-abortion states, and even domestic-abuse victims as the real perpetrators of Louisiana's harms. But, as just explained, if the Court stays the 2023 REMS, then the whole mail-order abortion scheme will fall apart—that is the best indication Louisiana has satisfied both traceability and redressability and thus has Article III standing.

All this is unsurprising. FDA and the manufacturers now brush aside the Biden Administration's statements about overriding pro-life state laws through widespread distribution of abortion drugs. And they ignore statements from abortion activists who admit that this was their plan all along. But history cannot be rewritten. It is thus unsurprising that an avowed assault on pro-life states through the 2023 REMS naturally gives those states standing to sue in defense of their sovereign

[1] Although Plaintiffs initially opposed Danco and GenBioPro's motions to intervene, they now do not oppose intervention in light of FDA's subsequent (a) concession that the 2023 REMS lacked legally adequate consideration and (b) refusal to defend the 2023 REMS.

and economic interests. As this Court said recently, where states "have unambiguously expressed their opposition to purely elective abortions by passing laws prohibiting the same," "principles of federalism" "clearly" give the states Article III standing to challenge a federal agency's intrusion upon that sovereign prerogative. *Louisiana v. EEOC*, 705 F. Supp. 3d 643, 653–54 (W.D. La. 2024).

That leaves only FDA's puzzling attempt to shelve this case for a few years. The Court can and should reject that request out of hand since, because Louisiana is entitled to preliminary relief, FDA cannot obtain a stay without satisfying the ordinary *Nken* factors—an impossible burden FDA does not even try to carry. And even if that were not so, FDA does not cite a single case where a court has stayed proceedings and denied preliminary relief even though the defendant (a) concedes that its conduct is unlawful and (b) would suffer no irreparable harm from the grant of preliminary relief. This Court should not be the first. The Court should preliminarily stay the 2023 REMS and deny FDA's motion to stay.

ARGUMENT

I. PLAINTIFFS HAVE STANDING.

Start with the attacks on this Court's jurisdiction. To establish standing, "a plaintiff must demonstrate (i) that she has suffered or likely will suffer an injury in fact, (ii) that the injury likely was caused or will be caused by the defendant, and (iii) that the injury likely would be redressed by the requested judicial relief." *FDA v. All. for Hippocratic Med. (Alliance)*, 602 U.S. 367, 380 (2024). Louisiana has suffered pocketbook and sovereign harms from the 2023 REMS—harms that led tragically to bodily harms for Plaintiff Rosalie.[2] Those injuries are traceable to FDA's removal of the in-person dispensing requirement. And those injuries are redressable by a decision staying or vacating the 2023 REMS.

[2] While there is no question that Rosalie suffered an Article III injury, Plaintiffs here focus on Louisiana's standing in particular for the sake of judicial efficiency.

A. Louisiana Has Suffered Injuries in Fact.

1. Louisiana suffers classic pocketbook injuries.

Classic pocketbook harms resolve this case. "Pocketbook harm is a traditional Article III injury." *Bost v. Ill. State Bd. of Elections*, No. 24-568, 2026 WL 96707, at *6 (U.S. Jan. 14, 2026) (Barrett, J., concurring) (citation omitted). After all, "an economic injury is the quintessential injury upon which to base standing." *Young Conservatives of Tex. Found. v. Smatresk*, 73 F.4th 304, 309 (5th Cir. 2023) (citation modified). Indeed, "[f]or standing purposes, a loss of even a small amount of money is ordinarily an 'injury.'" *Czyzewski v. Jevic Holding Corp.*, 580 U.S. 451, 464 (2017); *United States v. Texas*, 599 U.S. 670, 687–88 (2023) (Gorsuch, J., concurring). These well-recognized economic injuries can often take the form of the "effect on the states' fiscs." *Texas v. United States (DAPA)*, 809 F.3d 134, 152 (5th Cir. 2015); *see also, e.g.*, *Biden v. Nebraska*, 600 U.S. 477, 490 (2023) (Missouri's "financial harm is an injury in fact"). Here, Louisiana has suffered two types of classic pocket injuries, either or both of which assure the Court's jurisdiction: (a) economic harms incurred while enforcing Louisiana law against violations caused by the 2023 REMS; and (b) the expenditure of Medicaid dollars to treat adverse events caused by the 2023 REMS.

a. Consider first the pocketbook harms from violations of Louisiana's pro-life laws. Pocketbook harm occurs when a plaintiff "reasonably incur[s] costs to mitigate or avoid" the "'substantial risk'" of a harm caused by government action. *Clapper v. Amnesty Int'l USA*, 568 U.S. 398, 414 n.5 (2013) (collecting cases). In *Monsanto Co. v. Geertson Seed Farms*, 561 U. S. 139, 153–154 (2010), for example, the question was whether alfalfa farmers could seek judicial relief against agency action permitting the planting of genetically modified alfalfa. The farmers "established a reasonable probability that their organic and conventional alfalfa crops [would] be infected with [an] engineered gene" through cross-contamination. *Id.* at 153 (internal quotation marks omitted). And because the farmers took costly preventative measures to "minimize the likelihood of potential contamination," they suffered an Article III injury. *Id.* at 154–55.

Justices Barrett and Kagan recently reprised that reasoning to confirm a congressman's standing in his challenge to a state election law: "Like the farmers in *Monsanto*," they said, the

congressman "will 'reasonably incur costs to mitigate or avoid' the 'substantial risk' of harm caused by the challenged statute." *Bost*, 2026 WL 96707, at *7 (Barrett, J., concurring) (quoting *Clapper*, 568 U.S. at 414 n.5). They noted that the congressman's campaign "has spent, and will spend, money, time, and resources" to avoid alleged harms from the challenged law. *Id.* Because those "expenditures mitigate a substantial risk of harm, [the congressman] has pleaded Article III injury." *Id.*

So here, as Louisiana explained in its opening brief, ECF 20-26 at 21, and as FDA, Danco, and GenBioPro do not dispute: Like the alfalfa farmers and the congressman, Louisiana has expended substantial money, time, and resources attempting to mitigate the avowedly intended harm caused by the 2023 REMS. As recounted in the Complaint and opening brief, for example, Louisiana has indicted two out-of-state prescribers who violated Louisiana law by sending FDA-approved mifepristone into Louisiana. The State has issued warrants for their arrest. And Governor Landry has completed the necessary paperwork and formally asked the governors of California and New York to extradite these fugitive prescribers.[3] To be even more precise: In just *three* distinct investigations alone regarding the unlawful mailing of mifepristone into Louisiana, the State has spent at least $17,604.40.[4] Through these efforts, Louisiana is incurring costs every day to bring criminal prescribers to justice and deter others from breaking the State's pro-life laws. *Cf. Texas*, 599 U.S. at 687–88 (Gorsuch, J., concurring) (discussing States' standing to "challenge [] Executive Branch policies that indirectly caused them monetary harms" where "the States have spent, and continue to spend, more money on law enforcement, incarceration, and social services").

Even though Plaintiffs raised these harms in support of their motion, ECF 20-26 at 21–23, neither FDA nor the manufacturers dispute these expenditures. Their failure to dispute these harms alone ends the injury-in-fact analysis.[5]

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[3] Governors Newsom and Hochul have refused extradition. ECF 1 ¶¶ 100–02; Governor Gavin Newsom (@GavinNewsom), X (Feb. 5, 2026, 8:43 PM), perma.cc/46CV-HMZ9.

[4] Ex. A, Toner Decl. ¶ 4–6.

[5] To add "extra icing on a cake already frosted," *Yates v. United States*, 574 U.S. 528, 557 (2015) (Kagan, J., dissenting), it bears noting that FDA's elimination of the in-person dispensing requirement also forced the Louisiana Legislature to take legislative action accounting for the dangers inherent in

b. If that were not enough, Louisiana's Medicaid pocketbook harms would be. Federal law places on state Medicaid programs the financial burden for Medicaid-covered women who suffer complications from mifepristone—which is why the State suffers quintessential pocketbook harm every time such complications arise. This is a demonstrable fact.

We know—and neither FDA nor the manufacturers dispute—that Louisiana already has spent over $90,000 in Medicaid dollars for emergency room care and hospitalizations directly traceable to just *two* FDA-approved mifepristone-induced abortions. ECF 20-26 at 6, 23. And the total amount spent is likely much higher, considering the number of abortions occurring and that prescribers are counseling women to conceal the fact that they took mifepristone. Louisiana's ongoing costs are thus plainly "certainly impending," or at the least there is a "substantial risk" these costs will occur. *Clapper*, 568 U.S. at 414 & n.5.

This fact is unsurprising because it is an obvious consequence of mifepristone's documented complication rate. When it removed the in-person dispensing requirement, FDA anticipated that emergency-room visits would increase—with the baseline being a 2016 warning that roughly 1 in 25 women would end up in the emergency room. *See generally* ECF 1-10. So, there was a "reasonable probability" and "substantial risk" that Medicaid-covered women would seek care, especially in Louisiana where half a million women are on Louisiana Medicaid. *See Monsanto*, 561 U.S. at 153–54; ECF 20-26 at 23. In the end, Medicaid costs are indisputable economic harm—and they plainly reinforce Louisiana's standing as a matter of dollars and cents.

2. Louisiana suffers classic sovereign harms.

In addition to its pocketbook harm, Louisiana has established injury to its sovereign interests in enforcing its pro-life laws. *See Texas v. United States*, 787 F.3d 733, 752 n.38 (5th Cir. 2015); *cf. Abbott*

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prescribing mifepristone without an in-person visit. *See* State Senator Sharon Hewitt (@sharonhewitt), X (May 21, 2022, 6:17 PM), perma.cc/4BCD-PYFK. The Legislature followed that up by also listing mifepristone as a controlled substance and outlawing coerced abortion, while the Louisiana Department of Health for its part was compelled to issue its own implementation guidance. *See* La. R.S. §§ 40:964(F), 14:87.6; La. Dep't of Health, *Memorandum and Guidance on Act 246 Regarding Mifepristone and Misoprostol* (effective Oct. 1, 2024), perma.cc/5K34-MSUW.

v. Perez, 585 U.S. 579, 602 n.17 (2018) ("[T]he inability to enforce its duly enacted plans clearly inflicts irreparable harm on the State[.]"). States have standing to vindicate their sovereign (or quasi-sovereign) interests. *Alfred L. Snapp & Son, Inc. v. Puerto Rico, ex rel., Barez*, 458 U.S. 592, 601–02 (1982). And as a corollary, they also have standing based on "federal interference with the enforcement of state law." *DAPA*, 809 F.3d at 153 (cleaned up and citations omitted). Those basic rules carry the day here: "Because the principles of federalism afford the states a sovereign interest in creating and enforcing their own laws and public policy," Louisiana "clearly ha[s] Article III standing to challenge" the 2023 REMS. *Louisiana*, 705 F. Supp. 3d at 654.

Louisiana's argument on this point is very simple: (a) it is undisputed that Louisiana law bars the dispensing of mifepristone within Louisiana to cause an unlawful abortion; (b) it is undisputed that some 1,000 such abortions are occurring every month in violation of Louisiana law; and (c) it is undisputed that it has become nearly impossible for Louisiana to prosecute those violations. Those undisputed—and unremedied—violations of Louisiana law are quintessential sovereign harms. Now, FDA and the manufacturers can dispute *who* is doing the violating and *who* bears responsibility for the violating, but that is better viewed as a *causation* question than a question about whether Louisiana is suffering sovereign injury in fact.

The closest FDA and the manufacturers come to squarely disputing Louisiana's injuries in fact is to say that the 2023 REMS does nothing to render "Louisiana's abortion laws unenforceable." ECF 52-4 at 6; ECF 51 at 14–16; ECF 54-4 at 9. But that, too, goes to whether the 2023 REMS is legally at fault versus whether Louisiana actually is suffering sovereign harms. And on that latter point, it is telling of course that neither FDA nor the manufacturers could identify a single instance in which Louisiana has been able to enforce its criminal code to stop the onslaught of illegal abortions. It also is important to recognize that FDA and the manufacturers rest on a false premise: that so long as a State can find some other way to stop a violation of its laws, the State lacks Article III standing to sue the federal government for causing the violation in the first place. That is emphatically wrong. Just as "federal interference with the *enforcement* of state law" is a sound basis for Article III standing, *DAPA*, 809 F.3d at 153 (emphasis added), so too is the federal government's "encourage[ment]" that "doctors

[] *violate* [Louisiana's] abortion laws" to begin with, *Texas v. Becerra*, 623 F. Supp. 3d 696, 714 (N.D. Tex. 2022) (emphasis added). Or, put in this Court's words, a State plainly may defend its "sovereign interest in creating ... [its] own laws and public policy" against the federal government's attack. *Louisiana*, 705 F. Supp. 3d at 654. Such an attack "interferes with adherence to—and, therefore, enforcement of—[Louisiana's] laws." *Texas*, 623 F. Supp. 3d at 714. This assault on state sovereignty constitutes a concrete injury-in-fact.

Whether viewed as making out an injury-in-fact or proving up causation, this assault on state sovereignty squarely provides Article III standing to an affected State. For present purposes, Louisiana respectfully submits that it is analytically clearer to resolve the injury-in-fact prong on the undisputed facts surrounding the ongoing violations of Louisiana law, which is sovereign harm—and save the question of FDA's and the 2023 REMS' responsibility for the traceability analysis.

B. Louisiana's Harms Are Traceable to the 2023 REMS.

Because it is undisputed that Louisiana is currently suffering sovereign and economic harms (in the form of violations of Louisiana law that, in turn, cause pocketbook injuries), the only real issue in the Article III standing analysis is traceability. But that is a straightforward issue best answered as a practical matter and as a historical matter—and the other side has no answer.

1. Practicality first. The best way to determine whether Louisiana's harms are traceable to the 2023 REMS is to ask whether those harms would be mitigated or eliminated if the 2023 REMS were vacated. *Cf. Alliance*, 602 U.S. at 380 ("The second and third standing requirements—causation and redressability—are often 'flip sides of the same coin.'"). The answer is yes. Pro-abortion groups like the ACLU (*see infra*) have publicly criticized Louisiana's filing of this lawsuit because, they say, doing away with the 2023 REMS would bar doctors in pro-abortion states from mailing mifepristone into pro-life states like Louisiana—for the reinstated in-person dispensing requirement would limit dispensing to, well, in-person visits. On this score, common sense leads the way: Why is this such an important case? Why does Louisiana care so much about reinstating the in-person dispensing requirement, and why do FDA's *amici* care so much about retaining the 2023 REMS? Because the in-

person dispensing requirement (or absence thereof) dictates whether some 1,000 abortions a month may continue to occur in Louisiana.

This reality explains the logical error in FDA's and the manufacturers' attempts to shift the blame elsewhere. For example, they claim that third-party providers and the anonymous people who order the drugs online (rather than FDA or the 2023 REMS) are responsible for the actual violations of Louisiana's law. They also emphasize that pro-abortion states' "shield" laws are what have made it nearly impossible for Louisiana to enforce its pro-life laws. But that is not how causation works: The third-party providers could not legally (under federal law) mail mifepristone into Louisiana without the 2023 REMS' removal of the in-person dispensing requirement, and the "shield" laws would be meaningless without the 2023 REMS because providers in "shield" law states could not legally mail mifepristone.

The 2023 REMS is the indispensable ingredient in the 1,000 abortions occurring in Louisiana every month—and that is why Louisiana easily satisfies the Article III causation standard. "Article III requires no more than *de facto* causality." *Dep't of Com. v. New York*, 588 U.S. 752, 768 (2019) (citation omitted). And for the practical reasons just explained, the 2023 REMS meets that standard.

2. History confirms as much because, if anything is clear from the record, it is that this assault on pro-life states like Louisiana was not just the "predictable" effect of the 2023 REMS, *id.*—it was the "whole point" of the 2023 REMS, *Tex. Corn Prod'rs v. EPA*, 141 F.4th 687, 700 (5th Cir. 2025). Indeed, this case presents one of the most egregious—and most stark—examples of "federal interference with the enforcement of state law," *DAPA*, 809 F.3d at 153, coupled with the obvious economic harms that would flow from such interference.[6]

[6] For this reason, to the extent FDA and the manufacturers worry about the ramifications of Louisiana's standing, that worry is unfounded. "It is only if the violation of the federal law or the Constitution interferes with state law that a state suffers a sovereign injury supporting sovereign standing." F. Andrew Hessick, *Quasi-Sovereign Standing*, 94 Notre Dame L. Rev. 1927, 1932 (2019), perma.cc/76HK-3MNS. And the key facts in this case are even more inherently limiting: agency action pursuant to a directive from the President of the United States to facilitate mailing mifepristone into pro-life states. If ever there were a case where state sovereignty established standing, this is it.

a. This story begins at least as far back as 1994, when the former Director of FDA's Office of Women's Health stated that mifepristone "was going to be very important especially in states where surgical abortions are not permitted. And if they overturn *Roe v. Wade*, it's going to be really important." ECF 1, ¶ 54. As abortion activists grew increasingly worried about *Roe*'s future in the 2010s, they began "to push harder to make abortion pills available by telemedicine and mail."[7] In March 2021, the ACLU wrote a letter to President Biden demanding that he direct FDA to review the REMS and "eliminate" these "barriers" to "accessing" abortion particularly in "state[s with] abortion restrictions."[8] Advocates even arranged for "high net-worth major donors" to personally meet with President Biden and lobby for him to remove the in-person dispensing requirement.[9] President Biden obliged one month later.

And by May 2022, abortion activists knew *Roe* would fall and thus argued that mifepristone would be necessary to ensure people could obtain abortions even where restricted.[10] President Biden was listening, and on the day the Supreme Court issued *Dobbs*, he explicitly directed the Secretary of HHS to protect access to "medication abortion" and identify all ways to make mifepristone as widely accessible as possible, including by "mail." ECF 1, ¶ 59. And he later recommitted to doing everything in his power to protect access to abortion, noting that some States are trying to "ban or severely restrict access to these medications." *Id.* at ¶ 57. This culminated in the 2023 REMS. *Id.* at ¶ 62. Evidence that undermining *Dobbs* was the avowed purpose for the 2023 REMS does not get much stronger.

b. This history brings this case squarely in line with precedents like *Texas Corn Producers* and *Diamond Alternative Energy, LLC v. EPA*, 606 U.S. 100 (2025)—precedents that say "the object" of a regulation obviously has standing to challenge it. FDA urges this Court to deny Louisiana standing on

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[7] Ex. B, Carrie Baker, Abortion Pills US History and Politics 93 (2024), perma.cc/24G8-ALWA.

[8] ACLU, *Reproductive Health, Rights, and Justice Groups Letter to Biden Administration on Mifepristone* (March 16, 2021) (perma.cc/VP9K-ETUN).

[9] Baker, *supra* n.7 at 115.

[10] Abigail Abrams and Jamie Ducharm, Inside the Effort to Promote Abortion Pills For a Post-Roe America, Time (May 31, 2022) (perma.cc/H6SD-BMGD).

the ground that it is not "the object" of the 2023 REMS. *See* ECF 51 at 16. But that is wrong on the law and the facts.

The Supreme Court recently explained that an entity can be "the object" of a regulatory regime even if other parties are "the directly regulated parties." *Diamond*, 606 U.S. at 115. That's because officials often "seek to indirectly target" people "through a conduit." *Id.* at 116. Whether an entity "is in fact an object of a regulation is a flexible inquiry rooted in common sense." *Contender Farms, L.L.P. v. U.S. Dep't of Agric.*, 779 F.3d 258, 265 (5th Cir. 2015). So private schools can be the object of a law barring parents from sending children to private schools, and sugar producers can be the target of FDA actions making it "harder for soda manufacturers to use sugar." *Diamond*, 606 U.S. at 115; *Energy Future Coal. v. EPA*, 793 F.3d 141, 144 (D.C. Cir. 2015) (Kavanaugh, J.). What matters is who the government "targets." *Diamond*, 606 U.S. at 115–16 (citing *Energy Future Coal.*, 793 F.3d at 144–145). If the government seeks to "impede[]" an entity by regulating intermediaries, the targeted entity is one of the "objects of the government action." *Id.* at 115.

In *Diamond*, for example, the Supreme Court said that fuel producers "might be considered an object" of California restrictions on automakers' use of gasoline in cars. *Id.* at 114. The "entire purpose of California's fleet-wide emissions standards and electric-vehicle mandate" was to reduce gas-powered cars. *Id.* at 112. Even though the fuel producers were not directly regulated, they were "the targets of government regulations" and had standing to challenge California's "regulations that threaten" their interests. *Id.* at 120.

So too here. FDA "target[ed]" pro-life states—through the "conduit" of abortion-drug prescribers—seeking to "impede" state pro-life laws. *Id.* at 116. "Indeed, that is the whole point of the regulations." *Id.* at 114.

FDA, Danco, and GenBioPro argue that *Diamond* doesn't apply here because Louisiana isn't in the "link" or "chain." ECF 51 at 16; ECF 52-4 at 9; ECF 54-4 at 9. Nonsense. Louisiana was the target—it's in the chain just as much as the fuel producers in *Diamond*. Though not a "directly regulated part[y]," *Diamond*, 606 U.S. at 115, Louisiana was the intended target of FDA's regulatory regime. ECF

20-26 at 24–25. The "whole point" was to increase access to mifepristone, especially in pro-life states. *Texas Corn Producers*, 141 F.4th at 700. So Louisiana has established both injury-in-fact and traceability.

c. Because Louisiana's standing is plain, the opposing parties offer a litany of distractions—none availing.

First, GenBioPro tries to rewrite history altogether. It claims, for example, that the story above is "pure fiction," ECF 54-4 at 9, and it revises the historical record to claim that the 2023 REMS was just an innocuous extension of the pandemic-era 2021 enforcement decision suspending the in-person dispensing requirement. *See* ECF 1, ¶ 51. This lawsuit, of course, does not challenge that temporary suspension, which no longer exists. But, more importantly, the Fifth Circuit already has determined that "FDA simply did not tether its [2023] action" in permanently removing the in-person dispensing requirement "to the continued existence of the public health emergency" that prompted the 2021 decision. *All. for Hippocratic Med. v. FDA (Alliance II)*, 78 F.4th 210, 248 (5th Cir. 2023), *rev'd and remanded sub nom. FDA v. All. for Hippocratic Med.*, 602 U.S. 367 (2024).

GenBioPro also tries to cover the Court's eyes to the fact that President Biden was quite literally directing this assault into pro-life states. These were all just statements from "various public officials," GenBioPro says—and besides, President Biden is not even an FDA official. ECF 54-4 at 10. With all respect, the idea that the Court should disregard the President's involvement in abridging pro-life states' laws is unserious.

Second, the parties on the other side run through a number of precedents—none of which help them. For example, FDA, Danco, and GenBioPro assert that *United States v. Texas* precludes any state standing based on indirect effects of federal agency actions. 599 U.S. 670 (2023). But that "extraordinarily unusual lawsuit" involved Texas's challenge to federal prosecutorial discretion—a core executive power. *Id.* at 684, 686. It addressed "only the narrow Article III standing question of whether the Federal Judiciary may in effect order the Executive Branch to take enforcement actions against violators of federal law," *id.* at 684–85—a question that is worlds away from the issues presented here. *See id.* at 686 ("The Court's standing decision today is narrow and simply maintains the longstanding jurisprudential status quo."). But, more fundamentally, insofar as *Texas* gestured at

"federal policies [that] frequently generate indirect effects on state revenues or state spending," *id.* at 680 n.3, the 2023 REMS is nothing of the sort: By design, the 2023 REMS was intended to authorize a *direct* attack on pro-life states, and that attack, in turn, has caused natural sovereign and economic harms. There is nothing "indirect" or coincidental about it.

The opposing parties also rely on the Ninth Circuit's nonbinding decision in *Washington v. FDA*, 108 F.4th 1163 (9th Cir. 2024). *Washington* deemed "highly speculative" a State's Medicaid costs incurred under the 2023 REMS, and it dismissed as based "heavily on speculation" the State's argument that the 2023 REMS would make it more difficult to enforce the State's pro-life laws. *Id.* at 1174, 1177. *Washington* is self-distinguishing because Louisiana does not need speculation: It has the Medicaid receipts to prove that the 2023 REMS has caused tens of thousands of dollars in unrecoverable financial harm. And subsequent to *Washington*, pro-abortion groups published rounds of data showing that, although Louisiana has significantly restricted abortion, there are nearly 1,000 abortions occurring in the State every month—all through mail-order abortion. ECF 20-26 at 5. The *Washington* court had none of this evidence and did not purport to issue a decision on facts like these.

Finally, the opposing parties try to shoehorn Louisiana into the *Alliance* decision where the Supreme Court found that plaintiff doctors did not have standing. That attempt is misplaced. The doctors' problem was that they did not show "that they could be forced to participate in an abortion or provide abortion-related medical treatment over their conscience objections." *Alliance*, 602 U.S. at 387. Here, by contrast, the State has demonstrated that it not only "could be" forced to pay for the medical costs attributable to FDA-approved mifepristone, but it also *has* been so forced—to the tune of tens of thousands of dollars. That is precisely the direct line of causation that the *Alliance* Court believed lacking. And that is in addition to the even-more-direct sovereign (and economic) harms that flow from the 2023 REMS' permitting doctors to mail mifepristone in violation of Louisiana law.

C. Plaintiffs' Injuries Are Redressable.

As the traceability discussion suggests, the redressability inquiry is open-and-shut—and indeed, no one contests this point: A judicial decision staying the 2023 REMS (in particular, its removal of the in-person dispensing requirement) would leave prescribers no choice but to comply with the

in-person dispensing requirement. Put otherwise, prescribers could not continue violating Louisiana law by mailing mifepristone into Louisiana. Just listen to the ACLU: "If the court grants Louisiana's motion, [requesters] will no longer be able to fill their mifepristone prescription by mail[.]"[11]

That is the very definition of redressability.[12] For, without the in-person dispensing requirement, prescribers cannot blanket Louisiana with mailed mifepristone. Without that flood of mifepristone, 1,000 illegal abortions each month in Louisiana cannot occur. And without 1,000 illegal abortions (and attendant emergency costs) each month, Louisiana's sovereignty and fisc are restored. Now, to be sure, that restoration may not be fully complete if a prescriber or two opt to violate the (newly reinstated) federal in-person dispensing requirement.[13] But redressability does not require certainty that the injury will be entirely eliminated; a substantial likelihood that the injury at least will be partially redressed is sufficient. *See Larson v. Valente*, 456 U.S. 228, 243 n.15 (1982). And that is the case here, illustrating that Plaintiffs satisfy all three elements of Article III standing.

D. Plaintiffs Fall Within the Relevant Zones of Interest.

Among other efforts to get around Plaintiffs' standing, Danco and GenBioPro (but not FDA) argue Plaintiffs are not within the zone of interests of the FDCA and the Comstock Act. ECF 52-4 at 14–15; ECF 54-4 at 12 n.2. They are wrong. The prudential zone-of-interests test "is not meant to be especially demanding and is applied in keeping with Congress's evident intent when enacting the APA to make agency action presumptively reviewable." *DAPA*, 809 F.3d at 162 (citation modified). This court-constructed test "looks to the law's substantive provisions to determine what interests (and hence which plaintiffs) are protected." *Simmons v. UBS Fin. Servs., Inc.*, 972 F.3d 664, 669 (5th Cir.

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[11] Press Release, Louisiana Lawsuit Seeks Immediate Nationwide Restrictions on Medication Abortion, ACLU (Dec. 17, 2025), perma.cc/MB39-DSAV.

[12] *See, e.g.*, Carrie Baker, *Mifepristone Manufacturers Move to Block GOP Lawsuit Seeking Nationwide Telehealth Abortion Ban*, Ms. Magazine, perma.cc/5P43-CBEJ ("Telehealth abortion from out of states is a critical avenue of access for women living in states that restrict abortion providers located inside the states from providing abortion services.").

[13] In this respect, GenBioPro appears to argue that—even without the 2023 REMS—there is no evidence that prescribers would be less likely to mail abortion drugs. The Court should be aware that this is a suggestion GenBioPro will not follow the law. GenBioPro has an affirmative duty to audit prescribers to ensure a REMS is being followed. ECF 20-16 at 4; 21 U.S.C. § 355-1.

2020). "That interest, at times, may reflect aesthetic, conservational, and recreational as well as economic values." *Ass'n of Data Processing Serv. Orgs., Inc. v. Camp*, 397 U.S. 150, 154 (1970) (citation modified). The "benefit of any doubt" must go to the plaintiff. *Simmons*, 972 F.3d at 666 n.3 (citation omitted). That "lenient approach" is necessary to preserve the APA's "generous review provisions," as well as a federal court's "virtually unflagging" obligation to hear cases within its jurisdiction, *Lexmark Int'l, Inc. v. Static Control Components, Inc.*, 572 U.S. 118, 126, 130 (2014) (internal marks omitted). "The test forecloses suit only when a plaintiff's interests are so marginally related to or inconsistent with the purposes implicit in the statute that it cannot reasonably be assumed that Congress intended to permit the suit." *DAPA*, 809 F.3d at 162 (internal marks omitted). In other words, "[t]here is no presumption against judicial review and in favor of administrative absolutism unless that purpose is fairly discernible in the statutory scheme." *Camp*, 397 U.S. at 157 (internal marks and citation omitted).

Danco and GenBioPro complain that Plaintiffs identify no particular provision of the FDCA protecting their interests. But "no explicit statutory provision" is necessary. *Id.* at 155. Moreover, Plaintiffs' interests are far more than "marginally related" to the purposes implicit in the FDCA. *DAPA*, 809 F.3d at 162. The FDCA prohibits the introduction and delivery of adulterated or misbranded drugs into interstate commerce. 21 U.S.C. § 331. The FDCA's mandates to "protect the public health," Public Law No. 87-781, 76 Stat. 780, "assure the safety, effectiveness, and reliability" of FDA-approved drugs, *id.*, and consider the "seriousness of any known or potential adverse events that may be related to the drug," 21 U.S.C. § 355-1(a)(1)(E), are intended "to ensure that the [FDCA] not be implemented haphazardly," *Bennett v. Spear*, 520 U.S. 154, 176 (1997). Certainly, Louisiana has an interest in protecting public health and safety and in keeping adulterated or misbranded drugs from entering its borders. And "[t]he threatened injury to a State's enforcement of its safety laws is within

the zone of interests of the Administrative Procedure Act[.]" *State of Ohio ex rel. Celebrezze v. U.S. Dep't of Transp.*, 766 F.2d 228, 233 (6th Cir. 1985).[14]

Likewise, Louisiana is within the zone of interests of the Comstock Act. This statute "indicates a national policy of discountenancing abortion as inimical to the national life." *Bours v. United States*, 229 F. 960, 964 (7th Cir. 1915); *see also Bolger v. Youngs Drug Prods. Corp.*, 463 U.S. 60, 70 n.19 (1983) (the "thrust" of the Act was "to prevent the mails from being used to corrupt the public morals"). Louisiana is well within this zone of interest because it has a "longstanding policy" protecting the "right to life of every unborn child from conception" and finding that abortion is "impermissible." La. R.S. § 40:1061.1(A)(2). It also has an interest in protecting public health and the well-being of its citizens, promoting public morals in seeing that the scheme passed by its Legislature is properly enforced, and in protecting its self-governing authority. *Sierra Club v. City of San Antonio*, 115 F.3d 311, 315 (5th Cir. 1997). As to both statutes, there is no evidence that Congress "sought to preclude judicial review of administrative rulings" by FDA "as to the legitimate scope of activities available" concerning chemical abortion drugs. *Camp*, 397 U.S. at 157. Accordingly, the zone-of-interests argument is meritless.

II. The Court Should Preliminarily Stay the 2023 REMS.

A. As FDA Does Not Dispute—and As Two Fifth Circuit Panels Have Held—Plaintiffs Are Likely to Succeed on the Merits.

Because Plaintiffs have standing, the rest of the preliminary-relief analysis is eminently straightforward under *Alliance I* and *Alliance II*, beginning with the merits.

1. Plaintiffs are likely to succeed on the merits of their arbitrary-and-capricious challenge to the 2023 REMS—so likely that FDA does not defend the 2023 REMS. Indeed, FDA itself agrees with "the *concerns* about removing the in-person dispensing requirement foreshadowed by the Fifth Circuit" in *Alliance II* and "the *lack of adequate consideration* underlying" the 2023 REMS. ECF 51 at 1 (emphases

[14] So, too, for Rosalie. As the *Alliance* district court recognized (before the Supreme Court reversed on standing grounds), patients are within the FDCA's zone of interests because they seek safe and effective medical procedures. *All. for Hippocratic Med. v. FDA*, 668 F. Supp. 3d 507, 530 (N.D. Tex. 2023).

added). That lack of adequate consideration is what led two prior Fifth Circuit panels to affirm a stay of the 2023 REMS, finding it "defect[ive]," "unreasonable," and "deeply troubling." *See All. for Hippocratic Med. v. FDA (Alliance I)*, No. 23-10362, 2023 WL 2913725, at *17 (5th Cir. Apr. 12, 2023); *Alliance II*, 78 F.4th at 249–50.

Danco claims that those conclusions by "some judges" improperly second-guessed FDA's scientific judgment. ECF 52-4 at 17; *see also* ECF 51 at 10. That is wrong. In determining that the 2023 REMS likely is neither reasonable nor reasonably explained, the Fifth Circuit panels did what judges do every day: They applied the APA to call an agency's strike a strike. Waving a "scientific judgment" flag does not magically relieve FDA from the APA's strictures.

Danco also recycles its failed *Alliance* argument that FDA reasonably relied on FAERS data in removing in-person dispensing. ECF 52-4 at 18–19. But FAERS data "are not an indicator of the safety profile of the drug." ECF 1-52 at 5. Rather, FDA itself warns that "[r]ates of occurrence [for an adverse event] cannot be established with [FAERS] reports." *Id.* Yet to approve the 2023 REMS, FDA "analyzed the FAERS data" from parts of 2020 and 2021 "to determine if there was a difference in adverse events when in-person dispensing was and was not enforced." ECF 1-10 at 27; *see also* ECF 1-50 at 64–65. But, as the Fifth Circuit recognized, "considerable evidence shows that FAERS data is insufficient to draw general conclusions about adverse events." *Alliance II*, 78 F.4th at 249. It was thus arbitrary for FDA to use data that "cannot be used to calculate the incidence of an adverse event," ECF 1-52 at 3, to determine the incidence of mifepristone's adverse events.

Danco waves away this problem because drug sponsors must report the adverse events that come to their attention. But abortion providers are not required to submit non-fatal adverse event reports to the drug sponsors. ECF 1-10 at 20 (acknowledging some events may not be reported because reporting is voluntary). And the sponsors have "no direct relationship with [mifepristone] patients and little ability to track events." *Alliance II*, 78 F.4th at 247. The Fifth Circuit thus correctly concluded that the sponsors' "residual reporting requirements do not cure this APA violation." *Id.*

Danco next says that FDA concluded that the published literature "supported" the 2023 REMS. ECF 52-4 at 18–19. That is not the full story. FDA also conceded the studies were "not

adequate on their own to establish the safety of … dispensing mifepristone by mail." ECF 1-10 at 35. They were merely "not inconsistent with [FDA's] conclusion" that removing the last remaining in-person doctor visit was safe. *Id.* at 28. As two different Fifth Circuit panels concluded, it was arbitrary and capricious for FDA to remove what it recently acknowledged was both "minimally burdensome" and "necessary to mitigate" mifepristone's "serious risks," Appl. for Stay, *FDA v. ACOG*, No. 20A34, 4, 7, 13 (U.S. Aug. 26, 2020), based on FAERS data that "cannot be used to calculate the incidence of an adverse event," plus studies that were "not adequate on their own to establish the safety of … dispensing mifepristone by mail." *See Alliance II*, 78 F.4th at 249, 250 (rejecting claim that studies "supported [FDA's] conclusion that mifepristone would still be safe and effective even with a relaxed in-person dispensing requirement").

2. Although this Court need not reach the Comstock Act issue Judge Ho reached, it also bears noting that the 2023 REMS directly conflicts with the Comstock Act. Indeed, "using the mails for the mailing of a drug for producing abortion is *precisely* what the Comstock Act prohibits." *Id.* at 267–68 (Ho, J., concurring) (citation modified and emphasis added).

Danco's responses are difficult to follow. For example, Danco claims that administrative agencies may disregard federal law outside of their enabling statutes—a claim directly refuted by (a) the APA's mandate to set aside actions that are "otherwise not in accordance with law" and (b) the Supreme Court's unqualified statement in *FCC v. NextWave Pers. Commc'ns Inc.*, 537 U.S. 293 (2003), that "otherwise not in accordance with law" means "any law." *Id.* at 300; *contra* ECF 52-4 at 21–22. More, Danco's argument would mean that federal agencies need not concern themselves with the Religious Freedom Restoration Act or a multitude of environmental statutes. That obviously is not the law.

Danco also notes that FDA routinely approves drugs that are subject to other statutes, like the Controlled Substances Act ("CSA"). But FDA approval does not authorize conduct prohibited by the CSA. Here, in contrast, the 2023 REMS authorizes using the mails to distribute an abortion-producing drug—conduct that the Comstock Act expressly forbids.

Finally, both Danco and GenBioPro would rewrite the Comstock Act to prohibit only "illegal abortions" based on post-enactment history. ECF 54-4 at 20–21; ECF 52-4 at 21–22. But the text contains no such limitation, and Congress in 1978 considered—and rejected—an amendment limiting the law to "illegal abortions." H.R. 13959, 95th Cong. §§ 6701(a)(2), 6702(1)(C)(i) (1978); *accord* Rep. of the Subcomm. on Crim. Just. on Recodification of Fed. Crim. L., H.R. Rep. No. 95-29, pt. 3, at 42 (1978) (explaining the amendment would "change[ ] current law by requiring proof … to produce an illegal abortion"); *see also* ECF 101 at 5; ECF 103-1 at 9. As a result, the post-enactment history of the Comstock Act "only reinforces the natural reading of the text." *Alliance II*, 78 F.4th at 270 (Ho, J., concurring). And to the extent the manufacturers cling to a smattering of old dicta from some circuit courts, the prior-construction canon modifies a statute's text only when the pre-enactment meaning is settled by "a uniform interpretation by inferior courts"—a standard plainly not satisfied here. *Tex. Dep't of Hous. & Cmty. Affs. v. Inclusive Cmtys. Project, Inc.*, 576 U.S. 519, 536 (2015) (citation omitted).

B. The Equities Favor Plaintiffs.

FDA's refusal to defend the 2023 REMS is dispositive on the equities. Neither FDA nor the public have an interest in enforcing a concededly unlawful regulation—and that is all the Court need say in resolving the equities. *Alliance II*, 78 F.4th at 251–52. But if the Court is inclined to say more, it need only identify Louisiana's undisputed irreparable harm, the public interest in favor of a stay, and FDA's failure to identify countervailing interests.

First, Louisiana faces concrete, irreparable harm absent preliminary relief. No one disputes that Louisiana is being blanketed by contraband mifepristone. For every month that the 2023 REMS remains in effect, nearly 1,000 FDA-approved mail-order abortion drugs enter Louisiana, causing abortions that violate Louisiana law and generating economic harms associated with those violations. For all the reasons Louisiana has standing, *see supra* Section I, its sovereign and economic harms are irreparable. *See Louisiana*, 705 F. Supp. 3d at 663 (finding Article III standing and irreparable harm "[f]or the same reasons"); ECF 20-26 at 15.

Second, the public interest here cuts in favor of women's health and thousands of unborn Louisiana children. The near-certain increase in emergency room visits caused by the 2023 REMS

(which FDA does not dispute) is reason enough to warrant a stay. *See* ECF 1 ¶¶ 32–40, 124–129, 156; ECF 20-26 at 15–16. But consider also that some women like Rosalie are forced to ingest abortion drugs against their will—a direct consequence of removing the in-person dispensing requirement. *See generally* ECF 1-92. Consider also that the "public interest" here arises from an express statement by the Louisiana people: their policy is to "protect the right to life of every unborn child from conception by prohibiting abortion." *Louisiana*, 705 F. Supp. 3d at 653 (quoting La. R.S. § 40:1061). The only way to vindicate the public interest in protecting mother and baby is to stay the 2023 REMS.

Third, and finally, FDA and the manufacturers identify no irreparable harm that *they* stand to suffer, nor anything that even comes close. Without elaboration (or a sworn declaration), FDA insists that this Court's review of the concededly unlawful 2023 REMS might somehow "disrupt" its own. *E.g.*, ECF 51 at 10. This argument is puzzling. FDA's review can continue apace with the in-person dispensing guardrail back in place. Whether FDA acted lawfully (it concedes it did not) is a legal question, not a scientific one, so it will not "short-circuit the agency's orderly review." ECF 51 at 3. And any "administrative inconvenience" cannot outweigh Louisiana's irreparable harms, especially where that inconvenience arises from the agency's own unlawful actions. *See Texas v. United States*, 40 F.4th 205, 229 (5th Cir. 2022) ("Despite the administrative inconvenience caused by this litigation, DHS has no interest in the perpetuation of unlawful agency action.") (citation modified); *Maryland v. King*, 567 U.S. 1301 (2012) (Roberts, C.J., in chambers).

FDA speculates about "administrative and judicial chaos" if Plaintiffs were to prevail here while another court vacates the 2023 REMS for different reasons. ECF 51 at 4. That speculation is misguided. The possibility of conflicting lower court rulings is, in part, why courts consider the "likelihood of success on the merits as an essential factor in determining when to grant emergency relief in individual cases." *Labrador v. Poe by & through Poe*, 144 S. Ct. 921, 931 (2024) (Kavanaugh, J., concurring). That standard minimizes such conflicts. And here FDA already has conceded that the 2023 REMS is unlawful. Regardless, our federal system leaves "determining the nationally uniform *interim* legal status ... of, say, the Clean Power Plan or Title IX regulations or mifepristone rules" to the Supreme Court—not the self-serving speculation of a federal agency in a district court. *Trump v.*

CASA, Inc., 606 U.S. 831, 876–77 (2025) (Kavanaugh, J., concurring) (describing the U.S. Supreme Court's "proper role" in deciding the interim status of new agency actions). The possibility that judges might disagree has never been cause to abdicate the judicial role.

For their part, Danco and GenBioPro speculate that reinstating the in-person dispensing requirement might take months to implement. Hardly. The infrastructure for this safeguard was in place for over 20 years. The Fifth Circuit was thus rightly unpersuaded by this speculation because Danco did "not deny" it "already has drug labels and documentation that comply with the [previous] mifepristone REMS." *Alliance II*, 78 F.4th at 252. The drug sponsors will have every incentive to swiftly recertify prescribers via an online two-page form. ECF 20-16 at 5. And to the extent GenBioPro set up a distribution model around mail-order mifepristone, ECF 54-4 at 24, that regime has been subject to uninterrupted litigation from its inception. GenBioPro cannot avoid a stay simply because it built its business on a rocky legal and regulatory foundation.

C. FDA's "Delay" Argument Is Meritless.

Apparently sensing that Plaintiffs are plainly entitled to a preliminary stay of the 2023 REMS, FDA (joined by Danco and GenBioPro) suggests that Plaintiffs' alleged "delay" in seeking such relief undercuts any claim of ongoing urgency. FDA misunderstands both the law and the facts. The standard for assessing whether a delay might weigh against preliminary relief is "reasonable diligence." *Benisek v. Lamone*, 585 U.S. 155, 159 (2018). And courts routinely "permit delays when determining the imminence of alleged irreparable harm where delays were 'caused by [plaintiff's] good faith efforts to investigate facts and law.'" *ADT, LLC v. Cap. Connect, Inc.*, 145 F. Supp. 3d 671, 699 (N.D. Tex. 2015) (collecting cases). FDA does not come close to displacing these principles.

First, as this Court is aware, Plaintiffs' interests were represented in the *Alliance* litigation. The *Alliance* lawsuit was initiated in November 2022 and the Fifth Circuit affirmed preliminary relief against the removal of the in-person dispensing requirement. The Supreme Court stayed that relief, however, which means that any lawsuit filed by Louisiana would almost certainly have been stayed pending the outcome in *Alliance*. In June 2024, the Supreme Court reversed on standing grounds, saying nothing

about the merits. And on remand, three state intervenors—which, again, represented Louisiana's interests—continued to press the argument that the 2023 REMS were unlawful.

Second, a presidential election occurred, and Louisiana sought to force an administrative reversal of the 2023 REMS through political negotiations—a possibility that seemed substantial given public statements by the new Administration. *See, e.g.*, ECF 51 at 1. When DOJ instead filed a reply in support of its motion to dismiss the still-pending *Alliance* litigation, Louisiana sought to intervene in that lawsuit. And when the *Alliance* court transferred the case to Missouri and dismissed Louisiana's intervention motion as moot, Louisiana filed this lawsuit six days later. And all the while, Louisiana has been pursuing its own criminal avenues attempting to stop the problem. That is diligence.

Third, and perhaps most significant, abortion providers began documenting illegal, mail-order abortions in July 2023, but it was not until October 2024—on the eve of the presidential election—that the nature and extent of Louisiana's harm became apparent. The Society of Family Planning's #WeCount data revealed for the first time the number of mail-order abortions taking place in Louisiana. And new data, showing that the number has ballooned to nearly 1,000 abortions a month, was released just days before Louisiana filed this suit.

FDA and the manufacturers take issue with the two months that passed between Plaintiffs' complaint and their motion for preliminary relief. But that brief interval reflects Plaintiffs' diligent pursuit of fact-intensive standing-related evidence reflected in the robust record Plaintiffs provided the court at this preliminary stage. That due diligence is not somehow fatal. *E.g.*, *ADT, LLC*, 145 F. Supp. 3d at 699 (eight-month delay with imminent need); *Optimus Steel, LLC v. U.S. Army Corps of Eng'rs*, 492 F. Supp. 3d 701, 719 (E.D. Tex. 2020) (eleven-month delay with "good explanation"). Nor does it compare to the examples of unreasonable delay cited by FDA. *E.g.*, *Parker v. Dacres*, 130 U.S. 43, 49 (1889) (waiting nine years to assert rights under a statute that required the same within six months); *Tate v. LeBlanc*, No. CIV.A. 13-1253-P, 2014 WL6455794, at *2 (W.D. La. Nov. 17, 2014) (waiting more than a year after the complaint to ask for preliminary relief).

In any event, Plaintiffs' supposed "delay" especially is not fatal given FDA's concession that the 2023 REMS is unlawful and Plaintiffs' victory on the equities. None of the cases Danco and

GenBioPro cite involve ongoing harms caused by conduct the defendant itself acknowledged to be unlawful. Those differences are dispositive. Here, FDA has conceded that the 2023 REMS is unlawful, and the ongoing and irreparable harms suffered by Plaintiffs warrant preliminary relief. That distinguishes FDA's best case, *AMID, Inc., v. Medic Alert Found. U.S.*, 241 F. Supp. 3d 788 (S.D. Tex. 2017), where the court declined to award relief on two claims—one because there was no likelihood of success and the other because there was no ongoing harm. Here, FDA does not dispute the merits, and Louisiana is suffering severe and ongoing harm. The Court should ignore FDA's attempt to manufacture a "delay" issue that ignores Plaintiffs' clear satisfaction of the preliminary-relief factors.

D. As the Fifth Circuit Has Held, a Universal Preliminary Stay Is the Appropriate Relief.

As Plaintiffs explained, ECF 20-26 at 16–17, all that is left is for the Court to enter the same relief that the Fifth Circuit previously entered: a preliminary stay of the 2023 REMS under 5 U.S.C. § 705, which would ensure that the longstanding in-person dispensing requirement "will continue to apply." *Alliance II*, 78 F.4th at 254.

FDA recycles (at 11) its failed *Alliance II* argument that a court may not "postpone" the effective date of any agency action already in effect. But the Fifth Circuit expressed "strong[] doubt[s]" about that argument for which FDA has "no authority." *Alliance II*, 78 F.4th at 255–56. And for good reason: Section 705 broadly authorizes a court to issue "all necessary and appropriate process to postpone the effective date of an agency action *or* to preserve status or rights pending conclusion of the review proceedings." 5 U.S.C. § 705 (emphasis added). Because that statutory disjunctive forecloses FDA's myopic focus on the word "postpone," FDA deflects by claiming that "to preserve" likewise can remedy only agency action that has not yet gone into effect. ECF 51 at 11. Wrong again. The "status quo" protected by section 705 is "'the status quo' *before the unlawful agency action took place*." *Louisiana v. EEOC*, 784 F. Supp. 3d 886, 909–10 (W.D. La. 2025) (emphasis added); *Wages & White Lion Invs., L.L.C. v. FDA*, 16 F.4th 1130, 1144 (5th Cir. 2021) ("[T]he relief sought here would simply suspend *administrative* alteration of the *status quo*."); *Nken v. Holder*, 556 U.S. 418, 429 & n.1 (2009) (status quo is "the state of affairs before" the challenged agency action). Thus, "[w]hether the effective

date of the [2023 REMS] has passed is irrelevant to this Court's ability to issue a Section 705 stay." *Texas v. Biden*, 646 F. Supp. 3d 753, 770 (N.D. Tex. 2022) (collecting cases); *see also Texas v. United States Dep't of Health & Hum. Servs.*, 770 F. Supp. 3d 940, 957 (E.D. Tex. 2025).

Relatedly, Danco argues that this Court may not award preliminary relief without a full administrative record. ECF 52-4 at 17. But the APA expressly allows a court to grant relief based on "the whole record or *those parts of it cited by a party*." 5 U.S.C. § 706 (emphasis added). That is why two panels of the Fifth Circuit affirmed preliminary relief in *Alliance I* and *II* based on a materially identical record. *Alliance II*, 78 F.4th at 250; *Alliance I*, 2023 WL 2913725, at *8. Were the rule otherwise, agencies could block preliminary relief indefinitely by, for example, hoarding part of the record in "cold storage." *See Alliance II*, Oral Arg. at 24:30 (5th Cir. May 17, 2023). Here, FDA has had years to produce any additional materials—beyond the "decisional documents" in the record—that it believes would advance its case. Its failure to do so does not deprive this Court of the power to issue preliminary relief.

E. The Manufacturers' Exhaustion Argument Is Meritless.

In the same desperate vein, the manufacturers assert that Plaintiffs failed to exhaust administrative remedies. That is doubly wrong.

First, the APA requires exhaustion only when required by statute or a rule "provides that the [agency] action ... is inoperative" during appeal. 5 U.S.C. § 704; *accord Darby v. Cisneros*, 509 U.S. 137, 154 (1993) (exhaustion required "*only* when expressly required by statute or when an agency rule requires appeal before review and the administrative action is made inoperative pending that review"). No such statute or rule exists here. Krupka, *Exasperated But Not Exhausted: Unlocking the Trap Set by the Exhaustion Doctrine on the FDA's REMS Petitioners*, 77 Vand. L. Rev. 937, 977–78, 980 (2024), perma.cc/3BHM-WRQE. Because FDA does not hold its REMS "inoperative" upon receiving a petition, exhaustion does not apply. *MCR Oil Tools, L.L.C. v. United States Dep't of Transp.*, 110 F.4th 677, 691 (5th Cir. 2024).

Second, and in any event, courts do not require exhaustion where one of the "traditionally recognized" exceptions applies. *Wash. Ass'n for Television & Child. v. FCC*, 712 F.2d 677, 682 (D.C. Cir. 1983). At least three are relevant here.

Start with administrative abuse of process. It is "well-established that where an agency fails to follow its own regulations, exhaustion may not be required." *Alliance I*, 2023 WL 2913725, at *16; *see also Way of Life Television Network, Inc. v. FCC*, 593 F.2d 1356, 1359–60 (D.C. Cir. 1979). FDA's own regulations require it to respond to citizen petitions within 180 days. *See* 21 C.F.R. § 10.30(e)(2). Yet the average REMS petition languishes for 937.6 days. *See* Krupka, *supra*, at 957–63. Worse, in *Alliance I*, FDA subjected plaintiffs to "sixteen years of delay, dawdle, and dithering," before eventually rejecting their petitions. *All. for Hippocratic Med. v. FDA*, 668 F. Supp. 3d 507, 538 (N.D. Tex. 2023). Plaintiffs here can expect no better. Based on "FDA's repeated failure to follow its own regulations," this Court should waive exhaustion (if such a requirement existed). *Alliance II*, 2023 WL 2913725, at *16.

Next take futility. "[T]he record shows that FDA would have denied any request for an administrative stay." *Alliance II*, 78 F.4th at 255. Indeed, FDA "expressly reaffirmed its commitment to mail-order abortion drugs" in a 2021 petition denial—the day FDA decided to permanently remove in-person dispensing and direct the abortion-drug companies to submit a proposed REMS without that requirement. *Alliance I*, 2023 WL 2913725, at *15. And FDA doubled down on its mail-order scheme by denying a similar petition on January 3, 2023—the day FDA formally approved the 2023 REMS. ECF 1-34. That is why the *Alliance II* Court concluded that it would have been clearly useless to raise the same challenge again. 78 F.4th at 255. In fact, another court found that a coalition of states did not need to file a petition that others had already filed and FDA had rejected because the agency could not "credibly argue that its decision on the Mifepristone REMS Program would change upon another citizen petition." Order Granting in part Pls.' Mot. Prelim. Inj., *Washington v. FDA*, No. 1:23-cv-03026 (E.D. Wash. Apr. 7, 2023), ECF No. 80 at 17 (perma.cc/J9Q4-85FU). Just so here.

Last, a typical exception "is where irreparable injury would result unless immediate judicial review is permitted." *Randolph-Sheppard Vendors of Am. v. Weinberger*, 795 F.2d 90, 107 (D.C. Cir. 1986) (collecting cases). That exception plainly applies here given the irreparable harms articulated above.

III. The Court Should Deny FDA's Request to Indefinitely Stay This Case.

The foregoing discussion also resolves FDA's puzzling attempt to shutter this case for years at the expense of quite literally thousands of unborn Louisiana children who would lose their lives in the meantime. When a party seeks to forestall adjudication of a motion for preliminary relief, a court must first decide whether the movant is entitled to preliminary relief. *E.g.*, *Procter & Gamble Co. v. Kraft Foods Global, Inc.*, 549 F.3d 842, 847–50 (Fed. Cir. 2008). Only after resolving that issue would the question of a stay properly arise—and at that juncture, the governing standard comes from *Nken v. Holder*, 556 U.S. 418, which FDA does not cite much less attempt to satisfy. *See, e.g.*, *Community Television of Utah, LLC v. Aereo, Inc.*, 997 F. Supp. 2d 1191, 1195–1205, 1209–11 (D. Utah 2014) (granting preliminary injunction and then considering *Nken* stay factors). And in all events, a free-floating *Landis* inquiry would not help FDA because Plaintiffs' satisfaction of the preliminary-relief factors all but forecloses any attempt to stay relief against a regulation that FDA refuses to legally defend. *See Alliance I*, 2023 WL 2913725, at *4, *21; *cf. Procter & Gamble Co.*, 549 F.3d at 849.

A. Begin with the *Nken* factors. *First*, for all the reasons explained above, FDA cannot muster the "strong showing" of a likelihood of success on the merits of Plaintiffs' APA claims—indeed, FDA does not even defend the 2023 REMS. *Nken*, 556 U.S. at 426.[15]

Second, FDA does not even try to claim irreparable harm. *Id.* The most FDA identifies is a worry that a challenge to the 2023 REMS—agency action FDA concedes is unlawful—might cause administrative burdens and disrupt FDA's own purported safety review. That is not irreparable harm. Thus, the two "most critical" factors—likelihood of success and irreparable injury—weigh decisively in Plaintiffs' favor. *Alliance I*, 2023 WL 2913725, at *4 (citing *Nken*, 556 U.S. at 434).

[15] Notwithstanding Defendants' and the manufacturers' objections to the applicability of the Comstock Act, the Fifth Circuit found that it "nevertheless undermines applicants' showing on the final three *Nken* factors." *Alliance I*, 2023 WL 2913725, at *20.

Third, FDA cannot carry its burden to show that a stay would not harm Plaintiffs. *Nken*, 556 U.S. at 426. Louisiana suffers irreparable sovereign and economic harms every day that the 2023 REMS remains in effect due to the 1,000 abortions that everyone agrees are occurring each month in Louisiana. And as Rosalie's tragic story shows, the 2023 REMS allows domestic abusers to order abortion drugs and force pregnant women to take them.

And *fourth*, FDA's nondefense of the 2023 REMS settles the public interest inquiry. As recounted above, hornbook law says there is no public interest in the perpetuation of unlawful agency action—much less indefinitely for years into the future. FDA counters that "it is not in the public interest to interrupt the administrative process." ECF 51 at 10 (quoting *Peak v. D.C.*, No. CV 06-0373 (JGP), 2006 WL 8445985, at *6 (D.D.C. Mar. 20, 2006)). But *Peak* merely said there was no need to disrupt an administrative process in the absence of a likelihood of success on the merits. *Id.* Here, FDA concedes the 2023 REMS is unlawful. FDA also says judicial relief "may prove [] unnecessary" if its purported safety review culminates in the agency's attempt to rescind the 2023 REMS. ECF 51 at 3. Setting aside FDA's speculation (through only a lawyer's pen, no less), FDA's post-hoc study cannot cure its prior unlawful action. *Dep't of Homeland Sec. v. Regents of the Univ. of Cal.*, 591 U.S. 1, 20–21 (2020). Meanwhile, Louisiana and its women and children suffer harm with each day that passes.

At bottom, FDA wants this Court to allow a "plainly unconstitutional or otherwise illegal [agency action]" to "remain in effect ... for several years pending" FDA's planned safety review. *Labrador*, 144 S. Ct. at 931 (2024) (Kavanaugh, J., concurring). FDA calls this the "status quo," ECF 51 at 11, which is just wrong as explained above: The status quo is the last lawful state of affairs—*i.e.*, before removal of the in-person dispensing requirement. If the status quo were the unlawful agency action, recalcitrant agencies could always avoid APA injunctions. That is not the law.

FDA also cites no case allowing an unlawful agency action that imposes irreparable harm to remain in place just because the agency said it was studying the unlawful action. *Ali v. Quarterman* vacated an administrative closure and directed the lower court to "*move forward with the case* so far as is practicable." 607 F.3d 1046, 1049 (5th Cir. 2010). In *Purcell*, the court granted an unopposed stay only once plaintiffs had secured relief from their alleged injuries. *Chelius v. Becerra*, No. CV 17-00493 JAO-

RT, 2023 WL 5041616, at *2–3 (D. Haw. Aug. 8, 2023). Similarly, the *Landis* plaintiffs faced no ongoing harm while their case was stayed. *Landis v. N. Am. Co.*, 299 U.S. 248, 251–52 (1936). And *Ricci v. Chicago Mercantile Exchange* upheld a stay where there was no ongoing or irreparable harm. 409 U.S. 289, 291, 305 (1973). Plus, FDA has had *five years* to study this issue since the Biden Administration first removed the in-person dispensing requirement. FDA made its bed, and now the APA provides for judicial review.[16]

B. The results do not change under *Landis*. FDA still "bears the burden of showing that the circumstances justify an exercise of [the Court's] discretion." *Nken*, 556 U.S. at 434. FDA "must make out a *clear case of hardship or inequity* in being required to go forward, if there is *even a fair possibility* that the stay for which he prays will work damage to some one [sic] else." *Landis*, 299 U.S. at 255 (emphases added). FDA identifies no hardship beyond the ordinary burdens of litigation and administrative review—generated by its own concededly unlawful action—while Plaintiffs face ongoing irreparable harm. FDA also makes no "showing that the difficulties inherent in the general situation, including potential judicial inefficiency, constitute a sufficient offset to the plaintiffs' rights to proceed without inordinate delay to a resolution of their claims." *Wedgeworth v. Fibreboard Corp.*, 706 F.2d 541, 546 (5th Cir. 1983). Particularly here, where the "realities of the hardship of a stay on the plaintiffs" is "substantial" and "permanent," and the stay "hinged on completion of" a study that "is manifestly 'indefinite,'" FDA can't sustain its burden under *Landis*. *Id.* at 545.

One last point about practicalities: The earliest time FDA could reasonably reinstate the in-person dispensing requirement is 2027. FDA (well, FDA's lawyer) says it might complete its study

[16] For similar reasons, the manufacturers' claim that this case is not ripe because FDA might change course in the future misunderstands the law. Ripeness ensures that federal courts do not adjudicate disputes prematurely—where, for example, an agency has not yet acted. *Abbott Laboratories v. Gardner*, 387 U.S. 136, 148–49 (1967) (explaining that ripeness "protect[s] the agencies from judicial interference until an administrative decision has been formalized and its effects felt in a concrete way by the challenging parties"). Here, there is no dispute that the 2023 REMS is final agency action. The lawfulness of that action is fully fit for judicial resolution—and in fact, there can be no further factual development vis-a-vis the 2023 REMS. *See Motor Vehicle Mfrs. Ass'n of the U.S., Inc. v. State Farm Mut. Auto. Ins.*, 463 U.S. 29, 41 (1983); *contra* ECF 52-4 at 16.

(but not its review) "sooner than" "a year or more." ECF 51 at 3.[17] But FDA puts forth zero evidence that it has even requested or commissioned the data necessary to initiate its purported review—other than vague statements on its own website that its efforts purportedly began in late January 2026. And this, after first promising this review over a year ago.[18] Worse, even once the agency achieves "Gold Standard Science and rigorous, transparent, and objective evidence," ECF 51 at 1, after "a year or more," that review is only the first step under 21 U.S.C. § 355-1. Next, the Secretary may direct the drug sponsor to modify the REMS "within 120 days or within [a] reasonable time." 21 U.S.C. § 355-1(g)(4)(B). At the expiration of the 120 days, the sponsor may challenge the REMS changes before the Drug Safety Oversight Board, which Danco and GenBioPro inevitably will. 21 U.S.C. § 355-1(h)(4)(A)(i); 21 U.S.C. § 355-1(j)(2). The Board reviews the parties' submissions, hears the dispute, and provides a written recommendation to the Secretary, who issues an action letter. 21 U.S.C. § 355-1(h)(4). All of this takes time. So even assuming that FDA takes the least time estimated for its study, by law the earliest FDA could restore in-person dispensing is about 18 months now. Worse, there is no evidence that FDA has even requested or commissioned the data it needs to start its review. Put another way, FDA's stay request asks this Court to ignore at least 18,000 illegal abortions, 18,000 unborn lives, at least 720 emergency room visits, and tens of thousands of dollars in unrecoverable costs from now—just in Louisiana.

CONCLUSION

The Court should preliminarily stay the 2023 REMS and deny FDA's motion to stay.

[17] U.S. Food & Drug Administration, Questions & Answers — Mifepristone Medical Termination of Pregnancy Through Ten Weeks Gestation (Feb. 2, 2026), perma.cc/M6YM-7MK5.

[18] Andrew Stanton, RFK Jr. Says He Would Study Abortion Pill Mifepristone Safety Issues, Newsweek (Jan. 29, 2025) perma.cc/5T8R-MU7S.

Dated: February 17, 2026

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on February 17, 2026, pursuant to Federal Rule of Civil Procedure 5(b)(2)(C), a true and correct copy of the foregoing memorandum, and all attachments thereto, was served by CM/ECF.

/s/ *Caitlin Huettemann*
Caitlin Huettemann

EXHIBIT A

UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF LOUISIANA
LAFAYETTE DIVISION

THE STATE OF LOUISIANA, by and through its Attorney General, LIZ MURRILL, and ROSALIE MARKEZICH, *Plaintiffs*, v. U.S. FOOD AND DRUG ADMINISTRATION, *et al.*, *Defendants*.	Case No.: 6:25-cv-01491-DCJ-DJA Judge David C. Joseph Magistrate Judge David J. Ayo

DECLARATION OF ERIN TONER

Pursuant to 28 U.S.C. § 1746, I, Erin Toner, affirm under penalty of perjury:

1. I am over the age of 18, have personal knowledge of the matters set forth herein, and am competent to make this Declaration.

2. I serve as the Human Resources Program Director in the Louisiana Department of Justice ("DOJ"). In my role, I manage the Louisiana DOJ's HR department, aligning HR strategy with business goals. I oversee talent acquisition, compensation, compliance, and employee relations. I also act as a vital link between staff and executive leadership.

3. The Louisiana Bureau of Investigation ("LBI") is a department of the Louisiana DOJ. LBI is responsible for the investigation of criminal activity, intelligence gathering, and case and technical support in Louisiana. LBI contains several "divisions," including the Criminal Investigations Division and the Special Investigations Division.[1]

[1] *See About the Bureau of Investigations*, Louisiana State Police, https://lsp.org/about/leadershipsections/bureau-of-investigations/ (last visited Feb. 12, 2026).

4. LBI is involved in the investigation of the shipment of abortion drugs into Louisiana for the purpose of causing illegal abortions within Louisiana's borders..

5. In just three distinct matters covered by that investigation, LBI reports that it has spent approximately 440 hours dedicated to investigation, travel, and other related operations.

6. The lead LBI investigator's current hourly rate is $40.01. Therefore, in the course of the 440 hours devoted to these three distinct matters, LBI has expended approximately $17,604.40 of the investigator's time, not including the investigator's travel and other operational expenses.

Executed in Louisiana, Louisiana, this 17 day of February 2026, 2026.

Signed by:
Erin Toner
CB07722D99CB48F...

Erin Toner

UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF LOUISIANA
LAFAYETTE DIVISION

THE STATE OF LOUISIANA, BY AND THROUGH ITS ATTORNEY GENERAL, LIZ MURRILL, AND ROSALIE MARKEZICH	**CIVIL DOCKET NO. 6:25-cv-01491**
VERSUS	**JUDGE DAVID C. JOSEPH**
U.S. FOOD AND DRUG ADMINISTRATION, ET AL	**MAGISTRATE JUDGE DAVID J. AYO**

MEMORANDUM RULING

This case was brought by the State of Louisiana and Louisiana resident Rosalie Markezich ("Plaintiffs") against the U.S. Food and Drug Administration ("FDA") and several related agency heads[1] (collectively, the "Government"), challenging the legality of FDA's 2023 agency action removing the in-person dispensing requirement for the abortion drug, mifepristone. Shortly after filing the lawsuit, Plaintiffs moved for preliminary injunctive relief, which was quickly followed by a flurry of motions by the Government and other parties in interest, including the drug's manufacturers, Danco Laboratories, LLC ("Danco") and GenBioPro, Inc. ("GenBioPro"). Also filed with the Court were twenty-two (22) amicus briefs authored by persons and organizations with a variety of viewpoints.[2]

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[1] The defendants in this matter are the U.S. Food and Drug Administration ("FDA"); Martin Makary, in his official capacity as Commissioner of Food and Drugs at FDA; George Francis Tidmarsh, in his official capacity as the Director of FDA's Center for Drug Evaluation and Research; the U.S. Department of Health and Human Services ("HHS"); and Robert F. Kennedy, Jr., in his official capacity as the Secretary of HHS.

[2] Amicus briefs were filed in support of the Plaintiffs' motion by the following entities: (i) Family Research Council and Martha Shuping, M.D. [Doc. 66]; (ii) Women Injured by

The Court heard oral argument on the pending motions on February 24, 2026, and at that time granted motions to intervene by the two drug manufacturers. [Docs. 52, 54, 229, 246]. Now before the Court for consideration are: (i) a MOTION FOR PRELIMINARY RELIEF UNDER 5 U.S.C. § 705 [Doc. 20] filed by Plaintiffs; (ii) a MOTION TO STAY THE CASE [Doc. 50] filed by the Government; (iii) a MOTION TO DISMISS [Doc. 230] filed by Intervenor-Defendant Danco; and (iv) a MOTION TO DISMISS [Doc. 232] filed by Intervenor-Defendant GenBioPro.[3]

Abortion, The Justice Foundation and its Center Against Forced Abortions, and the National Association of Christian Lawmakers [Doc. 92]; (iii) American Association of Pro-Life Obstetricians and Gynecologists and Samaritan's Purse [Doc. 96]; (iv) The American Center for Law and Justice [Doc. 99]; (v) Ethics and Public Policy Center [Doc. 101]; (vi) Women and Families Harmed by Mifepristone and Former Abortion Providers [Doc. 118]; (vii) Advancing American Freedom, Inc., et al [Doc. 123]; (viii) Concerned Women for America [Doc. 128]; (ix) Dr. Calum Miller [Doc. 130]; (x) Heartbeat International [Doc. 132]; (xi) Students for Life of America [Doc. 136]; (xii) Senator Bill Cassidy, M.D., Representative Christopher H. Smith, and 58 Members of Congress [Doc. 141]; and (xiii) the States of Nebraska, Alabama, Alaska, Arkansas, Georgia, Idaho, Indiana, Iowa, Kansas, Mississippi, Missouri, Montana, North Dakota, Ohio, Oklahoma, South Carolina, South Dakota, Texas, Utah, West Virginia, and Wyoming [Doc. 121].

Amicus briefs were filed in opposition to the Plaintiffs' Motion by the following entities: (i) IGH PLLC d/b/a Abortion on Demand, Hey Jane, and The Reproductive Health Initiative for Telehealth Equity & Solutions (RHITES) [Doc. 204]; (ii) National Domestic Violence Hotline and Legal Voice [Doc. 206]; (iii) Former Commissioners and Acting Commissioners of the U.S. Food and Drug Administration [Doc. 208]; (iv) the States of New York, Arizona, California, Colorado, Connecticut, Delaware, Hawaii, Illinois, Maine, Maryland, Massachusetts, Minnesota, Nevada, New Jersey, New Mexico, Oregon, Rhode Island, Vermont, Washington, and the District of Columbia filed an amicus brief in opposition to the Defendants' Motion to Stay [Doc. 210]; (v) Over 100 Reproductive Health, Rights, and Justice Organizations [Doc. 218]; (vi) Former U.S. Department of Justice Officials [Doc. 220]; (vii) Disability Rights Education and Defense Fund and Others [Doc. 222]; (viii) American College of Obstetricians & Gynecologists, et al [Doc. 224]; and (ix) Medical Students for Choice [Doc. 226].

[3] Plaintiffs' Motion for Preliminary Injunction is opposed by the Defendants [Doc. 51] and by the Intervenors [Docs. 230, 231], and Plaintiffs filed a single brief both in reply to the Defendants' opposition brief and in opposition to the Defendants' Motion to Stay [Doc. 111]. Plaintiffs oppose the Motions to Dismiss filed by Danco and GenBioPro [Doc. 253], and Danco and GenBioPro filed reply briefs [Docs. 256, 257, respectively].

After a review of the record and the complex regulatory and judicial history of this subject matter, the Court declines to grant the Plaintiffs § 705 relief at this time. The record shows that FDA is currently in the process of "conducting its own review of the evidence" with respect to the current Risk Evaluation and Mitigation Strategies ("REMS"), "to determine whether modifications are necessary." [Doc. 1-110]. And "courts owe significant deference to the politically accountable entities with the 'background, competence, and expertise to assess public health.'" *FDA v. Am. Coll. of Obstetricians & Gynecologists,* 141 S. Ct. 578, 578-79 (2021) (Roberts, C.J., concurring in grant of application for stay).

Indeed, given the information available – and, importantly, the dearth of information upon which FDA previously acted to significantly loosen safety restrictions for prescribing mifepristone – the equities and the public interest weigh heavily in favor of FDA completing the job that the law requires it to do. Put differently, at this juncture, it is the completion of FDA's promised good faith, evidence-based, and expeditious review of the mifepristone REMS, not "government by lawsuit," that this Court finds to be in the public interest. *See United States v. Texas*, 599 U.S. 670, 704 (2023) (Gorsuch, J., concurring).

The Motions to Dismiss filed by the drug manufacturers Danco and GenBioPro [Docs. 230, 232, respectively] move to dismiss on the bases that Plaintiffs: (i) lack Article III standing; (ii) are outside "zone of interests" of the APA and Comstock Act; (iii) have failed to exhaust their claims administratively pursuant to 21 C.F.R. § 10.45(b); (iv) have asserted claims not yet ripe for adjudication; and (v) that on the merits their claims fail to state a claim upon which relief can be granted. This ruling addresses the Intervenors' primary contention – the threshold jurisdictional issue of the Plaintiffs' standing to bring this action. But because the Court grants the Governments motion to stay this case pending completion of FDA's mifepristone REMS review, the Court declines to substantively address the remaining issues raised by Intervenors at this time. Intervenors may renew their Motions to Dismiss upon the Court's lifting of the stay.

For these reasons and as further detailed below, the Court finds that the Government's Motion to Stay the Case [Doc. 50] should be GRANTED. Plaintiffs' Motion for Preliminary Relief Under 5 U.S.C. § 705 [Doc. 20] is DENIED without prejudice to refiling upon the Court lifting the stay. Likewise, the two Motions to Dismiss filed by Intervenors [Docs. 230, 232] are DENIED without prejudice to refiling upon the Court lifting the stay. This action will remain STAYED until further order of the Court.

FACTUAL BACKGROUND AND PROCEDURAL HISTORY

I. Regulatory History of Mifepristone[4]

This case arises under the Federal Food, Drug, and Cosmetic Act, as amended, 21 U.S.C. ch. 9., the principal federal statute governing the regulation of food, drugs, medical devices, and cosmetics in the United States. The U.S. Department of Health and Human Services ("HHS") is charged with the responsibility for implementing that law and has delegated the obligation to FDA, its subagency. Under federal law, FDA is responsible for ensuring that drugs marketed in the United States are safe and effective.

To that end, a drug sponsor seeking approval – typically the manufacturer or prospective marketer – must submit an application to FDA demonstrating that the drug is safe and effective for its intended use. *Alliance IV*, 602 U.S. at 375, *citing* 21 U.S.C. § 355(d). The application must generally include proposed labeling that

[4] Although the Court provides herein a summary of the complex regulatory history pertinent to its ruling, a more exhaustive regulatory history is provided in *All. for Hippocratic Med. v. FDA*, 78 F.4th 210, 233 (5th Cir. 2023) ("*Alliance III*"), *rev'd and remanded sub nom., FDA v. All. for Hippocratic Med.,* 602 U.S. 367, 375 (2024) ("*Alliance IV*").

specifies, among other things, the drug's dosage, directions for use, and the specific conditions the drug is approved to treat. *Id.* at 375, *citing* 21 C.F.R. §§ 201.5, 314.50 (2022). FDA may also impose additional conditions on a drug's prescription and use when it finds that enhanced safety measures are necessary. *Id.*, *citing* 21 U.S.C. § 355-1(f)(3). Such conditions may include prescriber training, dispensing limitations, or patient-monitoring requirements. *Id.*

In 2000, FDA approved a new drug application for mifepristone tablets under its Subpart H regulations, 21 C.F.R. § 314.500. *Id.* This newly approved drug was marketed under the brand name Mifeprex and was used to terminate pregnancies through seven weeks of gestation (the "2000 Approval").[5] *Alliance IV*, 602 U.S. at 375. To help ensure that Mifeprex would be used safely and effectively, FDA placed further restrictions on the drug's use and distribution. *Id.* Among other requirements, only physicians were permitted to prescribe or supervise the prescription of Mifeprex, and patients were required to follow a regimen involving three in-person visits with a physician. *Id.* FDA also required prescribing physicians to report hospitalizations, blood transfusions, and other serious adverse events to the drug sponsor, which in turn was obligated to report those events to FDA. *Id.*

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[5] In 1992, FDA promulgated the "Subpart H" regulations, which permit the accelerated approval of drugs intended to treat serious or life-threatening illnesses based on evidence of meaningful therapeutic benefit. *See* 21 C.F.R. § 314.500. Recognizing that such approvals rest on an expedited evidentiary basis, Subpart H also authorized post-approval restrictions "to assure safe use." *Id.* § 314.520. Mifepristone was approved under this framework. In 2007, Congress codified and expanded these post-approval safety authorities by establishing Risk Evaluation and Mitigation Strategies (REMS), which are designed to ensure that a drug's benefits outweigh its risks. *See All. for Hippocratic Med. v. FDA,* 2023 WL 2913725, at *21 (5th Cir. Apr. 12, 2023) ("*Alliance II*"), *citing* 21 U.S.C. § 355-1 (a)(1)-(2).

In 2015, Mifeprex's distributor, Danco, submitted a supplemental new drug application seeking to amend Mifeprex's labeling and to relax some of the restrictions that FDA had imposed. *Id.* In 2016, FDA approved the proposed changes, which: (i) deemed Mifeprex safe to terminate pregnancies up to ten weeks rather than seven weeks; (ii) allowed healthcare providers such as nurse practitioners to prescribe Mifeprex; and (iii) approved a dosing regimen that reduced the number of required in-person visits from three to one. *Id.* at 375-76. In addition, FDA approved a change in the prescribers' adverse event reporting obligations to require prescribers to report only fatalities (collectively, the "2016 Amendments"). *Id.* at 376.

In April 2019, FDA approved an application for generic mifepristone, manufactured by GenBioPro (the "2019 Generic Application"). *Id.* FDA established the same conditions of use for generic mifepristone as for Mifeprex. *Id.* Then, in April 2021, at the height of the COVID-19 pandemic, FDA again relaxed the requirements for Mifeprex and generic mifepristone, announcing that it would temporarily "exercise enforcement discretion" to allow "dispensing mifepristone through the mail ... or through mail-order pharmacy" (the "2021 Nonenforcement Decision"). *Id.*

In January 2023, FDA issued its most recent REMS for mifepristone (the "2023 REMS"), which codified and refined prior changes, including, among other things: (i) the removal of an in-person dispensing requirement; (ii) permitting certified pharmacies to dispense mifepristone (including by mail); and (iii) otherwise continuing the post-2016 framework, including limited adverse-event reporting (primarily deaths). *Alliance III*, 78 F.4th at 247.

II. History of Mifepristone Litigation in the Fifth Circuit

In 2022, physicians providing pregnancy-related health care, including emergency care after unsuccessful medication abortions using mifepristone, and national organizations of such physicians, brought an action in a Texas district court under the Administrative Procedure Act ("APA") against FDA, HHS, and agency officials. *See All. for Hippocratic Med. v. FDA*, 668 F. Supp. 3d 507, 560 (N.D. Tex. Apr. 7, 2023) ("*Alliance I*"). These plaintiffs challenged both the lawfulness of FDA's initial approval of mifepristone (which had occurred more than 20 years earlier), and each post-approval action (at that time, the 2016 Amendments, 2019 Generic Approval, and 2021 Nonenforcement Decision). *Id.* After concluding that the plaintiffs had standing, the *Alliance I* district court entered a preliminary injunction staying the 2000 Approval of mifepristone and each of the subsequent agency actions – effectively removing the drug from the market pending a full trial on the merits. *Id.*

FDA and Danco appealed the injunction to the Fifth Circuit and asked for an emergency stay of the district court's order pending appeal. The Fifth Circuit granted a partial stay, temporarily reinstating FDA's original 2000 Approval of Mifeprex. *Alliance II*, 2023 WL 2913725, at *21. This partial stay permitted the drug to remain available only under the earlier, more restrictive conditions but left in place the district court's injunction as to later regulatory changes. *Id.* Specifically, the *Alliance II* court found that the plaintiffs were likely to succeed on the merits of their claims under 5 U.S.C. § 706(2)(A) in at least two respects. *Id.* at *17.

First, the *Alliance II* court determined that FDA had failed to examine the relevant data when adopting the 2016 Amendments – relying instead on data that included the very safeguards the 2016 REMS had therein dispensed with. *Id.* And second, in a similar vein, FDA thereafter relied on the absence of non-fatal adverse-event reports in FDA's Adverse Event Reporting System ("FAERS") after eliminating the requirement that such events even be reported. *Id.* As to the latter error, the Fifth Circuit pointedly explained that "[i]t's unreasonable for an agency to eliminate a reporting requirement for a thing and then use the resulting absence of data to support its decision." *Id.*

Thus, the Fifth Circuit concluded that the *Alliance* plaintiffs were likely to succeed on the merits of their APA challenges with respect to FDA's decisions beginning with the 2016 Amendments and "all subsequent actions." *Id.* at *17-21. Following the Fifth Circuit's partial stay, FDA and Danco sought a full stay from the United States Supreme Court, which they obtained, thereby preserving the current regulatory regime during the pendency of the appeal. *Danco Lab'ys, LLC v. All. for Hippocratic Med.*, 143 S. Ct. 1075 (2023).

Then, in August 2023, a different panel of the Fifth Circuit addressed the merits appeal of the *Alliance I* administrative stay and preliminary injunction. *See generally Alliance III*, 78 F.4th at 233. The merits panel agreed with the *Alliance II* court's determination that both the individual doctors and the plaintiff medical associations had Article III standing. And in assessing FDA's 2016 Amendments and the 2021 Nonenforcement Decision, the *Alliance III* court agreed that FDA had acted arbitrarily and capriciously and otherwise abused its discretion under 5 U.S.C.

§ 706(2)(A) when it, among other things: (i) failed to consider the cumulative effect of the 2016 Amendments; (ii) failed to consider whether it needed to continue to collect data of non-fatal adverse events in light of the "major" 2016 changes to the mifepristone REMS; (iii) gave dispositive weight in making the 2021 Non-Enforcement Decision to FAERS data that had been compromised by FDA's 2016 removal of non-fatal reporting requirements; and (iv) relied on literature that did not support its position in making the 2021 Nonenforcement Decision.[6] *Id.*

Specifically, the *Alliance III* court found that the studies underpinning FDA's approval of the 2016 Amendments failed to consider any data that cumulatively evaluated the effect of implementing each of its proposed "major" changes, which included:

> … increasing the maximum gestational age from forty-nine days to seventy days; allowing non-physicians to prescribe mifepristone; removing the requirement that the administration of misoprostol and the subsequent follow-up appointment be conducted in person; eliminating prescribers' obligation to report non-fatal adverse events; switching the method of administration for misoprostol from oral to buccal; and changing the dose of mifepristone (600 mg to 200 mg) and misoprostol (400 mcg to 800 mcg).

Id. at 246.

Instead, the *Alliance III* court found that the "FDA neither considered the effects as a whole, nor explained why it declined to do so[,]" even though FDA had acknowledged that "[t]he cumulative effect of the 2016 Amendments is

[6] The merits panel disagreed with the district court's determination that plaintiffs were likely to succeed on their challenge to FDA's 2000 Approval of Mifeprex and 2019 Approval of generic mifepristone. *Id.* at 256. Accordingly, the Fifth Circuit vacated the district court's order as to those agency actions. *Id.*

unquestionably an important aspect of the problem[.]" *Id.* The court also determined that FDA's failure to consider whether it needed to continue to collect data of non-fatal adverse events in light of the "major" changes to the mifepristone REMS was likely arbitrary and capricious. *Id.* at 246-47.

As to the 2021 Nonenforcement decision (that was later formalized in the 2023 REMS at issue here), the *Alliance III* court found, in essence, that FDA had based its decision on the absence of data that it had only five years previously intentionally eliminated – finding that "considerable evidence shows that FAERS data is insufficient to draw general conclusions about adverse events." *Id.* at 249. The Court also found that FDA had "relied on various literature relating to remote prescription of mifepristone" in spite of "FDA's admission that the literature did not affirmatively support its position." *Id.* at 250.

In 2024, the Supreme Court reversed, finding that the *Alliance* plaintiffs lacked Article III standing to challenge FDA's regulatory actions. *Alliance IV*, 602 U.S. at 396-97. The Court explained that Article III's case-or-controversy requirement confines federal judicial power to actual "personal stake" injuries. And because the plaintiff doctors and physician associations did not prescribe, use, manufacture, sell, or otherwise face regulation stemming from FDA's actions, their asserted injuries were speculative and not fairly traceable to the challenged FDA actions. *Id.* at 385-86.

In so finding, the Court emphasized that sincere legal, moral, ideological, and policy objections to another's conduct – here, the prescription and use of mifepristone – standing alone, do not satisfy Article III's standing requirements. *Id.* at 396.

Accordingly, the Supreme Court reversed the Fifth Circuit and remanded for further proceedings consistent with its opinion. *Id.* at 397.

III. Recent Actions of FDA

Important to the Court's determination here, on September 19, 2025, undoubtedly aware of the mifepristone regulatory deficiencies identified by the Fifth Circuit in the *Alliance* cases, FDA agreed to undergo a thorough review of the mifepristone REMS. Specifically, in direct response to a letter sent to HHS by the Attorneys General of 22 states,[7] HHS Secretary Kennedy and FDA Commissioner Makary responded with a letter agreeing to conduct a comprehensive safety review of the mifepristone REMS, including the 2023 REMS at issue here. [Doc. 1-110].

In their letter, Secretary Kennedy and Commissioner Makary stated that, "[s]ince its original approval, the FDA has received reports of serious adverse events in patients who took mifepristone," and consequently, FDA's review would "study[] the adverse consequences reported in relation to mifepristone to ensure the REMS are sufficient to protect women from unstated risks." [*Id.*]. FDA premised this review on a frank acknowledgement of the "lack of adequate consideration underlying the prior REMS approvals" as well as "recent studies raising concerns about the safety of mifepristone as currently administered," including those that "indicate potential dangers that may attend offering mifepristone without sufficient medical support or supervision." [*Id.*]. The letter promised to ensure that FDA's analysis and any

[7] The letter, sent by Kansas Attorney General Kris Kobach and 21 other AGs on July 31, 2025, asked for a comprehensive review of mifepristone or, alternatively, a removal of the drug from the market pending additional safety testing.

resulting revisions to the mifepristone REMS would be "grounded in Gold Standard Science." [*Id.*]. Commissioner Makary publicly acknowledged that the review of mifepristone safety was underway as of January 2026.[8]

IV. The Instant Lawsuit

On October 6, 2025, the State of Louisiana and Rosalie Markezich filed the instant lawsuit, challenging FDA's January 2023 REMS, and particularly, the removal of the in-person dispensing requirement and authorization of dispensation of the drug by mail and telehealth.[9] Plaintiffs claimed injuries include: (i) harm to state sovereignty; (ii) increased Medicaid expenditures, including over $92,000 in 2025 emergency room and hospitalization costs from two mifepristone-induced abortions and projections of hundreds of thousands of dollars in similar costs; and (iii) public-health harms, including statistically-certain emergency room visits and risks of serious and sometimes fatal infections and bleeding. Plaintiffs seek preliminary relief to stay or set aside the 2023 REMS under 5 U.S.C. § 705, or an injunction mandating that FDA enforce mifepristone's previous in-person dispensing requirement. In response, the Government asks this Court to stay the litigation while FDA conducts its review of the mifepristone REMS.

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[8] *Questions and Answers on Mifepristone for Medical Termination of Pregnancy Through Ten Weeks Gestation,* FDA, https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/questions-and-answers-mifepristone-medical-termination-pregnancy-through-ten-weeks-gestation (last updated Feb. 2, 2026).

[9] Plaintiff Markezich alleges that in October 2023, her then-boyfriend used her email address to obtain mifepristone (and a second drug, misoprostol) from a physician in California via mail order. [Doc. 1, ¶ 10]. She alleges that she did not want to take the drug, was pressured by him, and that the result of taking the medication caused the termination of her pregnancy and ongoing distress and trauma. [*Id.*].

On February 24, 2026, the Court granted the Motions to Intervene filed by mifepristone manufacturers Danco and GenBioPro [Docs. 52 and 54, respectively], and thereafter, the Intervenors' Motions to Dismiss were filed into the record. [Docs. 230 and 232, respectively].

LAW AND ANALYSIS

I. Legal Standards

A. APA Standard of Review

The APA was designed by Congress to act as "a check upon administrators whose zeal might otherwise have carried them to excesses not contemplated in legislation creating their offices." *United States v. Morton Salt Co.*, 338 U.S. 632, 644 (1950). It requires federal courts to "hold unlawful and set aside agency action, findings, and conclusions found to be arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with the law." 5 U.S.C. § 706(2)(A). The standard set forth by the Fifth Circuit is clear:

> … [A]n agency must "examine the relevant data and articulate a satisfactory explanation for its action including a 'rational connection between the facts found and the choice made.'" An agency violates these rules where it "entirely fail[s] to consider an important aspect of the problem," or offers "an explanation for its decision that runs counter to the evidence before the agency, or is so implausible that it could not be ascribed to a difference in view or the product of agency expertise."

Alliance III, 78 F.4th at 245 (internal citations omitted).

To be sure, the arbitrary and capricious standard is narrow, and courts must be careful not to "substitute" their own "policy judgment for that of the agency." *FCC v. Prometheus Radio Project*, 592 U.S. 414, 423 (2021). But ultimately, Congress has vested federal courts with the responsibility to "ensure that the agency 'examined the

relevant data and articulated a satisfactory explanation for its action.'" *Sierra Club v. EPA*, 939 F.3d 649, 664 (5th Cir. 2019). And applying this standard, courts may vacate agency decisions containing "unexplained inconsistencies in the rulemaking record." *Id.*

If an agency's deliberative process falls short of the APA's requirements, Section 705 authorizes courts to stay an agency action while the action undergoes judicial review. 5 U.S.C. § 705. "In the same way that a preliminary injunction is the temporary form of a permanent injunction, a stay is the temporary form of vacatur." *Alliance III*, 78 F.4th at 254*, quoting Monsanto Co. v. Geerston Seed Farms*, 561 U.S. 139, 165 (2010).

B. Injunctive Relief Pursuant to 5 U.S.C. § 705

Here, Plaintiffs urge the Court in their Motion for Preliminary Relief to issue an order under § 705 of the APA, "staying or postponing the effective date of the [2023 REMS]." [Doc. 20]. Because "a stay [under the APA] has the practical effects of an injunction," the preliminary injunction factors applicable to Federal Rule of Civil Procedure 65 motions apply. *Alliance III*, 78 F.4th at 242*, citing* 28 U.S.C. § 1292(a) *and Alliance II*, 2023 WL 291375, at *3 n.3; *see also Colorado v. EPA*, 989 F.3d 874, 883 (10th Cir. 2021). "Injunctive relief is an extraordinary and drastic remedy, not to be granted routinely, but only when the movant, by a clear showing, carries the burden of persuasion." *Louisiana v. Biden*, 575 F. Supp. 3d 680, 691 (W.D. La. Dec. 16, 2021), *aff'd*, 55 F.4th 1017 (5th Cir. 2022), *citing Holland Am. Ins. Co. v. Succession of Roy*, 777 F.2d 992, 997 (5th Cir. 1985). "To be entitled to a preliminary injunction, a movant must establish: (1) a likelihood of success on the merits; (2) a

substantial threat of irreparable injury; (3) that the threatened injury if the injunction is denied outweighs any harm that will result if the injunction is granted; and (4) that the grant of an injunction will not disserve the public interest." *Id.* at 691, *quoting Ladd v. Livingston*, 777 F.3d 286, 288 (5th Cir. 2015); *Alliance III*, 78 F.4th at 241.

C. Motion to Stay

The above notwithstanding, a district court always retains the inherent authority to stay a proceeding "to control the disposition of the causes on its docket …." *Crimson Bldg. Co. v. Plutus Grp., LLC*, 2020 WL 13616911, at *1 (N.D. Tex. Feb. 24, 2020), *quoting United States v. Rainey*, 757 F.3d 234, 241 (5th Cir. 2014) (internal quotation marks omitted). In staying a case pursuant to this authority, the Court should "balance between the harm of moving forward [with the litigation] and the harm of holding back." *Ali v. Quarterman*, 607 F.3d 1046, 1049 (5th Cir. 2010). Additionally, the Court should consider whether a stay is warranted in light of activity in a related action and other "present day realities." *In re Beebe*, 1995 WL 337666, at *3-4 (5th Cir. May 15, 1995); *see also Landis v. N. Am. Co.*, 299 U.S. 248, 258 (1936).

As the Supreme Court has explained, "[e]specially in cases of extraordinary public moment, [a plaintiff] may be required to submit to delay not immoderate in extent and not oppressive in its consequences if the public welfare or convenience will thereby be promoted." *Clinton v. Jones*, 520 U.S. 681, 706-07 (1997), *citing Landis*, 299 U.S. at 256. And district courts regularly stay proceedings to allow an agency to pursue further action on the rulemaking at issue. *See, e.g., Town & Cnty. of*

Nantucket v. Burgum, 2025 WL 3120419, at *2 (D.D.C. 2025), *citing Code v. McHugh*, 139 F. Supp. 3d 465, 466 (D.D.C. 2015); *FBME Bank Ltd. v. Lew*, 142 F. Supp. 3d 70, 76 (D.D.C. 2015); *Sierra Club v. Van Antwerp*, 560 F. Supp. 2d 21, 26 (D.D.C. 2008).

II. Standing

As a threshold matter, the Court is first charged with the important jurisdictional task of determining whether the Plaintiffs have standing to challenge the 2023 REMS. As previously discussed, the *Alliance* litigation was ultimately dismissed by the Supreme Court for those plaintiffs' lack of standing to challenge the mifepristone REMS. *Alliance IV*, 602 U.S. at 396-97. And here, both the Government and Intervenors argue in their briefing that the Plaintiffs lack standing for their requested relief. [Docs. 51, 230, 231]. Intervenors Danco and GenBioPro also specifically seek dismissal of this action on that basis. [Docs. 230, 232].

The Court will therefore first carefully evaluate Plaintiffs' Article III standing. Standing is "built on a single basic idea – the idea of the separation of power." *Alliance IV*, 602 U.S. at 378. "Article III requires a plaintiff to show that she has suffered an injury-in-fact that is fairly traceable to the defendant's allegedly unlawful conduct and likely to be redressed by the requested relief." *Haaland v. Brackeen*, 599 U.S. 255, 291-92 (2023), *citing California v. Texas*, 593 U.S. 659, 668-69 (2021); *see also Lujan v. Defenders of Wildlife*, 504 U.S. 555, 560 (1992).

To establish standing, "a plaintiff must demonstrate: (i) that she has suffered or likely will suffer an injury-in-fact; (ii) that the injury likely was caused or will be caused by the defendant; and (iii) that the injury likely would be redressed by the requested judicial relief." *Texas v. United States*, 126 F.4th 392, 407 (5th Cir. 2025),

quoting Alliance IV, 602 U.S. at 380. "The second and third standing requirements – causation and redressability – are often 'flip sides of the same coin,'" meaning if "a defendant's action causes an injury, enjoining the action or awarding damages for the action will typically redress that injury. So the two key questions in most standing disputes are injury-in-fact and causation." *Texas*, 126 F.4th at 407, *quoting Alliance IV*, 602 U.S. at 380-81.

The Court is also cognizant that at earlier stages of litigation, such as in adjudicating a motion for injunctive relief, the manner and degree of evidence required to show standing may be less than at later stages. *Speech First, Inc. v. Fenves*, 979 F.3d 319, 329-30 (5th Cir. 2020), *as revised* (Oct. 30, 2020), *citing Lujan*, 504 U.S. at 561 ("each element [of standing] must be supported ... with the manner and degree of evidence required at the successive stages of the litigation"); s*ee also Barber v. Bryant*, 860 F.3d 345, 352 (5th Cir. 2017), *citing Lujan*, 504 U.S. at 561 ("Since they are not mere pleading requirements but rather an indispensable part of the plaintiff's case, each element must be supported ... with the manner and degree of evidence required at the successive stages of litigation."). Thus, at this stage, it is the Plaintiffs' burden to put forth facts establishing that they have standing to seek the requested § 705 relief.

Louisiana argues that it has standing both because: (i) the 2023 REMS causes sovereign harm by facilitating abortions that violate numerous Louisiana state

laws,[10] [Doc. 20-26, p. 24]; and (ii) it continues to suffer ongoing financial injury resulting from the 2023 REMS and has already paid hundreds of thousands of dollars through Louisiana Medicaid for emergency room medical care stemming from mifepristone use by residents. [*Id.*, p. 26]. In response, Defendants argue primarily that Louisiana lacks standing because it "do[es] not prescribe or use mifepristone" and the 2023 REMS Modification does not "require[] [Louisiana] to do anything or to refrain from doing anything" and the indirect causal chain between the REMS and Louisiana's alleged injury is too speculative or attenuated to establish standing. [Docs. 51, 230, 231]. Put another way, because Louisiana is not a regulated party, the Defendants allege that Louisiana is unable to establish traceability between

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[10] Louisiana prohibits all abortions except those that are determined to be medically necessary to prevent the death or substantial risk of death of the mother. *See* La. R.S. § 40:1061, La. R.S. § 14:87.7, and La. R.S. § 14:87.8.1.

Important here, Louisiana has also enacted a criminal prohibition on the prescribing and dispensing of mifepristone for purposes of inducing an abortion and classifies mifepristone as a Schedule IV controlled and dangerous substance under its drug laws. *See* La. R.S. § 14:87.1(2)(a) ("'Abortion-inducing drug' means any drug or chemical, or any combination of drugs or chemicals, or any other substance when used with the intent to cause an abortion."); La. R.S. § 40:964.

And if those criminal prohibitions were not clear, Louisiana's longstanding policy, enacted into statute, states, in part:

> It is the intention of the Legislature of Louisiana to regulate, prohibit, or restrict abortion to the fullest extent permitted by the decisions of the Supreme Court of the United States. The legislature does solemnly declare, find, and reaffirm the longstanding public policy of this state that every unborn child is a human being from the moment of conception and is, therefore, a legal person for purposes under the laws of this state and Constitution of Louisiana.

La. R.S. § 40:1061.1 (A)(1).

Louisiana's claimed sovereign and financial injuries and FDA's promulgation of the 2023 REMS. [*Id*].

Although the Supreme Court has observed that establishing standing is "ordinarily substantially more difficult" for unregulated parties – particularly where causation rests on "the unfettered choices of independent actors" – it has also made clear that standing may exist where such actors predictably respond to the challenged action. *Lujan*, 504 U.S. at 560-61; *see also California*, 593 U.S. at 675*, citing Dep't of Com v. New York*, 588 U.S. 752, 768 (2019). The Fifth Circuit treats this inquiry as part of the traceability analysis, not injury-in-fact. *See Reule v. Jackson*, 114 F.4th 360, 367 (5th Cir. 2024), *cert. denied*, 145 S. Ct. 1431 (2025). Thus, even where injury is undisputed, standing fails if the causal chain is too speculative. *Alliance IV*, 602 U.S. at 383.

As previously discussed, in *Alliance IV*, the Supreme Court dismissed for lack of standing where the plaintiff doctors and medical associations had no direct involvement with mifepristone, no cognizable economic injury, and no obligation to participate in abortion care, rendering any causal chain to FDA's actions too speculative. 602 U.S. at 385-86, 393-94. In the same vein, the Government attempts to distinguish this Court's standing analysis in *Louisiana v. EEOC*, 784 F. Supp. 3d 886 (W.D. La. 2025), arguing that, unlike the regulatory mandate there, the 2023 REMS imposes no obligations on the State. The Government further argues that any Medicaid-based economic harm is too attenuated.

After careful consideration, the Court finds that Defendants' arguments fall short at this stage. Here, the evidence in the record shows that the "independent

actors" – that is, the out-of-state medical providers prescribing mifepristone via telemedicine or mail – responded to the 2023 REMS by expanding mifepristone access to pro-life states like Louisiana in ways that were entirely predictable. On July 8, 2022, then-President Biden issued Executive Order 14076,[11] which expressly sought to protect and expand access to "*healthcare service delivery* and promote access to critical reproductive healthcare services, including abortion" in the wake of *Dobbs*. [Doc. 1-45, pp. 2-3] (emphasis added). And in a "Factsheet" issued by the White House

[11] Section 1 of EO 14076, enacted just one week after the *Dobbs* decision was issued, is entitled "Policy" and states:

> Nearly 50 years ago, *Roe* v. *Wade,* 410 U.S. 113 (1973), articulated the United States Constitution's protection of women's fundamental right to make reproductive healthcare decisions. These deeply private decisions should not be subject to government interference. Yet today, fundamental rights — to privacy, autonomy, freedom, and equality — have been denied to millions of women across the country.
>
> Eliminating the right recognized in *Roe* has already had and will continue to have devastating implications for women's health and public health more broadly. Access to reproductive healthcare services is now threatened for millions of Americans, and especially for those who live in States that are banning or severely restricting abortion care. Women's health clinics are being forced to close — including clinics that offer other preventive healthcare services such as contraception — leaving many communities without access to critical reproductive healthcare services. Women seeking abortion care — especially those in low-income, rural, and other underserved communities — now have to travel to jurisdictions where services remain legal notwithstanding the cost or risks.
>
> *In the face of this health crisis, the Federal Government is taking action to protect healthcare service delivery and promote access to critical reproductive healthcare services, including abortion.* It remains the policy of my Administration to support women's right to choose and to protect and defend reproductive rights. Doing so is essential to justice, equality, and our health, safety, and progress as a Nation.

Exec. Order No. 14,076, 88 Fed. Reg. 42,831 (July 7, 2023) (emphasis added).

on April 12, 2023, the administration touted, among other things, actions taken by FDA to "protect[] access to [abortion] care nationwide." [Doc. 1-60].

Thus, in that post-*Dobbs* regulatory environment, there is evidence that the 2023 REMS was approved without adequate consideration, at least in part, as part of an effort to circumvent anti-abortion states' ability to regulate abortion. Likewise, there is evidence that the consequences of this action were predictable – out-of-state providers and related entities would expand access to mifepristone in ways designed to reach into jurisdictions like Louisiana. These actions cause concrete and ongoing injury to Louisiana, as further discussed below.

But first, Louisiana's claimed injury must be put within the appropriate framework. The Constitution's Supremacy Clause declares that federal laws "shall be the supreme law of the land" when conflicting with state laws. U.S. CONST. art. VI, cl. 2. This includes the Food, Drug, and Cosmetic Act, 21 U.S.C. § 301, *et seq.*, and the resulting authority vested in FDA to approve and regulate drugs. Nevertheless, respect for the federal nature of our government is also paramount – "a system in which … the National Government, anxious though it may be to vindicate and protect federal rights and federal interests, always endeavors to do so in ways that will not unduly interfere with the legitimate activities of the [states]." *Younger v. Harris*, 401 U.S. 37, 44 (1971). The Supreme Court has consistently considered federalism concerns when, for example, determining the reach of federal law. *See, e.g., Sackett v. EPA*, 598 U.S. 651, 683 (2023); *U.S. Forest Serv. v. Cowpasture River Pres. Ass'n*, 590 U.S. 604, 621 (2020).

Here, Louisiana alleges that an unlawful use of federal regulatory power by an administrative agency directly undermines the enforcement of its own laws and forces it to incur additional costs.[12] *See Texas v. United States*, 809 F.3d 134, 153 (5th Cir. 2015) ("States have a sovereign interest in the power to create and enforce a legal code."). Of course, if this Court or others ultimately determine that FDA acted lawfully in its removal of the in-person dispensing requirement for mifepristone, then Louisiana would have no judicial recourse under the APA.[13] After all, this would directly implicate the Constitution's Supremacy Clause and the power vested by Congress in FDA to regulate drugs. U.S. CONST. art. VI, cl. 2; *see also GenBioPro, Inc.*, 144 F.4th at 273 (4th Cir. 2025) (finding that although state law determines whether "abortion may be performed at all," federal law "permits the FDA to regulate how mifepristone must be prescribed and dispensed *if and when* a medication abortion is performed.").

On the other hand, if FDA did not act lawfully under the APA but rather exceeded or abused the power vested in it by Congress as Plaintiffs contend, then Louisiana clearly has an interest in vindicating its sovereign prerogative under basic principles of federalism. And the Fifth Circuit has twice indicated in *Alliance II* and *Alliance III* that FDA was likely arbitrary and capricious under the APA in removing

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12 *See supra* note 10.

13 For the avoidance of doubt, this does not mean that medical providers would then be free to ignore the laws of the states in which they prescribe mifepristone without fear of criminal prosecution. As recently put by the Fourth Circuit Court of Appeals, "the text of the [Food, Drug and Cosmetic Act] suggests that Congress intended to create a regulatory floor, not a ceiling" on drug regulation by the states. *GenBioPro, Inc. v. Raynes*, 144 F.4th 258, 274 (4th Cir. 2025). But that issue is not before the Court here.

mifepristone's in-person dispensing requirement. *Alliance II*, 2023 WL 2913725, at *17; *Alliance III*, 78 F.4th at 241-48.

To be sure, there are factors other than the 2023 REMS that influence the arrival of mifepristone in Louisiana. For example, some states have enacted "shield laws" to protect medical practitioners in their states from extradition for prescribing and illegally shipping mifepristone into jurisdictions where it has been prohibited. *See generally What Are Shield Laws?*, CTR. FOR REPROD. RTS., (Oct. 9, 2025), https://reproductiverights.org/resources/what-are-shield-laws/; *see also, e.g.,* CAL. PENAL CODE § 847.5(b)-(c). There are also the usual practical and investigatory impediments faced by state law enforcement when engaging in drug interdiction efforts. And these may be even more significant than the 2023 REMS in influencing the accessibility of mifepristone to Louisiana residents. But there can be little doubt that the 2023 REMS is a factor, which is all that is required for Louisiana to show injury-in-fact and traceability. *See Texas v. United States*, 50 F.4th 498, 519 (5th Cir. 2022) ("DACA is not the sole cause of the State's injury, but DACA has exacerbated it. That is sufficient."). Thus, even if the 2023 REMS is not the "sole cause" of Louisiana's sovereign harms, it has surely "exacerbated" them; "that is sufficient" for standing to assert its claims. *Id.*

Furthermore, "[m]onetary costs are of course an injury" for standing purposes. *Texas*, 599 U.S. at 676. And "even one dollar's worth of harm is traditionally enough to" confer standing. *Id.* at 688 (Gorsuch, J., concurring). A state's increased medical costs, such as increased Medicaid costs due to a federal agency action, can constitute

a "pocket-book injury" sufficient to satisfy the injury-in-fact requirement of standing. *Texas v. United States*, 126 F.4th 392, 411 n.22 (5th Cir. 2025) (collecting cases).

Here, Louisiana has put forth sufficient evidence to demonstrate that it has suffered and continues to suffer pocketbook injury. Under the federal Medicaid statute, Louisiana is required to cover medical assistance for eligible pregnant women, which includes inpatient and outpatient medical services. 42 U.S.C. §§ 1396(a)(viii), (a)(1)-(2). Louisiana is required to pay a portion of the total Medicaid costs, *id.* § 1396a(a)(2), and the federal government will pay between 50 percent and 83 percent, *id.* § 1396d(b). Crucially, FDA's "own documents" show that "emergency room care is statistically certain" in mifepristone cases. *Alliance II*, 2023 WL 2913725, at *10. And according to FDA's own 2023 label, 2.9-4.6 percent of women who receive an in-person visit with a doctor, are prescribed mifepristone, and take it as directed will require an emergency room visit. [Doc. 1-9, p. 9]. Empirical evidence indicates that the emergency room visitation and hospitalization rate may be closer to ten percent for patients with an estimated gestational duration of 78-84 days. [Doc. 1-13, p. 2]; [Doc. 20-4, p. 2].[14] And rates may also be higher when mifepristone is dispensed by mail. [Doc. 1-10, pp. 34-35].

Plaintiffs further estimate that, on average, about 1,000 mifepristone-induced abortions are occurring per month in Louisiana. [Doc. 20-2, p. 36]; [Doc. 20-22, pp. 1-2]. And, according to Plaintiffs' expert, many of these women obtaining abortions are likely to be on Medicaid. [Doc. 20-22, pp. 2-3]. In support of this

[14] *See* https://www.contraceptionjournal.org/article/S0010-7824(25)00308-7/abstract for the complete study.

contention, Plaintiffs have supplied evidence from the Louisiana Department of Health identifying more than $92,000 in Medicaid costs incurred for emergency room care and hospitalizations required because of two mifepristone-induced abortions in 2025 in which the drugs were received from out-of-state prescribers. [Doc. 20-20, pp. 4-5, ¶¶ 11-12]. These two incidents alone are sufficient to establish Louisiana's standing, but it is likely that many more Medicaid patients have required similar care due to complications from mifepristone. [*Id.*, pp. 4-5, ¶¶ 10, 13-15]; [Doc. 20-19, pp. 3-4, ¶¶ 7-8]; [Doc. 20-23, p. 4, ¶¶ 14-16].

And regardless of whether Louisiana's financial harm is the $92,000 previously discussed or far more than that, Louisiana's harm is more than zero. *See Texas*, 50 F.4th at 517-18 ("The record does not indicate precisely what portion of all costs for illegal aliens is spent on DACA recipients, but no one disputes that some are."). Accordingly, because "even one dollar's worth of harm" is sufficient, Louisiana has put forth sufficient evidence to demonstrate a substantial likelihood of success in proving it has suffered financial injury for standing purposes. *Texas*, 599 U.S. at 688 (Gorsuch, J., concurring).

For all of these reasons, Louisiana has established injury that is traceable to FDA's actions and redressable, at least in part, by the relief requested herein. Louisiana therefore has standing to challenge the 2023 REMS on the record before the Court.[15]

[15] Because the Court determines that the State of Louisiana has standing, it need not consider standing for Markezich. *Biden v. Nebraska*, 600 U.S. 477, 489 (2023) ("If at least one plaintiff has standing, the suit may proceed."), *citing Rumsfeld v. Forum for Acad. & Institutional Rts., Inc.*, 547 U.S. 47, 52 n.2 (2006).

III. Analysis Under Rule 65

With standing established for these purposes, the Court next considers whether Plaintiffs have carried their burden under the Rule 65 framework applicable to the Plaintiffs' requested § 705 relief.[16]

A. Likelihood of Success on the Merits

"The exact quantum of evidence that a plaintiff must present to satisfy the likelihood-of-success factor varies from case to case." *League of United Latin Am. Citizens v. Abbott*, 809 F. Supp. 3d 502, 546 (W.D. Tex. 2025), *citing Jefferson Cmty. Health Care Ctrs., Inc. v. Jefferson Par. Gov't*, 849 F.3d 615, 626 (5th Cir. 2017) ("[T]here is no particular degree of likelihood of success that is required in every case. …"). "The Fifth Circuit applies a 'sliding scale' approach, whereby a plaintiff who makes a strong showing on the other three preliminary injunction factors bears a lesser burden on the likelihood-of-success requirement (and vice versa)." *Id.*, *citing TitleMax of Texas, Inc v. City of Dallas*, 142 F.4th 322, 328 (5th Cir. 2025). Thus, "[w]here the other factors are strong," the movant need only show "some likelihood of success on the merits" to obtain a preliminary injunction. *Id.*

As discussed above, in *Alliance III*, the Fifth Circuit found that FDA, in promulgating the 2021 Nonenforcement Decision, had based its decision on the absence of data that it had only five years previously intentionally eliminated – finding that "considerable evidence shows that FAERS data is insufficient to draw

[16] The Plaintiffs do not squarely address in their briefing the application of the Rule 65 factors as they apply to Plaintiff Markezich. The Court therefore limits its analysis to Plaintiff Louisiana.

general conclusions about adverse events." *Alliance III*, 78 F.4th at 249. The Court also found that FDA had "relied on various literature relating to remote prescription of mifepristone – despite FDA's admission that the literature did not affirmatively support its position." *Id.* at 250.

To be sure, the 2023 REMS had not yet been put into effect when suit was filed in *Alliance I*. Therefore, those plaintiffs did not specifically challenge the 2023 REMS, as the Plaintiffs do here. But the Fifth Circuit's analysis in *Alliance III* found fault with both the 2016 Amendments and the 2021 Nonenforcement Decision – and included in its discussion that "in January 2023, FDA amended mifepristone's REMS … formalizing the change" rendered in the 2021 Nonenforcement Decision. *Id.* at 247. Likewise, in rejecting a mootness challenge by FDA, the *Alliance III* court described the 2023 REMS as merely a "final form of a previous, identical policy," removing mifepristone's in-person dispensing requirement. *Id.* at 248-49.

Accordingly, Plaintiffs' challenge to the 2023 REMS focuses on the very same failure to engage in reasoned decision-making under the APA when FDA modified the mifepristone regulatory regime. *Id.* at 245, 255. And the Supreme Court, in vacating the Fifth Circuit's opinion in *Alliance III*, addressed only those plaintiffs' lack of Article III standing to bring an APA challenge. *Alliance IV*, 602 U.S. at 396-97. The *Alliance III* court's reasoning is therefore due strong consideration in weighing Plaintiffs' likelihood of success on the merits.

Further, HHS Secretary Kennedy and FDA Commissioner Makary essentially acknowledged APA procedural deficits with respect to mifepristone in their September 19, 2025, letter, stating that FDA's intention to review the mifepristone

regulatory framework was precipitated by "the lack of adequate consideration underlying the prior REMS approvals" and recent safety concerns. [Doc. 1-110]. Thus, the Court concludes that Plaintiffs are likely to succeed on the merits of their 2023 REMS challenge.

B. Irreparable Injury

The Court has already found that Louisiana demonstrated an injury-in-fact, and those same facts establish irreparable harm. An irreparable harm is one that has "no adequate remedy at law." *Louisiana v. Biden*, 55 F.4th 1017, 1033-34 (5th Cir. 2022). Here, the 2023 REMS operates, arguably, in derogation of Louisiana law and interferes with Louisiana's ability to enforce its laws and implement the policy choices of its citizens. *Louisiana v. EEOC*, 705 F. Supp. 3d 643, 653 (W.D. La. 2024).

No remedy at law can redress that sovereign harm. By permitting medical providers to prescribe mifepristone remotely, the 2023 REMS facilitates the distribution of mifepristone into Louisiana notwithstanding contrary law. Louisiana suffers sovereign harm each time those laws are circumvented. And Louisiana has also demonstrated financial injury that cannot be "remedied where, as here, the defendant is entitled to sovereign immunity." *Alliance III*, 78 F.4th at 251.

C. Balance of Harms/Public Interest

No one disputes that "[a]bortion presents a profound moral issue." *Dobbs*, 597 U.S. at 223; s*ee also Alliance IV*, 602 U.S. at 376, 396 (noting both the longstanding controversy surrounding mifepristone and plaintiffs' "sincere legal, moral, ideological, and policy objections"). But this Court is not a forum for resolving moral or policy disagreements. Its task is to apply established legal standards to the record

before it. That inquiry turns on legally cognizable harms to the parties and the public interest, not on the weight of competing moral views. And where, as here, the issues implicate scientific and medical judgments committed by Congress to an agency with specialized knowledge, that limitation carries particular force.

Having previously discussed the ongoing harm suffered by Plaintiff Louisiana, the Court starts its analysis by looking at the interests of the Government. First, the Court notes that "anytime the Government is enjoined … 'it suffers a form of irreparable injury.'" *Alliance III*, 78 F.4th at 251*, quoting Maryland v. King*, 567 U.S. 1301, 1303 (2012) (Roberts, C.J., in chambers). Specific to this matter, FDA is charged with implementing federal statutes governing the safety and efficacy of drugs through an evidence-based administrative rule-making process. *Alliance IV*, 602 U.S. at 374-75.

In carrying out that mandate, the agency evaluates scientific and clinical data, makes factual findings based on the administrative record, and, where appropriate, considers public comments. *See Weinberger v. Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609, 617 (1973) (explaining that FDA approval requires adequate, well-controlled clinical investigations by qualified experts, not anecdotal or uncontrolled data). The agency must also "articulate a satisfactory explanation for its action including a rational connection between the facts found and the choice made." *Motor Vehicle Mfrs. Ass'n of the United States, Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983). This science-based regime derives from and is limited to the confines of its Congressional mandate.

And FDA, being a component of the Executive Branch, operates as an agency ultimately accountable to the President. The public interest in the proper function of FDA and its scientifically grounded, congressionally authorized protocol is substantial. The Intervenors also have a substantial financial interest in this matter. Any change in the current regulatory regime governing the prescription of mifepristone, which has now been in place for five years, would affect their profit margins and compliance costs.

No doubt Louisiana has a great interest in this issue as well. *Dobbs* returned the issue of abortion to the people of the States and their elected representatives, including regulation of abortion methods, procedures, and the use of related drugs. 597 U.S. at 302. The 2023 REMS clearly facilitates easier access to mifepristone for Louisiana residents. But the Court must also take into consideration that any interim relief ordered by this Court would not relieve Louisiana of its duty to enforce its own laws. In practice, even with the remedy requested herein, mifepristone would likely continue to reach those who seek it, as our country's decades of experience with the war on illegal drugs clearly and painfully demonstrates.[17] Meanwhile, Louisiana retains many meaningful, boots-on-the-ground law enforcement mechanisms to mitigate its sovereign and financial harms while FDA completes its ongoing review.

The Court next turns to the public interest and begins with the premise, as recognized by the *Alliance III* court, that "[t]here is generally no public interest in the

[17] In 2025, for instance, cocaine production reached record levels despite fifty-five years of counter-narcotics enforcement efforts by the United States and other nations. *World Drug Report 2025*, UNITED NATIONS OFF. ON DRUGS & CRIME (June 13, 2025).

perpetuation of unlawful agency action." *Louisiana,* 55 F.4th at 1035. But the Court also notes that the Supreme Court fully stayed the preliminary injunction issued by the *Alliance I* district court, as affirmed in part by the Fifth Circuit in *Alliance II*, (including its injunction of the 2021 Nonenforcement Decision). *Danco Lab'ys, LLC*, 143 S. Ct. 1075. This effectively allowed the challenged FDA actions with respect to mifepristone to continue throughout the course of the appeal. And, of course, that injunction was ultimately vacated for lack of standing. *Alliance IV*, 602 U.S. at 396-97.

Here, unlike in the *Alliance* cases, FDA does not defend its decision-making on the merits but instead acknowledges deficits and requests a stay to complete a fulsome review of the merits of Plaintiffs' claims – a review that was announced before this lawsuit was filed and has already been initiated. [Doc. 1-110]. FDA also has the authority to take interim actions to ensure drug safety if new information is discovered during the pendency of its review. *See generally* [Doc. 250].

Also weighing on its analysis is the Court's understanding that this case arises amid multiple parallel lawsuits across the country addressing the same regulatory issues surrounding access to mifepristone, creating a substantial risk of inconsistent judicial outcomes on a question of nationwide importance.[18] Although not styled as

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[18] *See Mifepristone Litigation and Federal Action Tracker*, UCLA LAW CTR. ON REPROD. HEALTH, LAW, & POLICY (last updated Apr. 2026), https://law.ucla.edu/academics/centers/center-reproductive-health-law-and-policy/mifepristone-litigation-and-federal-action-tracker.

At the time of the parties' briefing, five other states are challenging either the approval of mifepristone or subsequent actions easing restrictions. *See Missouri v. FDA*, No. 4:25-cv-1580-CMS (E.D. Mo.) (Missouri, Idaho, and Kansas challenging actions easing REMS restrictions); *Florida v. FDA*, No. 7:25-cv-126-O (N.D. Tex.) (Florida and Texas challenging

a universal injunction, the relief sought by Plaintiffs would, as a practical matter, have a nationwide effect. As the Supreme Court recently observed, such sweeping relief creates asymmetry because a plaintiff "must win just one suit to secure sweeping relief," whereas the Government "must win everywhere" to avoid it. *Trump v. CASA, Inc.*, 606 U.S. 831, 855 (2025). It also risks "rushed, high-stakes, [and] low-information" decision-making in consequential cases. *Id.* at 855-56, *quoting Labrador v. Poe ex rel. Poe*, 144 S. Ct. 921, 927 (2024) (Gorsuch, J., concurring).

These concerns are reinforced by settled limits on equitable relief, which require that remedies be tailored to the plaintiff's injury and may not be "more burdensome … than necessary." *Texas*, 599 U.S. at 702 (Gorsuch, J., concurring), *quoting Califano v. Yamasaki*, 442 U.S. 682, 702 (1979) (internal quotation marks omitted). "Faithful application of those principles suggests that an extraordinary remedy like vacatur would demand truly extraordinary circumstances to justify it." *Id.* at 702 (Gorsuch, J., concurring).

This is because, like "universal injunctions, vacatur can stymie the orderly review of important questions, lead to forum shopping … and facilitate efforts to evade the APA's normal rulemaking processes." *Id.* at 703 (Gorsuch, J., concurring). "Vacatur can also sweep up nonparties who may not wish to receive the benefit of the

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approval of mifepristone and actions easing REMS restrictions). Other plaintiffs have challenged FDA's restrictions as too burdensome. *See Purcell v. Kennedy*, 2025 WL 3101785 (D. Haw. Oct. 30, 2025) (finding that FDA violated the APA by failing to provide a reasoned explanation for its burdensome conditions on the prescription of mifepristone, which that court determined appeared to be unwarranted relative to the drug's safety); *Washington v. FDA*, No. 1:23-cv-3026-TOR, 2025 WL 1888794 (E.D. Wash. 2025) (plaintiffs challenge REMS as too restrictive); *Whole Woman's Health All. v. FDA*, No. 3:23-cv-19 (W.D. Va.) (same). This list does not include a multitude of citizen petitions.

court's decision," which, here, would include the 18 states and other amici that filed briefs urging denial of Plaintiffs' Motion. *Id.* (Gorsuch, J., concurring); *see also, e.g., supra* note 2. As a result, vacatur improperly applied, "strains our separation of powers" because "it exaggerates the role of the Judiciary in our constitutional order, allowing individual judges to act more like a legislature by decreeing the rights and duties of people nationwide." *Id.* (Gorsuch, J., concurring). All told, although federal courts are vested with much authority, the Constitution does not establish, nor does this Court condone, "government by lawsuit." *Id.* at 704, *quoting* ROBERT H. JACKSON, THE STRUGGLE FOR JUDICIAL SUPREMACY 286-87 (1941).

Next, the Court finds it appropriate to look at the substance of the alleged deficiencies pointed to by Plaintiffs in weighing the equities of issuing interim relief. No doubt, the State has shown evidence of ongoing harm owing to the 2023 REMS. But the APA deficiencies pointed to by the Plaintiffs and found by the Fifth Circuit in *Alliance III* show only that the 2023 REMS was "taken without sufficient consideration of the effects those changes would have on patients" due to a lack of underlying data. *Alliance III*, 78 F.4th at 253. Those same deficiencies likewise prevent this Court from determining whether FDA's in-person dispensing requirement is scientifically necessary to ensure mifepristone is "safe" and "effective." *Id.* at 245; *see also* 21 U.S.C. § 355(b)(1)(i).

On the one hand, a proper science-driven evaluation may lead FDA to conclude that the in-person dispensing requirement is necessary to comply with FDA's mandate to ensure that mifepristone is "safe and effective" for use, 21 U.S.C. § 355(b)(1)(i), and Plaintiffs offer substantial evidence supporting that possibility. On

the other hand, FDA may determine, after a thorough and scientifically-driven process, that such a requirement is not required. This Court is ill-equipped to make this determination, particularly where FDA has thus far failed to even collect the data necessary to comply with the APA's requirement that it "examine the relevant data and articulate a satisfactory explanation for its action including a 'rational connection between the facts found and the choice made.'" *Alliance III*, 78 F.4th at 245, *quoting Motor Vehicle Mfrs.*, 463 U.S. at 43. And ultimately it is FDA, not this Court, that possesses the expertise to evaluate scientific evidence and make public health judgments.[19]

At bottom, the APA does not charge the judiciary with the task of supplanting the role of federal agencies in promulgating regulations. *See Prometheus Radio Project*, 592 U.S. at 423. Rather, it is quite simply meant to be "a check" upon administrators to ensure that they are doing their job as directed by Congress. *Morton Salt Co.*, 338 U.S. at 644 (1950). Here, FDA has acknowledged its own deficits and has initiated an ongoing review of mifepristone.

Finally, this Court finds that prudence in issuing injunctive relief is warranted here because the 2023 REMS has governed a nationally integrated regulatory scheme

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[19] *See, e.g.*, *FDA,* 141 S. Ct. at 578-79 (Roberts, C.J., concurring in grant of application for stay) ("[C]ourts owe significant deference to the politically accountable entities with the 'background, competence, and expertise to assess public health.'"); *Cytori Therapeutics, Inc.* v. *Food & Drug Admin.*, 715 F.3d 922, 927 (D.C. Cir. 2013) (Kavanaugh, J.) ("A court is ill-equipped to second-guess that kind of agency scientific judgment under the guise of the APA's arbitrary and capricious standard."); *Otsuka Pharm. Co.* v. *Burwell*, 302 F. Supp. 3d 375, 403 (D.D.C. 2016) (Jackson, J.) ("To begin with, the FDA is an expert agency charged with making precisely these sorts of highly technical determinations, and its interpretation … is premised on 'the agency's evaluations of scientific data within its area of expertise.'"), *aff'd sub nom. Otsuka Pharm. Co.* v. *Price*, 869 F.3d 987 (D.C. Cir. 2017).

for five years (since the promulgation of the 2021 Nonenforcement Decision), and imposing sweeping relief now risks the "patchwork" of judicial remedy the Court has warned against. *CASA*, 606 U.S. at 872 (Kavanaugh, J., concurring). There are now at least five other lawsuits in federal courts around the nation addressing issues similar to those before the Court. *See supra* note 18. And again, FDA's ongoing review of the mifepristone REMS indicates both responsiveness to Congress's directive that drugs be "safe and effective," 21 U.S.C. § 355, as well as accountability to the public. *See DHS v. Regents of the Univ. of California*, 591 U.S. 1, 16 (2020), *quoting Franklin v. Massachusetts*, 505 U.S. 788, 796 (1992) ("The APA 'sets forth the procedures by which federal agencies are accountable to the public and their actions subject to review by the courts.'"). FDA's review should be conducted and completed free from judicial interference.

Therefore, for the reasons discussed, the Court declines to grant the Plaintiffs § 705 relief at this time. Given the length of time the 2023 REMS has been in effect, reliance interests on that scheme throughout the nation, the sweeping effect any remedy would have across states with differing abortion laws, and most importantly, FDA's recognition of its own shortcomings in regulating mifepristone and ongoing fulsome review of the mifepristone REMS, the Court will afford the agency a time-limited period of deference to complete its review and carry out the responsibilities assigned to it by Congress. This case will therefore be stayed.

But the stay granted to FDA will not remain open-ended. FDA has an obligation to act with all deliberate speed to review its past actions and complete a thorough analysis that addresses the deficiencies it has acknowledged. The parties

and the American public deserve nothing less. Should the agency fail to complete its review and make any necessary revisions to the REMS within a reasonable timeframe, the Court's analysis – and the weight accorded to these factors – will inevitably change.

CONCLUSION

Considering the foregoing,

IT IS HEREBY ORDERED that Defendants' MOTION TO STAY THE CASE [Doc. 50] is GRANTED, and this matter is STAYED pending completion of FDA's ongoing review of the mifepristone REMS and issuance of any resulting agency decision.

IT IS FURTHER ORDERED that Plaintiffs' MOTION FOR PRELIMINARY RELIEF UNDER 5 U.S.C. § 705 [Doc. 20] is DENIED WITHOUT PREJUDICE and with permission to refile, as appropriate, following completion of FDA's review or upon a lifting of the stay upon a material change in circumstances.

IT IS FURTHER ORDERED, pursuant to Plaintiffs' request at the motions hearing on February 24, 2026, that FDA produce the entirety of the administrative record to Plaintiffs' counsel within sixty (60) days.

IT IS FURTHER ORDERED that Danco's MOTION TO DISMISS [Doc. 230] and GenBioPro's MOTION TO DISMISS [Doc. 232] are hereby DENIED WITHOUT PREJUDICE and with permission to refile, as appropriate, following completion of FDA's review or upon a lifting of the stay upon a material change in circumstances.

IT IS FURTHER ORDERED that FDA shall file a report on or before six (6) months from the date of this Order providing the Court with the status of its review in terms of process and any updated timeframe for completion of review. Within

fourteen (14) days after FDA completes its REMS review, FDA shall file a brief advising the Court of any agency action and proposing a schedule for further proceedings, if necessary.

THUS, DONE AND SIGNED in Chambers on this 7th day of April 2026.

DAVID C. JOSEPH
UNITED STATES DISTRICT JUDGE

No. 26-30203

In the United States Court of Appeals for the Fifth Circuit

STATE OF LOUISIANA, BY AND THROUGH ITS ATTORNEY GENERAL, LIZ MURRILL ; ROSALIE MARKEZICH,
Plaintiffs-Appellants

v.

FOOD & DRUG ADMINISTRATION ; MARTY MAKARY, COMMISSIONER, U.S. FOOD AND DRUG ADMINISTRATION ; RICHARD PAZDUR, IN HIS OFFICIAL CAPACITY AS DIRECTOR, CENTER FOR DRUG EVALUATION & RESEARCH, U.S. FOOD & DRUG ADMINISTRATION ; UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES ; ROBERT F. KENNEDY, JR., SECRETARY, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES,
Defendants-Appellees

v.

DANCO LABORATORIES, L.L.C. ; GENBIOPRO, INCORPORATED,
Intervenors-Appellees

On Appeal from the United States District Court
for the Western District of Louisiana
No. 6:25-cv-01491-DCJ-DJA, Hon. David C. Joseph

MOTION FOR § 705 STAY OR INJUNCTION PENDING APPEAL

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CERTIFICATE OF INTERESTED PERSONS

Louisiana, et al. v. Food and Drug Administration, et al.

The undersigned counsel of record certifies that the following listed persons and entities as described in the fourth sentence of Rule 28.2.1 have an interest in the outcome of this case. These representations are made in order that the judges of this court may evaluate possible disqualification or recusal.

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Rosalie Markezich

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TABLE OF CONTENTS

CERTIFICATE OF INTERESTED PERSONS i

TABLE OF AUTHORITIES xviii

MOTION 1

STATEMENT 2

JURISDICTIONAL STATEMENT 7

STANDARD OF REVIEW 8

ARGUMENT 8

I. AS THIS COURT AND THE DISTRICT COURT HAVE CONCLUDED, PLAINTIFFS ARE LIKELY TO SUCCEED ON THE MERITS. 9

A. The 2023 REMS Is Unlawful. 9

B. Louisiana Has Standing. 12

II. AS THE DISTRICT COURT CONCLUDED, LOUISIANA IS SUFFERING IRREPARABLE HARM. 17

III. THE BALANCE OF EQUITIES AND PUBLIC INTEREST FAVOR A STAY OR INJUNCTION. 18

A. The Remaining Factors Are Straightforward. 18

B. The District Court's Considerations Are Misplaced. 20

CONCLUSION 26

CERTIFICATE OF SERVICE 28

CERTIFICATE OF COMPLIANCE 29

TABLE OF AUTHORITIES

Cases

All. for Hippocratic Med. v. FDA,
2023 WL 2913725 (5th Cir. Apr. 12, 2023) ..... passim

All. for Hippocratic Med. v. FDA,
78 F.4th 210 (5th Cir. 2023) ..... passim

Bost v. Ill. State Bd. of Elections,
146 S. Ct. 513 (2026) 16

Buenrosto-Mendez v. Bondi,
166 F.4th 494 (5th Cir. 2026) 22

Career Colls. & Schs. of Tex. v. U.S. Dep't of Educ.,
98 F.4th 220 (5th Cir. 2024) 23

Clapper v. Amnesty Int'l USA,
568 U.S. 398, 414 n.5 (2013) 13

Diamond Alt. Energy, LLC v. EPA,
606 U.S. 100 (2025) 16

Dobbs v. Jackson Women's Health Organization,
597 U.S. 215 (2022) 2

FDA v. All. for Hippocratic Med.,
602 U.S. 367 (2024) 4, 21

In re Flint Water Cases,
960 F.3d 820 (6th Cir. 2020) 1

Larson v. Valente,
456 U.S. 228 (1982) 16

Moore v. Tangipahoa Par. Sch. Bd.,
507 F. App'x 389 (5th Cir. 2013) 5, 8, 18

Nken v. Holder,
556 U.S. 418 (2009) 9

Simon v. City & Cnty. of San Francisco,
135 F.4th 784 (9th Cir. 2025) 1

Speech First, Inc. v. Killeen,
968 F.3d 628 (7th Cir. 2020) 18

Texas v. United States,
126 F.4th 392 (5th Cir. 2025) 12, 13

Texas v. United States,
50 F.4th 498 (5th Cir. 2022) 17

Texas v. United States,
809 F.3d 134 (5th Cir. 2015) 12

TitleMax of Tex., Inc. v. City of Dallas,
142 F.4th 322 (5th Cir. 2025) 8, 18

Trump v. CASA, Inc.,
606 U.S. 831 (2025) 23, 24

United States v. Abbott,
110 F.4th 700 (5th Cir. 2024) 5, 8, 18

Vapor Tech. Ass'n v. Graham,
167 F.4th 302 (5th Cir. 2026) 8

Wages & White Lion Invs., LLC v. FDA,
16 F.4th 1130 (5th Cir. 2021) 8, 10

Statutes

28 U.S.C. § 1292(a)(1) 7

5 U.S.C. § 705 ..... passim

La. R.S. 40:1061.1(A)(1) 13

Other Authorities

Questions and Answers on Mifepristone for Medical Termination of Pregnancy Through Ten Weeks Gestation, U.S. Food & Drug Admin., perma.cc/4TMY-SWYQ 6

Rules

Fed. R. App. P. 8(a)(1) 1

MOTION

Under Federal Rules of Appellate Procedure 8 and 27, Plaintiffs-Appellants the State of Louisiana and Rosalie Markezich move the Court for a stay under 5 U.S.C. § 705 pending appeal or, alternatively, an injunction pending appeal. The subject of the stay or injunction is the U.S. Food and Drug Administration's (FDA) "2023 agency action removing the in-person dispensing requirement for the abortion drug, mifepristone," also known as the "2023 REMS." Ex. A (Dist.Ct.Op.) at 1.[1]

Although a movant "ordinarily" must first seek relief pending appeal in the district court, Fed. R. App. P. 8(a)(1), that is not the case where such a formal request would be futile, *see, e.g.*, *Simon v. City & Cnty. of San Francisco*, 135 F.4th 784, 815 n.22 (9th Cir. 2025); *In re Flint Water Cases*, 960 F.3d 820, 825 (6th Cir. 2020). That is the situation here, as the district court has both (a) denied the precise preliminary relief Plaintiffs now seek from this Court and (b) stayed the lawsuit, preventing any further proceedings below.

[1] The Intervenors oppose this relief and intend to respond; the Federal Defendants intend to respond.

STATEMENT

For decades, FDA closely regulated the abortion drug mifepristone. One such regulation was an in-person dispensing requirement, which, among other things, ensured that a woman was operating free from coercion and that mifepristone would not pose a unique danger to her health.

In 2023, however, the Biden Administration changed mifepristone's Risk Evaluation and Mitigation Strategy (REMS) to remove the in-person dispensing requirement. The Biden Administration's avowed purpose was to undermine *Dobbs v. Jackson Women's Health Organization*, 597 U.S. 215, 232 (2022). Fearing that pro-life states would provide strong protections for unborn babies and their mothers after *Dobbs*, the Biden Administration sought to ensure that prescribers outside those states (say, in New York and California) could still effectuate abortions in pro-life states. The key to that scheme was the 2023 REMS: the permanent removal of the in-person dispensing requirement, which allowed the "dispensing [of] mifepristone through the mail ... or through mail-order pharmacy" into pro-life states. Dist.Ct.Op.6 (citation omitted). The net result is that some 1,000 Louisiana babies are

illegally aborted using FDA-approved mifepristone every month. Dist.Ct.Op.24.

In this case, Louisiana and one of its citizens—Rosalie Markezich, who was coerced to take mifepristone to abort a baby she wanted—have sued for vacatur of the 2023 REMS under the Administrative Procedure Act (APA).[2] *See* Dist.Ct.ECF.1 (complaint). Louisiana has sought a stay of the 2023 REMS under 5 U.S.C. § 705 or a preliminary injunction against its enforcement. *See* Dist.Ct.ECF.20-26 (preliminary-relief motion); Dist.Ct.ECF.111 (preliminary-relief reply). FDA has refused to defend the 2023 REMS. Ex. B (Tr.) at 35 ("We're not taking a position on any merits issue with respect to this motion."). In fact, FDA's position is that the 2023 REMS reflects a "lack of adequate consideration," Dist.Ct.Op.28 (citation omitted), and that the "Biden [A]dministration removed mifepristone's in-person dispensing rule without studying the safety risks," Dist.Ct.ECF.1 at 4 (citation omitted).

There is virtually no question that the 2023 REMS is unlawful under basic APA review. Two panels of this Court already have said as

[2] Because the district court focused its analysis on Louisiana, *see* Dist.Ct.Op.25 n.15, 26 n.16, this motion likewise focuses on Louisiana.

much, criticizing FDA's "ostrich's-head-in-the-sand approach" and twice upholding a § 705 stay of the 2023 REMS. *All. for Hippocratic Med. v. FDA* (*Alliance I*), 2023 WL 2913725, at *17 (5th Cir. Apr. 12, 2023); *All. for Hippocratic Med. v. FDA* (*Alliance II*), 78 F.4th 210, 249–51 (5th Cir. 2023).[3] (The Supreme Court later reversed that stay solely on standing grounds. *FDA v. All. for Hippocratic Med.*, 602 U.S. 367 (2024).) The district court below similarly agreed that "Plaintiffs are likely to succeed on the merits of their 2023 REMS challenge." Dist.Ct.Op.28.

There is also virtually no question that Louisiana has standing to sue and is suffering irreparable harm. Here, too, the district court below agreed that, "[b]y permitting medical providers to prescribe mifepristone remotely, the 2023 REMS facilitates the distribution of mifepristone into Louisiana," causing illegal abortions in Louisiana. *Id.* "Louisiana suffers sovereign harm each time [its] laws are circumvented," the court explained, and "[n]o remedy at law can redress that sovereign harm." *Id.*

[3] As the district court explained, the *Alliance II* Court technically considered a 2021 Nonenforcement Decision, not the 2023 REMS; however, "the *Alliance II* court described the 2023 REMS as merely a 'final form of a previous, identical policy,' removing mifepristone's in-person dispensing requirement"—*i.e.*, the 2021 Nonenforcement Decision. Dist.Ct.Op.27. So the Court's reasoning directly maps onto the 2023 REMS as well.

Further, Louisiana suffers unrecoverable (due to FDA's sovereign immunity) "financial injury" given the economic costs of this scheme. *Id.* The "same facts" that establish Louisiana's standing also "establish irreparable harm." *Id.*

Because the district court correctly concluded that Louisiana (a) is likely to succeed in this challenge to the 2023 REMS and (b) suffers irreparable harm every day that the 2023 REMS remains in effect, preliminary relief is plainly warranted. *See, e.g.*, *United States v. Abbott*, 110 F.4th 700, 706 (5th Cir. 2024) (en banc) ("The first factor—likelihood of success on the merits—is 'the most important.'"); *Moore v. Tangipahoa Par. Sch. Bd.*, 507 F. App'x 389, 399 (5th Cir. 2013) (likelihood of success on the merits and irreparable harm are "the most important" preliminary-relief factors). But, in a strange turn of events, the court denied Louisiana's relief and imposed an *indefinite* stay under the heading "Balance of Harms/Public Interest." Dist.Ct.Op.28.

The district court erred in denying relief. Consider just two reasons why: (1) while Louisiana is suffering irreparable harm, the district court identified no irreparable harm from entering a § 705 stay, which means the balance favors Louisiana; and (2) this Court already held that the

public has no interest in the illegal 2023 REMS, FDA and the public "will not be injured by" a § 705 stay, and "the public interest is disserved by a drug that does not afford adequate protections to its users." *Alliance II*, 78 F.4th at 251–53. A § 705 stay is warranted.

The only thing that has changed since *Alliance II* is that FDA has now proclaimed for over a year that it will "study" and "review" the 2023 REMS. But when pressed by the district court in February 2026, FDA said (a) "I don't have a timeline I can give Your Honor," (b) some part of the review (but "*not* the whole review") might be complete by 2027, and (c) FDA "can't talk specifically about what they are doing" but they are somewhere "in the data collection phase of the study." Tr.33–34; *accord* Dist.Ct.ECF.20-26 at 8. In other words, as of February 2026 (and still today[4]), FDA did not even have the data sufficient to conduct a review.

The district court nevertheless relied on FDA's purported study to deny preliminary relief to Louisiana and then indefinitely stay this lawsuit to see what, if anything, comes of the supposed review.

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[4] Remarkably, the day after the decision below, FDA (non)updated its website to say that, "[a]s of April 2026," FDA *still* does not have sufficient data for its "saftey [sic] study on mifepristone." *Questions and Answers on Mifepristone for Medical Termination of Pregnancy Through Ten Weeks Gestation*, U.S. Food & Drug Admin., perma.cc/4TMY-SWYQ.

This motion challenges the denial of preliminary relief (rather than the stay decision). For there is no justification—given Louisiana's, FDA's, and the district court's agreement that the 2023 REMS is unlawful—for forcing Louisiana to suffer ongoing irreparable harm unless and until FDA decides what it wants to do (or not do) with the 2023 REMS at some unidentified future date. (The district court has requested only a status update in six months.) Such a result flips the APA on its head—the whole point of which is to ensure timely judicial review and vacatur of unlawful agency actions. *See* § 705 ("Relief pending review").

Each month that passes is not just time lost; it is some 1,000 Louisiana lives lost. For these reasons, the Court should enter the same § 705 stay it upheld in *Alliance I* and *Alliance II* or, alternatively, enjoin enforcement of the 2023 REMS pending appeal.

JURISDICTIONAL STATEMENT

On April 7, the district court issued its decision denying Plaintiffs' motion for preliminary relief and granting the Federal Defendants' motion to stay the case. Ex. A. The State appealed that ruling the next day. Dist.Ct.ECF.269. This Court has jurisdiction under 28 U.S.C. § 1292(a)(1).

STANDARD OF REVIEW

Plaintiffs request a stay of the 2023 REMS or, alternatively, a preliminary injunction pending appeal. *See* 5 U.S.C. § 705; Fed. R. Civ. P. 65. Plaintiffs thus "must show '(1) a strong likelihood of success on the merits; (2) irreparable injury in the absence of an injunction; (3) that the balance of hardships weighs in their favor if injunctive relief is granted; and (4) that the public interest favors such relief.'" *Vapor Tech. Ass'n v. Graham*, 167 F.4th 302, 305 (5th Cir. 2026) (citation omitted); *see Wages & White Lion Invs., LLC v. FDA*, 16 F.4th 1130, 1143–44 (5th Cir. 2021) (applying these factors under § 705). The first two are the "most important." *Abbott*, 110 F.4th at 706; *Moore*, 507 F. App'x at 399. This Court applies a "sliding-scale" approach to these factors, such that Plaintiffs' strong showing on one or more factors requires only "some" showing on the others. *TitleMax of Tex., Inc. v. City of Dallas*, 142 F.4th 322, 328–29 (5th Cir. 2025).

ARGUMENT

The issue before this Court is remarkably narrow because the district court resolved nearly the entire preliminary-relief analysis in Plaintiffs' favor. *First*, the district court concluded—as two panels of this Court concluded—that Plaintiffs are likely to succeed in their APA

challenge to the 2023 REMS. *Second*, the district court concluded that Louisiana not only has standing but is suffering irreparable harm every day that the 2023 REMS remains in effect.

That leaves only the *third* issue: whether the equities and public-interest inquiries, which merge in this context, *see Nken v. Holder*, 556 U.S. 418, 435 (2009), somehow override Louisiana's entitlement to preliminary relief and warrant an indefinite stay of this litigation while Louisiana undisputedly continues to suffer irreparable harm. They do not. The proper course is to enter preliminary relief, just what this Court preserved in *Alliance I* and *Alliance II*.

I. AS THIS COURT AND THE DISTRICT COURT HAVE CONCLUDED, PLAINTIFFS ARE LIKELY TO SUCCEED ON THE MERITS.[5]

A. The 2023 REMS Is Unlawful.

Start with the merits analysis that this Court has twice conducted—and in which the district court concurred. Arbitrary-and-capricious review "requires that agency action be reasonable and reasonably explained," meaning that the agency "has reasonably

[5] Given current space constraints, this analysis is necessarily more abbreviated than the analyses preserved below and in this Court's prior decisions. *See* Dist.Ct.ECF.20-26 at 9–14 (APA), 17–25 (standing); Dist.Ct.ECF.111 at 2–13 (standing), 15–18 (APA).

considered the relevant issues and reasonably explained the decision." *Wages & White Lion*, 16 F.4th at 1136 (citation omitted). The fatal defect in the 2023 REMS is that the Biden FDA removed the in-person dispensing requirement with no legitimate justification for doing so. *Alliance I*, 2023 WL 2913725, at *17–18; *Alliance II*, 78 F.4th at 249–51. The district court well summarized the two bases for this Court's conclusions in *Alliance I* and *Alliance II*. Dist.Ct.Op.7–11.

First, FDA based its removal of the in-person dispensing requirement "on the absence of data that [FDA] had only five years previously intentionally eliminated," using that absence to justify deeming mifepristone safe without an in-person dispensing requirement. Dist.Ct.Op.26–27 (citing *Alliance II*, 78 F.4th at 249). This Court was astounded by FDA's "declar[ation] [that] the absence of non-fatal adverse-event reports means mifepristone is 'safe.'" *Alliance I*, 2023 WL 2913725, at *17. "This ostrich's-head-in-the-sand approach is deeply troubling," the Court said. *Id.* "It's unreasonable for an agency to eliminate a reporting requirement for a thing and then use the resulting absence of data to support its decision"—and thus "it [is] unlikely that

plaintiffs' arbitrary-and-capricious challenges will fail on the merits." *Id.* at *17–18; *accord Alliance II*, 78 F.4th at 249–50.

Second, FDA also "relied on various literature relating to remote prescription of mifepristone—despite FDA's admission that the literature did not affirmatively support its position." Dist.Ct.Op.27 (quoting *Alliance II*, 78 F.4th at 250). That makes this an easy arbitrary-and-capricious case: "Especially in light of the unreliability of the adverse-event data, it was not reasonable for FDA to depend on the published literature to support its decision." *Alliance II*, 78 F.4th at 250. Because FDA "did not refer to any literature that affirmatively supported the notion that mifepristone would remain safe and effective even without the in-person dispensing requirement," Plaintiffs "are likely to succeed in showing that [the 2023 REMS] violated the APA." *Id.* at 251.

This Court's own prior merits determinations are correct—and that is even truer today because "HHS Secretary Kennedy and FDA Commissioner Makary [have] essentially acknowledged APA procedural deficits," "stating that FDA's intention to review the mifepristone regulatory framework was precipitated by 'the lack of adequate consideration underlying the prior REMS approvals' and recent safety

concerns." Dist.Ct.Op.27–28. Plaintiffs are thus likely to "succeed on the merits of their 2023 REMS challenge." Dist.Ct.Op.28.[6]

B. Louisiana Has Standing.

The district court likewise rightly held that Louisiana has Article III standing to challenge the 2023 REMS. "To establish standing, 'a plaintiff must demonstrate: (i) that she has suffered or likely will suffer an injury-in-fact; (ii) that the injury likely was caused or will be caused by the defendant; and (iii) that the injury likely would be redressed by the requested judicial relief." Dist.Ct.Op.16 (citing *Texas v. United States*, 126 F.4th 392, 407 (5th Cir. 2025)). Each element is satisfied. Dist.Ct.Op.16–25.

1. The district court correctly determined that Louisiana suffers at least two distinct injuries in fact.

First is the harm to Louisiana's "sovereign interest in the power to create and enforce a legal code." Dist.Ct.Op.22 (quoting *Texas v. United States*, 809 F.3d 134, 153 (5th Cir. 2015)). Louisiana expressly prohibits

[6] Omitted here for efficiency, Louisiana also has an APA claim based on the Comstock Act, which is an independent basis for likelihood of success on the merits. *See* Dist.Ct.ECF.20-26 at 13–14; *Alliance II*, 78 F.4th at 267–70 (Ho, J., concurring in part and dissenting in part).

abortion (with narrow exceptions), including the dispensing of mifepristone to induce an abortion. Dist.Ct.Op.18 n.10 (collecting statutes). Louisiana law also expressly "reaffirm[s] the longstanding public policy of this state that every unborn child is a human being from the moment of conception." *Id.* (quoting La. R.S. 40:1061.1(A)(1)). Yet Louisiana law is violated some 1,000 times a month when mifepristone is mailed into Louisiana to effectuate illegal abortions. "Louisiana suffers sovereign harm each time those laws are circumvented." Dist.Ct.Op.28. That is a textbook injury-in-fact.[7]

Second is monetary injury. As the district court recounted from this Court's precedents, "[a] state's increased medical costs, such as increased Medicaid costs due to a federal agency action, can constitute a 'pocket-book injury' sufficient to satisfy the injury-in-fact requirement of standing." Dist.Ct.Op.23–24; *see Texas*, 126 F.4th at 408, 411, 413 n.26. And that is the case here: Louisiana's unrebutted record evidence shows that many of the 1,000 mifepristone abortions per month in Louisiana

[7] Louisiana also independently established monetary harm in the form of its reasonable "costs to mitigate or avoid" these legal violations. *See* Dist.Ct.ECF.111 at 3–4 & n.4 (citing *Clapper v. Amnesty Int'l USA*, 568 U.S. 398, 414 n.5 (2013)).

are for women on Medicaid. Dist.Ct.Op.24. That record evidence also shows that, by FDA's own telling, roughly 1 in 25 women who take mifepristone will end up in the emergency room. *Id.*; *accord Alliance I*, 2023 WL 2913725, at *10 ("emergency room care is statistically certain"). The same evidence shows that Louisiana has incurred "more than $92,000 in [such] Medicaid costs" due to only two mifepristone-induced abortions requiring emergency care in 2025—a number that is "likely" severely underinclusive. Dist.Ct.Op.25. "[B]ecause 'even one dollar's worth of harm' is sufficient, Louisiana has put forth sufficient evidence to demonstrate a substantial likelihood of success in proving it has suffered financial injury for standing purposes." *Id.* (citation omitted).

2. The only real question below was traceability and redressability, which "are often flip sides of the same coin" since "if a defendant's action causes an injury, enjoining the action ... will typically redress that injury." Dist.Ct.Op.17 (citation modified). On this question, the district court made two key points.

First, the district court rejected FDA's claim that the above harms are not traceable to the 2023 REMS since "Louisiana is not a regulated party." Dist.Ct.Op.18. That is because "standing may exist where

[independent] actors predictably respond to the challenged action" in a manner that generates those harms. Dist.Ct.Op.19 (collecting cases). That is the case here because "the evidence in the record shows that the 'independent actors'—that is, the out-of-state medical providers prescribing mifepristone via telemedicine or mail—responded to the 2023 REMS by expanding mifepristone access to pro-life states like Louisiana in ways that were entirely predictable." Dist.Ct.Op.19–20.

In fact, this was not just the *predictable* consequence of the REMS, but its *intended* consequence. The Biden Administration openly advertised that it was seeking to preserve abortion in pro-life states after *Dobbs*. Dist.Ct.Op.20–21; *accord* Dist.Ct.ECF.20-26 at 4; Dist.Ct.ECF.111 at 9. The district court thus correctly held that "there is evidence that the 2023 REMS was approved without adequate consideration, at least in part, to circumvent anti-abortion states' ability to regulate abortion." Dist.Ct.Op.21.

That is the end of the traceability analysis: "The government generally may not target a [state] through stringent and allegedly unlawful regulation, and then evade the resulting lawsuit[] by claiming that the target[] of its regulation should be locked out of court as [an]

unaffected bystander[]." *Diamond Alt. Energy, LLC v. EPA*, 606 U.S. 100, 125 (2025); *Bost v. Ill. State Bd. of Elections*, 146 S. Ct. 513, 520–21 (2026). It is also the end of the redressability analysis since "the fact that a regulation was designed to produce a particular effect on the market ordinarily means that the likely result of vacating that regulation would be to reduce that effect on the market." *Diamond*, 606 U.S. at 117.

Second, the district court correctly recognized that Louisiana need not show that the 2023 REMS is *solely* responsible for Louisiana's harms, or that vacating the REMS would *completely* eliminate Louisiana's harms. *See Larson v. Valente*, 456 U.S. 228, 243 n.15 (1982). There are, of course, other actors "influenc[ing] the arrival of mifepristone in Louisiana," including pro-abortion states and out-of-state prescribers. Dist.Ct.Op.23. "But there can be little doubt that the 2023 REMS is a factor, which is all that is required for Louisiana to show injury-in-fact and traceability." *Id.* After all, *but for the 2023 REMS*, no out-of-state prescriber could legally (under federal law) mail mifepristone into Louisiana. In that way, the 2023 REMS is the indispensable ingredient in the nearly 1,000 mifepristone abortions occurring in Louisiana every month. "Thus, even if the 2023 REMS is not the 'sole cause' of Louisiana's

[] harms, it has surely 'exacerbated' them; 'that is sufficient' for standing to assert its claims." Dist.Ct.Op.23 (citing *Texas v. United States*, 50 F.4th 498, 519 (5th Cir. 2022)).

II. AS THE DISTRICT COURT CONCLUDED, LOUISIANA IS SUFFERING IRREPARABLE HARM.

The district court also correctly concluded that Louisiana "establish[ed] irreparable harm." Dist.Ct.Op.28.

First, the 2023 REMS operates "in derogation of Louisiana law and interferes with Louisiana's ability to enforce its laws and implement the policy choices of its citizens." *Id.* In particular, "[b]y permitting medical providers to prescribe mifepristone remotely, the 2023 REMS facilitates the distribution of mifepristone into Louisiana notwithstanding contrary law." *Id.* "Louisiana suffers sovereign harm each time those laws are circumvented," the court explained. *Id.* And because "[n]o remedy at law can redress that sovereign harm," *id.*, it is irreparable, *see Alliance II*, 78 F.4th at 251.

Second, the district court recognized that Louisiana is suffering irreparable economic harm. Specifically, as discussed above, the 2023 REMS is causing direct and predictable economic injuries to Louisiana—and those injuries "cannot be 'remedied where, as here, the defendant is

entitled to sovereign immunity.'" Dist.Ct.Op.28 (citing *Alliance II*, 78 F.4th at 251).

III. THE BALANCE OF EQUITIES AND PUBLIC INTEREST FAVOR A STAY OR INJUNCTION.

So far, Louisiana has satisfied the two "most important" factors. *Abbott*, 110 F.4th at 706; *Moore*, 507 F. App'x at 399. In fact, Louisiana is so strong on those two core factors that, under this Court's "sliding-scale" approach, *TitleMax of Tex., Inc.*, 142 F.4th at 329, even a negligible showing on the "less significant" equities and public-interest inquiries, *Moore*, 507 F. App'x at 399, would warrant a § 705 stay. *See, e.g.*, *Speech First, Inc. v. Killeen*, 968 F.3d 628, 637 (7th Cir. 2020) ("If the plaintiff is likely to win on the merits, the balance of harms need not weigh as heavily in his favor.").

In all events, those remaining inquiries are easily resolved for Louisiana—and the district court's reasoning otherwise is misplaced.

A. The Remaining Factors Are Straightforward.

Begin with the equities and recall the district court's emphatic determination that Louisiana is suffering irreparable harm. The district court did not identify any cognizable irreparable harm to any other party that would be caused by the § 705 stay requested by Plaintiffs. *See*

Alliance II, 78 F.4th at 251 ("This risk of irreparable harm must be weighed against any injury FDA and [the drug manufacturers] would sustain as a result of the [§ 705] stay order, as well as against the public interest."). Common sense and the law of gravity suggest, therefore, that Louisiana must win any balancing analysis.[8]

That point is reinforced by this Court's own determination that it would be *against the public interest* to allow the 2023 REMS to remain in effect. *First*, although "anytime the Government is enjoined from enforcing its statutes, or regulations, 'it suffers a form of irreparable injury,'" "neither the FDA nor the public has any interest in enforcing a regulation that violates federal law." *Alliance II*, 78 F.4th at 251 (citation omitted). "In this regard, the government/public-interest analysis collapses with the merits"—and "[i]t follows that FDA and the public will not be injured by an order staying" the 2023 REMS. *Id.* at 251–52.[9]

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[8] The district court asserted in passing that the drug manufacturers "have a substantial financial interest" because "[a]ny change in the current regulatory regime ... would affect their profit margins and compliance costs." Dist.Ct.Op.30. But the district court did not elaborate, deem that interest an irreparable harm, or even weigh it against Louisiana's irreparable harm.

[9] The court "note[d]" that the Supreme Court stayed the *Alliance* district court's § 705 stay, thereby "allow[ing] the challenged FDA actions with respect to mifepristone to continue throughout the course of the

Second, the Court recognized that, "of course, the public interest is disserved by a drug that does not afford adequate protections to its users." *Id.* at 253. And this preliminary-relief record shows that the 2023 REMS lacks "sufficient consideration of the effects [its] changes would have on patients." *Id.*[10]

These basic facts confirm that preliminary relief is warranted: (a) Louisiana is suffering irreparable harm absent a § 705 stay, (b) no other party will suffer irreparable harm with a § 705 stay, and (c) the public interest is decidedly against keeping the 2023 REMS in effect.

B. The District Court's Considerations Are Misplaced.

Rather than take this straightforward path, the district court offered several thoughts under the heading "Balance of Harms/Public

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appeal." Dist.Ct.Op.31. This statement implies that perhaps the public *does* have an interest in the enforcement of illegal regulations. That is incorrect. As the ultimate *Alliance* decision illustrates, the Supreme Court believed there was no Article III standing. Thus, the "no public interest in enforcing a regulation that violates federal law" principle was not triggered. Not so here, where the district court agreed that Louisiana has standing and is likely to succeed on the merits.

[10] These points address the district court's puzzling assertion that there are cognizable "reliance interests on [the 2023 REMS]" that should be preserved. Dist.Ct.Op.35. *Alliance II* said exactly the opposite in emphasizing that the public has no interest in the perpetuation of this unlawful and unreasoned regulation.

Interest" that led the court to deny preliminary relief. Each consideration is misplaced.

1. The district court principally resisted becoming "a forum for resolving moral or policy disagreements" (or "scientific or medical judgments"). Dist.Ct.Op.28–29. But as this Court's (and the district court's) merits analyses reflect, this lawsuit asks no court to resolve moral, policy, scientific, or medical disagreements; it asks only for a plain APA analysis, which courts run every day. *See Alliance II*, 78 F.4th at 249–50 (explaining why the 2023 REMS "was [likely] arbitrary and capricious"); *accord* Dist.Ct.Op.26–28. To the extent the district court was invoking the Supreme Court's discussion of moral and policy objections in *Alliance*, that discussion was in the context of explaining why such objections do not establish Article III standing. *See* 602 U.S. at 396. That is not an issue here.

2. The district court also worried "that this case arises amid multiple parallel lawsuits across the country addressing the same regulatory issues surrounding access to mifepristone, creating a substantial risk of inconsistent judicial outcomes on a question of

nationwide importance." Dist.Ct.Op.31, 35. That worry appears to come in two parts, each unavailing.

First is a concern that a court elsewhere considering similar issues might reach a different conclusion. But that is an unremarkable feature of high-profile litigation, which often occurs on multiple fronts and leads to diverse results. Taken to its logical conclusion, this concern would paralyze every judge, preventing them from independently deciding important issues in their best judgment. *Cf. Buenrosto-Mendez v. Bondi*, 166 F.4th 494 (5th Cir. 2026) (resolving immigration issue over which district courts have split nationwide). That is not the proper judicial role.

More fundamentally, the *Alliance I* Court already rejected a similar concern. There, the Court expressed "every respect for fellow federal courts," but refused to "embrace an argument that would, in effect, allow the decision of an out-of-circuit district court to impel us towards [a stay] that would be otherwise inappropriate." 2023 WL 2913725, at *19. So here: The Court should reject the notion that the mere possibility of contrary decisions elsewhere in the Nation can be a basis for denying preliminary relief Louisiana needs.

Second is a concern that the universal scope of a § 705 stay would run into "settled limits on equitable relief." Dist.Ct.Op.31–33. Four important points in response.

One, that chafes against this Court's precedents. This Court has held that "the scope of preliminary relief under Section 705 aligns with the scope of ultimate relief under Section 706, which is not party-restricted and allows a court to 'set aside' an unlawful agency action." *Career Colls. & Schs. of Tex. v. U.S. Dep't of Educ.*, 98 F.4th 220, 255 (5th Cir. 2024). That is why *Alliance I* and *Alliance II* upheld a universal § 705 stay.

Two, the district court's conflation (Dist.Ct.Op.32) of the *equitable* relief considered in *Trump v. CASA, Inc.*, 606 U.S. 831 (2025), with the *legal* relief provided by § 705 runs into the same problem. By its own terms, *CASA* expressly avoided the "distinct" question of vacatur under the APA. *CASA*, 606 U.S. at 847 n.10; Dist.Ct.ECF.20-26 at 17. Accordingly, *CASA* does not excuse the district court from applying this Court's own vacatur precedents.

Three, it is not Louisiana's fault that only a universal § 705 stay could remedy Louisiana's harm. Louisiana would be open to a Louisiana-

specific remedy—except that no one can figure out how to build one considering the indiscriminate, nationwide attacks from doctors and activists in pro-abortion states that FDA has facilitated. The court below directly addressed that issue, and the federal government threw up its hands. *See* Tr.53 (Q: "I asked plaintiffs' counsel if she could conceive of any remedy limited to the parties of this case, Rule 65 remedy. Can you think of any?" A: "We aren't proposing any narrowing of relief...." Q: "All right. I'm asking you: Can you think of any way, as a technical matter, to do that in this case?" A: "I can't, Your Honor.").

Because only a universal § 705 stay appears workable, the right answer is not to level down and deny Louisiana the relief it needs just because the relief would sweep more broadly. For all the district court's reliance on *CASA*, *CASA* squarely holds in the equity context that "courts generally 'may administer complete relief *between the parties*'" even if doing so happens to benefit others. 606 U.S. at 851–52 (using the example of ordering a neighbor to turn loud music down or off; that order "will necessarily benefit the defendant's surrounding neighbors too; there is no way 'to peel off just the portion of the nuisance that harmed the plaintiff'"). All the same here.

Four, it bears noting that none of this is relevant to the remaining preliminary-relief factors—the equities and public interest. This discussion at most goes to *scope* of relief, not whether Louisiana is *entitled* to relief. The district court thus erred multiple times over in citing this discussion to deny Louisiana preliminary relief.

3. Last and "most important[]" in the district court's view is that FDA is entitled to a stay because it says it is "review[ing]" the 2023 REMS. Dist.Ct.Op.35. The lower court held "the APA deficiencies [as] found by the Fifth Circuit"—that the 2023 REMS was based on inadequate data—somehow "prevent[ed]" it from issuing preliminary relief because "ultimately it is FDA, not this Court, that possesses the expertise to evaluate scientific evidence and make public health judgments." Dist.Ct.Op.33–34. The lower court was willing to overlook clear "evidence of ongoing harm owing to the 2023 REMS," because "FDA has acknowledged its own deficits and has initiated an ongoing review of mifepristone." *Id.* At bottom, the court concluded that "FDA's review should be conducted and completed free from judicial interference." Dist.Ct.Op.35.

This reasoning is badly mistaken. To start, it would allow the government to avoid preliminary review in *every* APA case. More, the question before the Court is legal not scientific: Is the 2023 REMS lawful? No amount of further study or agency action will change that answer (which this Court has twice answered in the negative). More fundamentally, it makes no sense to *deny* preliminary relief on the grounds that agency action is *so* unlawful that the agency openly concedes a review is necessary. That is the strongest point in favor of *granting* preliminary relief, not giving FDA a free pass to maintain a concededly unlawful regulation. In short, FDA's review cannot magically render the 2023 REMS lawful, nor does it provide grounds to refuse to set aside unlawful action as ensured by § 705.

CONCLUSION

The Court should stay the 2023 REMS under § 705 pending appeal or, alternatively, enjoin its enforcement pending appeal.

Respectfully submitted,

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CERTIFICATE OF SERVICE

I certify that on April 17, 2026, I filed the foregoing brief with the Court's CM/ECF system, which will automatically send an electronic notice of filing to all counsel of record.

/s/ J. Benjamin Aguiñaga
J. BENJAMIN AGUIÑAGA

CERTIFICATE OF COMPLIANCE

Pursuant to Fifth Circuit Rule 32.3, the undersigned certifies that this motion complies with:

(1) the type-volume limitations of Federal Rule of Appellate Procedure 27(d)(2) because it contains 5,199 words; and

(2) the typeface requirements of Rule 32(a)(5) and the type-style requirements of Rule 32(a)(6) because it has been prepared in a proportionally spaced typeface (14-point Century Schoolbook) using Microsoft Word 2016 (the same program used to calculate the word count).

/s/ J. Benjamin Aguiñaga
J. BENJAMIN AGUIÑAGA

Dated: April 17, 2026

EXHIBIT A

UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF LOUISIANA
LAFAYETTE DIVISION

THE STATE OF LOUISIANA, BY AND THROUGH ITS ATTORNEY GENERAL, LIZ MURRILL, AND ROSALIE MARKEZICH	**CIVIL DOCKET NO. 6:25-cv-01491**
VERSUS	**JUDGE DAVID C. JOSEPH**
U.S. FOOD AND DRUG ADMINISTRATION, ET AL	**MAGISTRATE JUDGE DAVID J. AYO**

MEMORANDUM RULING

This case was brought by the State of Louisiana and Louisiana resident Rosalie Markezich ("Plaintiffs") against the U.S. Food and Drug Administration ("FDA") and several related agency heads[1] (collectively, the "Government"), challenging the legality of FDA's 2023 agency action removing the in-person dispensing requirement for the abortion drug, mifepristone. Shortly after filing the lawsuit, Plaintiffs moved for preliminary injunctive relief, which was quickly followed by a flurry of motions by the Government and other parties in interest, including the drug's manufacturers, Danco Laboratories, LLC ("Danco") and GenBioPro, Inc. ("GenBioPro"). Also filed with the Court were twenty-two (22) amicus briefs authored by persons and organizations with a variety of viewpoints.[2]

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[1] The defendants in this matter are the U.S. Food and Drug Administration ("FDA"); Martin Makary, in his official capacity as Commissioner of Food and Drugs at FDA; George Francis Tidmarsh, in his official capacity as the Director of FDA's Center for Drug Evaluation and Research; the U.S. Department of Health and Human Services ("HHS"); and Robert F. Kennedy, Jr., in his official capacity as the Secretary of HHS.

[2] Amicus briefs were filed in support of the Plaintiffs' motion by the following entities: (i) Family Research Council and Martha Shuping, M.D. [Doc. 66]; (ii) Women Injured by

The Court heard oral argument on the pending motions on February 24, 2026, and at that time granted motions to intervene by the two drug manufacturers. [Docs. 52, 54, 229, 246]. Now before the Court for consideration are: (i) a MOTION FOR PRELIMINARY RELIEF UNDER 5 U.S.C. § 705 [Doc. 20] filed by Plaintiffs; (ii) a MOTION TO STAY THE CASE [Doc. 50] filed by the Government; (iii) a MOTION TO DISMISS [Doc. 230] filed by Intervenor-Defendant Danco; and (iv) a MOTION TO DISMISS [Doc. 232] filed by Intervenor-Defendant GenBioPro.[3]

Abortion, The Justice Foundation and its Center Against Forced Abortions, and the National Association of Christian Lawmakers [Doc. 92]; (iii) American Association of Pro-Life Obstetricians and Gynecologists and Samaritan's Purse [Doc. 96]; (iv) The American Center for Law and Justice [Doc. 99]; (v) Ethics and Public Policy Center [Doc. 101]; (vi) Women and Families Harmed by Mifepristone and Former Abortion Providers [Doc. 118]; (vii) Advancing American Freedom, Inc., et al [Doc. 123]; (viii) Concerned Women for America [Doc. 128]; (ix) Dr. Calum Miller [Doc. 130]; (x) Heartbeat International [Doc. 132]; (xi) Students for Life of America [Doc. 136]; (xii) Senator Bill Cassidy, M.D., Representative Christopher H. Smith, and 58 Members of Congress [Doc. 141]; and (xiii) the States of Nebraska, Alabama, Alaska, Arkansas, Georgia, Idaho, Indiana, Iowa, Kansas, Mississippi, Missouri, Montana, North Dakota, Ohio, Oklahoma, South Carolina, South Dakota, Texas, Utah, West Virginia, and Wyoming [Doc. 121].

Amicus briefs were filed in opposition to the Plaintiffs' Motion by the following entities: (i) IGH PLLC d/b/a Abortion on Demand, Hey Jane, and The Reproductive Health Initiative for Telehealth Equity & Solutions (RHITES) [Doc. 204]; (ii) National Domestic Violence Hotline and Legal Voice [Doc. 206]; (iii) Former Commissioners and Acting Commissioners of the U.S. Food and Drug Administration [Doc. 208]; (iv) the States of New York, Arizona, California, Colorado, Connecticut, Delaware, Hawaii, Illinois, Maine, Maryland, Massachusetts, Minnesota, Nevada, New Jersey, New Mexico, Oregon, Rhode Island, Vermont, Washington, and the District of Columbia filed an amicus brief in opposition to the Defendants' Motion to Stay [Doc. 210]; (v) Over 100 Reproductive Health, Rights, and Justice Organizations [Doc. 218]; (vi) Former U.S. Department of Justice Officials [Doc. 220]; (vii) Disability Rights Education and Defense Fund and Others [Doc. 222]; (viii) American College of Obstetricians & Gynecologists, et al [Doc. 224]; and (ix) Medical Students for Choice [Doc. 226].

[3] Plaintiffs' Motion for Preliminary Injunction is opposed by the Defendants [Doc. 51] and by the Intervenors [Docs. 230, 231], and Plaintiffs filed a single brief both in reply to the Defendants' opposition brief and in opposition to the Defendants' Motion to Stay [Doc. 111]. Plaintiffs oppose the Motions to Dismiss filed by Danco and GenBioPro [Doc. 253], and Danco and GenBioPro filed reply briefs [Docs. 256, 257, respectively].

After a review of the record and the complex regulatory and judicial history of this subject matter, the Court declines to grant the Plaintiffs § 705 relief at this time. The record shows that FDA is currently in the process of "conducting its own review of the evidence" with respect to the current Risk Evaluation and Mitigation Strategies ("REMS"), "to determine whether modifications are necessary." [Doc. 1-110]. And "courts owe significant deference to the politically accountable entities with the 'background, competence, and expertise to assess public health.'" *FDA v. Am. Coll. of Obstetricians & Gynecologists,* 141 S. Ct. 578, 578-79 (2021) (Roberts, C.J., concurring in grant of application for stay).

Indeed, given the information available – and, importantly, the dearth of information upon which FDA previously acted to significantly loosen safety restrictions for prescribing mifepristone – the equities and the public interest weigh heavily in favor of FDA completing the job that the law requires it to do. Put differently, at this juncture, it is the completion of FDA's promised good faith, evidence-based, and expeditious review of the mifepristone REMS, not "government by lawsuit," that this Court finds to be in the public interest. *See United States v. Texas*, 599 U.S. 670, 704 (2023) (Gorsuch, J., concurring).

The Motions to Dismiss filed by the drug manufacturers Danco and GenBioPro [Docs. 230, 232, respectively] move to dismiss on the bases that Plaintiffs: (i) lack Article III standing; (ii) are outside "zone of interests" of the APA and Comstock Act; (iii) have failed to exhaust their claims administratively pursuant to 21 C.F.R. § 10.45(b); (iv) have asserted claims not yet ripe for adjudication; and (v) that on the merits their claims fail to state a claim upon which relief can be granted. This ruling addresses the Intervenors' primary contention – the threshold jurisdictional issue of the Plaintiffs' standing to bring this action. But because the Court grants the Governments motion to stay this case pending completion of FDA's mifepristone REMS review, the Court declines to substantively address the remaining issues raised by Intervenors at this time. Intervenors may renew their Motions to Dismiss upon the Court's lifting of the stay.

For these reasons and as further detailed below, the Court finds that the Government's Motion to Stay the Case [Doc. 50] should be GRANTED. Plaintiffs' Motion for Preliminary Relief Under 5 U.S.C. § 705 [Doc. 20] is DENIED without prejudice to refiling upon the Court lifting the stay. Likewise, the two Motions to Dismiss filed by Intervenors [Docs. 230, 232] are DENIED without prejudice to refiling upon the Court lifting the stay. This action will remain STAYED until further order of the Court.

FACTUAL BACKGROUND AND PROCEDURAL HISTORY

I. Regulatory History of Mifepristone[4]

This case arises under the Federal Food, Drug, and Cosmetic Act, as amended, 21 U.S.C. ch. 9., the principal federal statute governing the regulation of food, drugs, medical devices, and cosmetics in the United States. The U.S. Department of Health and Human Services ("HHS") is charged with the responsibility for implementing that law and has delegated the obligation to FDA, its subagency. Under federal law, FDA is responsible for ensuring that drugs marketed in the United States are safe and effective.

To that end, a drug sponsor seeking approval – typically the manufacturer or prospective marketer – must submit an application to FDA demonstrating that the drug is safe and effective for its intended use. *Alliance IV*, 602 U.S. at 375, *citing* 21 U.S.C. § 355(d). The application must generally include proposed labeling that

[4] Although the Court provides herein a summary of the complex regulatory history pertinent to its ruling, a more exhaustive regulatory history is provided in *All. for Hippocratic Med. v. FDA*, 78 F.4th 210, 233 (5th Cir. 2023) ("*Alliance III*"), *rev'd and remanded sub nom., FDA v. All. for Hippocratic Med.,* 602 U.S. 367, 375 (2024) ("*Alliance IV*").

specifies, among other things, the drug's dosage, directions for use, and the specific conditions the drug is approved to treat. *Id.* at 375, *citing* 21 C.F.R. §§ 201.5, 314.50 (2022). FDA may also impose additional conditions on a drug's prescription and use when it finds that enhanced safety measures are necessary. *Id.*, *citing* 21 U.S.C. § 355-1(f)(3). Such conditions may include prescriber training, dispensing limitations, or patient-monitoring requirements. *Id.*

In 2000, FDA approved a new drug application for mifepristone tablets under its Subpart H regulations, 21 C.F.R. § 314.500. *Id.* This newly approved drug was marketed under the brand name Mifeprex and was used to terminate pregnancies through seven weeks of gestation (the "2000 Approval").[5] *Alliance IV*, 602 U.S. at 375. To help ensure that Mifeprex would be used safely and effectively, FDA placed further restrictions on the drug's use and distribution. *Id.* Among other requirements, only physicians were permitted to prescribe or supervise the prescription of Mifeprex, and patients were required to follow a regimen involving three in-person visits with a physician. *Id.* FDA also required prescribing physicians to report hospitalizations, blood transfusions, and other serious adverse events to the drug sponsor, which in turn was obligated to report those events to FDA. *Id.*

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[5] In 1992, FDA promulgated the "Subpart H" regulations, which permit the accelerated approval of drugs intended to treat serious or life-threatening illnesses based on evidence of meaningful therapeutic benefit. *See* 21 C.F.R. § 314.500. Recognizing that such approvals rest on an expedited evidentiary basis, Subpart H also authorized post-approval restrictions "to assure safe use." *Id.* § 314.520. Mifepristone was approved under this framework. In 2007, Congress codified and expanded these post-approval safety authorities by establishing Risk Evaluation and Mitigation Strategies (REMS), which are designed to ensure that a drug's benefits outweigh its risks. *See All. for Hippocratic Med. v. FDA,* 2023 WL 2913725, at *21 (5th Cir. Apr. 12, 2023) ("*Alliance II*"), *citing* 21 U.S.C. § 355-1 (a)(1)-(2).

In 2015, Mifeprex's distributor, Danco, submitted a supplemental new drug application seeking to amend Mifeprex's labeling and to relax some of the restrictions that FDA had imposed. *Id.* In 2016, FDA approved the proposed changes, which: (i) deemed Mifeprex safe to terminate pregnancies up to ten weeks rather than seven weeks; (ii) allowed healthcare providers such as nurse practitioners to prescribe Mifeprex; and (iii) approved a dosing regimen that reduced the number of required in-person visits from three to one. *Id.* at 375-76. In addition, FDA approved a change in the prescribers' adverse event reporting obligations to require prescribers to report only fatalities (collectively, the "2016 Amendments"). *Id.* at 376.

In April 2019, FDA approved an application for generic mifepristone, manufactured by GenBioPro (the "2019 Generic Application"). *Id.* FDA established the same conditions of use for generic mifepristone as for Mifeprex. *Id.* Then, in April 2021, at the height of the COVID-19 pandemic, FDA again relaxed the requirements for Mifeprex and generic mifepristone, announcing that it would temporarily "exercise enforcement discretion" to allow "dispensing mifepristone through the mail ... or through mail-order pharmacy" (the "2021 Nonenforcement Decision"). *Id.*

In January 2023, FDA issued its most recent REMS for mifepristone (the "2023 REMS"), which codified and refined prior changes, including, among other things: (i) the removal of an in-person dispensing requirement; (ii) permitting certified pharmacies to dispense mifepristone (including by mail); and (iii) otherwise continuing the post-2016 framework, including limited adverse-event reporting (primarily deaths). *Alliance III*, 78 F.4th at 247.

II. History of Mifepristone Litigation in the Fifth Circuit

In 2022, physicians providing pregnancy-related health care, including emergency care after unsuccessful medication abortions using mifepristone, and national organizations of such physicians, brought an action in a Texas district court under the Administrative Procedure Act ("APA") against FDA, HHS, and agency officials. *See All. for Hippocratic Med. v. FDA*, 668 F. Supp. 3d 507, 560 (N.D. Tex. Apr. 7, 2023) ("*Alliance I*"). These plaintiffs challenged both the lawfulness of FDA's initial approval of mifepristone (which had occurred more than 20 years earlier), and each post-approval action (at that time, the 2016 Amendments, 2019 Generic Approval, and 2021 Nonenforcement Decision). *Id.* After concluding that the plaintiffs had standing, the *Alliance I* district court entered a preliminary injunction staying the 2000 Approval of mifepristone and each of the subsequent agency actions – effectively removing the drug from the market pending a full trial on the merits. *Id.*

FDA and Danco appealed the injunction to the Fifth Circuit and asked for an emergency stay of the district court's order pending appeal. The Fifth Circuit granted a partial stay, temporarily reinstating FDA's original 2000 Approval of Mifeprex. *Alliance II*, 2023 WL 2913725, at *21. This partial stay permitted the drug to remain available only under the earlier, more restrictive conditions but left in place the district court's injunction as to later regulatory changes. *Id.* Specifically, the *Alliance II* court found that the plaintiffs were likely to succeed on the merits of their claims under 5 U.S.C. § 706(2)(A) in at least two respects. *Id.* at *17.

First, the *Alliance II* court determined that FDA had failed to examine the relevant data when adopting the 2016 Amendments – relying instead on data that included the very safeguards the 2016 REMS had therein dispensed with. *Id.* And second, in a similar vein, FDA thereafter relied on the absence of non-fatal adverse-event reports in FDA's Adverse Event Reporting System ("FAERS") after eliminating the requirement that such events even be reported. *Id.* As to the latter error, the Fifth Circuit pointedly explained that "[i]t's unreasonable for an agency to eliminate a reporting requirement for a thing and then use the resulting absence of data to support its decision." *Id.*

Thus, the Fifth Circuit concluded that the *Alliance* plaintiffs were likely to succeed on the merits of their APA challenges with respect to FDA's decisions beginning with the 2016 Amendments and "all subsequent actions." *Id.* at *17-21. Following the Fifth Circuit's partial stay, FDA and Danco sought a full stay from the United States Supreme Court, which they obtained, thereby preserving the current regulatory regime during the pendency of the appeal. *Danco Lab'ys, LLC v. All. for Hippocratic Med.*, 143 S. Ct. 1075 (2023).

Then, in August 2023, a different panel of the Fifth Circuit addressed the merits appeal of the *Alliance I* administrative stay and preliminary injunction. *See generally Alliance III*, 78 F.4th at 233. The merits panel agreed with the *Alliance II* court's determination that both the individual doctors and the plaintiff medical associations had Article III standing. And in assessing FDA's 2016 Amendments and the 2021 Nonenforcement Decision, the *Alliance III* court agreed that FDA had acted arbitrarily and capriciously and otherwise abused its discretion under 5 U.S.C.

§ 706(2)(A) when it, among other things: (i) failed to consider the cumulative effect of the 2016 Amendments; (ii) failed to consider whether it needed to continue to collect data of non-fatal adverse events in light of the "major" 2016 changes to the mifepristone REMS; (iii) gave dispositive weight in making the 2021 Non-Enforcement Decision to FAERS data that had been compromised by FDA's 2016 removal of non-fatal reporting requirements; and (iv) relied on literature that did not support its position in making the 2021 Nonenforcement Decision.[6] *Id.*

Specifically, the *Alliance III* court found that the studies underpinning FDA's approval of the 2016 Amendments failed to consider any data that cumulatively evaluated the effect of implementing each of its proposed "major" changes, which included:

> … increasing the maximum gestational age from forty-nine days to seventy days; allowing non-physicians to prescribe mifepristone; removing the requirement that the administration of misoprostol and the subsequent follow-up appointment be conducted in person; eliminating prescribers' obligation to report non-fatal adverse events; switching the method of administration for misoprostol from oral to buccal; and changing the dose of mifepristone (600 mg to 200 mg) and misoprostol (400 mcg to 800 mcg).

Id. at 246.

Instead, the *Alliance III* court found that the "FDA neither considered the effects as a whole, nor explained why it declined to do so[,]" even though FDA had acknowledged that "[t]he cumulative effect of the 2016 Amendments is

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[6] The merits panel disagreed with the district court's determination that plaintiffs were likely to succeed on their challenge to FDA's 2000 Approval of Mifeprex and 2019 Approval of generic mifepristone. *Id.* at 256. Accordingly, the Fifth Circuit vacated the district court's order as to those agency actions. *Id.*

unquestionably an important aspect of the problem[.]" *Id.* The court also determined that FDA's failure to consider whether it needed to continue to collect data of non-fatal adverse events in light of the "major" changes to the mifepristone REMS was likely arbitrary and capricious. *Id.* at 246-47.

As to the 2021 Nonenforcement decision (that was later formalized in the 2023 REMS at issue here), the *Alliance III* court found, in essence, that FDA had based its decision on the absence of data that it had only five years previously intentionally eliminated – finding that "considerable evidence shows that FAERS data is insufficient to draw general conclusions about adverse events." *Id.* at 249. The Court also found that FDA had "relied on various literature relating to remote prescription of mifepristone" in spite of "FDA's admission that the literature did not affirmatively support its position." *Id.* at 250.

In 2024, the Supreme Court reversed, finding that the *Alliance* plaintiffs lacked Article III standing to challenge FDA's regulatory actions. *Alliance IV*, 602 U.S. at 396-97. The Court explained that Article III's case-or-controversy requirement confines federal judicial power to actual "personal stake" injuries. And because the plaintiff doctors and physician associations did not prescribe, use, manufacture, sell, or otherwise face regulation stemming from FDA's actions, their asserted injuries were speculative and not fairly traceable to the challenged FDA actions. *Id.* at 385-86.

In so finding, the Court emphasized that sincere legal, moral, ideological, and policy objections to another's conduct – here, the prescription and use of mifepristone – standing alone, do not satisfy Article III's standing requirements. *Id.* at 396.

Accordingly, the Supreme Court reversed the Fifth Circuit and remanded for further proceedings consistent with its opinion. *Id.* at 397.

III. Recent Actions of FDA

Important to the Court's determination here, on September 19, 2025, undoubtedly aware of the mifepristone regulatory deficiencies identified by the Fifth Circuit in the *Alliance* cases, FDA agreed to undergo a thorough review of the mifepristone REMS. Specifically, in direct response to a letter sent to HHS by the Attorneys General of 22 states,[7] HHS Secretary Kennedy and FDA Commissioner Makary responded with a letter agreeing to conduct a comprehensive safety review of the mifepristone REMS, including the 2023 REMS at issue here. [Doc. 1-110].

In their letter, Secretary Kennedy and Commissioner Makary stated that, "[s]ince its original approval, the FDA has received reports of serious adverse events in patients who took mifepristone," and consequently, FDA's review would "study[] the adverse consequences reported in relation to mifepristone to ensure the REMS are sufficient to protect women from unstated risks." [*Id.*]. FDA premised this review on a frank acknowledgement of the "lack of adequate consideration underlying the prior REMS approvals" as well as "recent studies raising concerns about the safety of mifepristone as currently administered," including those that "indicate potential dangers that may attend offering mifepristone without sufficient medical support or supervision." [*Id.*]. The letter promised to ensure that FDA's analysis and any

[7] The letter, sent by Kansas Attorney General Kris Kobach and 21 other AGs on July 31, 2025, asked for a comprehensive review of mifepristone or, alternatively, a removal of the drug from the market pending additional safety testing.

resulting revisions to the mifepristone REMS would be "grounded in Gold Standard Science." [*Id.*]. Commissioner Makary publicly acknowledged that the review of mifepristone safety was underway as of January 2026.[8]

IV. The Instant Lawsuit

On October 6, 2025, the State of Louisiana and Rosalie Markezich filed the instant lawsuit, challenging FDA's January 2023 REMS, and particularly, the removal of the in-person dispensing requirement and authorization of dispensation of the drug by mail and telehealth.[9] Plaintiffs claimed injuries include: (i) harm to state sovereignty; (ii) increased Medicaid expenditures, including over $92,000 in 2025 emergency room and hospitalization costs from two mifepristone-induced abortions and projections of hundreds of thousands of dollars in similar costs; and (iii) public-health harms, including statistically-certain emergency room visits and risks of serious and sometimes fatal infections and bleeding. Plaintiffs seek preliminary relief to stay or set aside the 2023 REMS under 5 U.S.C. § 705, or an injunction mandating that FDA enforce mifepristone's previous in-person dispensing requirement. In response, the Government asks this Court to stay the litigation while FDA conducts its review of the mifepristone REMS.

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[8] *Questions and Answers on Mifepristone for Medical Termination of Pregnancy Through Ten Weeks Gestation,* FDA, https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/questions-and-answers-mifepristone-medical-termination-pregnancy-through-ten-weeks-gestation (last updated Feb. 2, 2026).

[9] Plaintiff Markezich alleges that in October 2023, her then-boyfriend used her email address to obtain mifepristone (and a second drug, misoprostol) from a physician in California via mail order. [Doc. 1, ¶ 10]. She alleges that she did not want to take the drug, was pressured by him, and that the result of taking the medication caused the termination of her pregnancy and ongoing distress and trauma. [*Id.*].

On February 24, 2026, the Court granted the Motions to Intervene filed by mifepristone manufacturers Danco and GenBioPro [Docs. 52 and 54, respectively], and thereafter, the Intervenors' Motions to Dismiss were filed into the record. [Docs. 230 and 232, respectively].

LAW AND ANALYSIS

I. Legal Standards

A. APA Standard of Review

The APA was designed by Congress to act as "a check upon administrators whose zeal might otherwise have carried them to excesses not contemplated in legislation creating their offices." *United States v. Morton Salt Co.*, 338 U.S. 632, 644 (1950). It requires federal courts to "hold unlawful and set aside agency action, findings, and conclusions found to be arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with the law." 5 U.S.C. § 706(2)(A). The standard set forth by the Fifth Circuit is clear:

> … [A]n agency must "examine the relevant data and articulate a satisfactory explanation for its action including a 'rational connection between the facts found and the choice made.'" An agency violates these rules where it "entirely fail[s] to consider an important aspect of the problem," or offers "an explanation for its decision that runs counter to the evidence before the agency, or is so implausible that it could not be ascribed to a difference in view or the product of agency expertise."

Alliance III, 78 F.4th at 245 (internal citations omitted).

To be sure, the arbitrary and capricious standard is narrow, and courts must be careful not to "substitute" their own "policy judgment for that of the agency." *FCC v. Prometheus Radio Project*, 592 U.S. 414, 423 (2021). But ultimately, Congress has vested federal courts with the responsibility to "ensure that the agency 'examined the

relevant data and articulated a satisfactory explanation for its action.'" *Sierra Club v. EPA*, 939 F.3d 649, 664 (5th Cir. 2019). And applying this standard, courts may vacate agency decisions containing "unexplained inconsistencies in the rulemaking record." *Id.*

If an agency's deliberative process falls short of the APA's requirements, Section 705 authorizes courts to stay an agency action while the action undergoes judicial review. 5 U.S.C. § 705. "In the same way that a preliminary injunction is the temporary form of a permanent injunction, a stay is the temporary form of vacatur." *Alliance III*, 78 F.4th at 254*, quoting Monsanto Co. v. Geerston Seed Farms*, 561 U.S. 139, 165 (2010).

B. Injunctive Relief Pursuant to 5 U.S.C. § 705

Here, Plaintiffs urge the Court in their Motion for Preliminary Relief to issue an order under § 705 of the APA, "staying or postponing the effective date of the [2023 REMS]." [Doc. 20]. Because "a stay [under the APA] has the practical effects of an injunction," the preliminary injunction factors applicable to Federal Rule of Civil Procedure 65 motions apply. *Alliance III*, 78 F.4th at 242*, citing* 28 U.S.C. § 1292(a) *and Alliance II*, 2023 WL 291375, at *3 n.3; *see also Colorado v. EPA*, 989 F.3d 874, 883 (10th Cir. 2021). "Injunctive relief is an extraordinary and drastic remedy, not to be granted routinely, but only when the movant, by a clear showing, carries the burden of persuasion." *Louisiana v. Biden*, 575 F. Supp. 3d 680, 691 (W.D. La. Dec. 16, 2021), *aff'd*, 55 F.4th 1017 (5th Cir. 2022), *citing Holland Am. Ins. Co. v. Succession of Roy*, 777 F.2d 992, 997 (5th Cir. 1985). "To be entitled to a preliminary injunction, a movant must establish: (1) a likelihood of success on the merits; (2) a

substantial threat of irreparable injury; (3) that the threatened injury if the injunction is denied outweighs any harm that will result if the injunction is granted; and (4) that the grant of an injunction will not disserve the public interest." *Id.* at 691, *quoting Ladd v. Livingston*, 777 F.3d 286, 288 (5th Cir. 2015); *Alliance III*, 78 F.4th at 241.

C. Motion to Stay

The above notwithstanding, a district court always retains the inherent authority to stay a proceeding "to control the disposition of the causes on its docket …." *Crimson Bldg. Co. v. Plutus Grp., LLC*, 2020 WL 13616911, at *1 (N.D. Tex. Feb. 24, 2020), *quoting United States v. Rainey*, 757 F.3d 234, 241 (5th Cir. 2014) (internal quotation marks omitted). In staying a case pursuant to this authority, the Court should "balance between the harm of moving forward [with the litigation] and the harm of holding back." *Ali v. Quarterman*, 607 F.3d 1046, 1049 (5th Cir. 2010). Additionally, the Court should consider whether a stay is warranted in light of activity in a related action and other "present day realities." *In re Beebe*, 1995 WL 337666, at *3-4 (5th Cir. May 15, 1995); *see also Landis v. N. Am. Co.*, 299 U.S. 248, 258 (1936).

As the Supreme Court has explained, "[e]specially in cases of extraordinary public moment, [a plaintiff] may be required to submit to delay not immoderate in extent and not oppressive in its consequences if the public welfare or convenience will thereby be promoted." *Clinton v. Jones*, 520 U.S. 681, 706-07 (1997), *citing Landis*, 299 U.S. at 256. And district courts regularly stay proceedings to allow an agency to pursue further action on the rulemaking at issue. *See, e.g., Town & Cnty. of*

Nantucket v. Burgum, 2025 WL 3120419, at *2 (D.D.C. 2025), *citing Code v. McHugh*, 139 F. Supp. 3d 465, 466 (D.D.C. 2015); *FBME Bank Ltd. v. Lew*, 142 F. Supp. 3d 70, 76 (D.D.C. 2015); *Sierra Club v. Van Antwerp*, 560 F. Supp. 2d 21, 26 (D.D.C. 2008).

II. Standing

As a threshold matter, the Court is first charged with the important jurisdictional task of determining whether the Plaintiffs have standing to challenge the 2023 REMS. As previously discussed, the *Alliance* litigation was ultimately dismissed by the Supreme Court for those plaintiffs' lack of standing to challenge the mifepristone REMS. *Alliance IV*, 602 U.S. at 396-97. And here, both the Government and Intervenors argue in their briefing that the Plaintiffs lack standing for their requested relief. [Docs. 51, 230, 231]. Intervenors Danco and GenBioPro also specifically seek dismissal of this action on that basis. [Docs. 230, 232].

The Court will therefore first carefully evaluate Plaintiffs' Article III standing. Standing is "built on a single basic idea – the idea of the separation of power." *Alliance IV*, 602 U.S. at 378. "Article III requires a plaintiff to show that she has suffered an injury-in-fact that is fairly traceable to the defendant's allegedly unlawful conduct and likely to be redressed by the requested relief." *Haaland v. Brackeen*, 599 U.S. 255, 291-92 (2023), *citing California v. Texas*, 593 U.S. 659, 668-69 (2021); *see also Lujan v. Defenders of Wildlife*, 504 U.S. 555, 560 (1992).

To establish standing, "a plaintiff must demonstrate: (i) that she has suffered or likely will suffer an injury-in-fact; (ii) that the injury likely was caused or will be caused by the defendant; and (iii) that the injury likely would be redressed by the requested judicial relief." *Texas v. United States*, 126 F.4th 392, 407 (5th Cir. 2025),

quoting Alliance IV, 602 U.S. at 380. "The second and third standing requirements – causation and redressability – are often 'flip sides of the same coin,'" meaning if "a defendant's action causes an injury, enjoining the action or awarding damages for the action will typically redress that injury. So the two key questions in most standing disputes are injury-in-fact and causation." *Texas*, 126 F.4th at 407, *quoting Alliance IV*, 602 U.S. at 380-81.

The Court is also cognizant that at earlier stages of litigation, such as in adjudicating a motion for injunctive relief, the manner and degree of evidence required to show standing may be less than at later stages. *Speech First, Inc. v. Fenves*, 979 F.3d 319, 329-30 (5th Cir. 2020), *as revised* (Oct. 30, 2020), *citing Lujan*, 504 U.S. at 561 ("each element [of standing] must be supported ... with the manner and degree of evidence required at the successive stages of the litigation"); s*ee also Barber v. Bryant*, 860 F.3d 345, 352 (5th Cir. 2017), *citing Lujan*, 504 U.S. at 561 ("Since they are not mere pleading requirements but rather an indispensable part of the plaintiff's case, each element must be supported ... with the manner and degree of evidence required at the successive stages of litigation."). Thus, at this stage, it is the Plaintiffs' burden to put forth facts establishing that they have standing to seek the requested § 705 relief.

Louisiana argues that it has standing both because: (i) the 2023 REMS causes sovereign harm by facilitating abortions that violate numerous Louisiana state

laws,[10] [Doc. 20-26, p. 24]; and (ii) it continues to suffer ongoing financial injury resulting from the 2023 REMS and has already paid hundreds of thousands of dollars through Louisiana Medicaid for emergency room medical care stemming from mifepristone use by residents. [*Id.*, p. 26]. In response, Defendants argue primarily that Louisiana lacks standing because it "do[es] not prescribe or use mifepristone" and the 2023 REMS Modification does not "require[] [Louisiana] to do anything or to refrain from doing anything" and the indirect causal chain between the REMS and Louisiana's alleged injury is too speculative or attenuated to establish standing. [Docs. 51, 230, 231]. Put another way, because Louisiana is not a regulated party, the Defendants allege that Louisiana is unable to establish traceability between

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[10] Louisiana prohibits all abortions except those that are determined to be medically necessary to prevent the death or substantial risk of death of the mother. *See* La. R.S. § 40:1061, La. R.S. § 14:87.7, and La. R.S. § 14:87.8.1.

Important here, Louisiana has also enacted a criminal prohibition on the prescribing and dispensing of mifepristone for purposes of inducing an abortion and classifies mifepristone as a Schedule IV controlled and dangerous substance under its drug laws. *See* La. R.S. § 14:87.1(2)(a) ("'Abortion-inducing drug' means any drug or chemical, or any combination of drugs or chemicals, or any other substance when used with the intent to cause an abortion."); La. R.S. § 40:964.

And if those criminal prohibitions were not clear, Louisiana's longstanding policy, enacted into statute, states, in part:

> It is the intention of the Legislature of Louisiana to regulate, prohibit, or restrict abortion to the fullest extent permitted by the decisions of the Supreme Court of the United States. The legislature does solemnly declare, find, and reaffirm the longstanding public policy of this state that every unborn child is a human being from the moment of conception and is, therefore, a legal person for purposes under the laws of this state and Constitution of Louisiana.

La. R.S. § 40:1061.1 (A)(1).

Louisiana's claimed sovereign and financial injuries and FDA's promulgation of the 2023 REMS. [*Id*].

Although the Supreme Court has observed that establishing standing is "ordinarily substantially more difficult" for unregulated parties – particularly where causation rests on "the unfettered choices of independent actors" – it has also made clear that standing may exist where such actors predictably respond to the challenged action. *Lujan*, 504 U.S. at 560-61; *see also California*, 593 U.S. at 675*, citing Dep't of Com v. New York*, 588 U.S. 752, 768 (2019). The Fifth Circuit treats this inquiry as part of the traceability analysis, not injury-in-fact. *See Reule v. Jackson*, 114 F.4th 360, 367 (5th Cir. 2024), *cert. denied*, 145 S. Ct. 1431 (2025). Thus, even where injury is undisputed, standing fails if the causal chain is too speculative. *Alliance IV*, 602 U.S. at 383.

As previously discussed, in *Alliance IV*, the Supreme Court dismissed for lack of standing where the plaintiff doctors and medical associations had no direct involvement with mifepristone, no cognizable economic injury, and no obligation to participate in abortion care, rendering any causal chain to FDA's actions too speculative. 602 U.S. at 385-86, 393-94. In the same vein, the Government attempts to distinguish this Court's standing analysis in *Louisiana v. EEOC*, 784 F. Supp. 3d 886 (W.D. La. 2025), arguing that, unlike the regulatory mandate there, the 2023 REMS imposes no obligations on the State. The Government further argues that any Medicaid-based economic harm is too attenuated.

After careful consideration, the Court finds that Defendants' arguments fall short at this stage. Here, the evidence in the record shows that the "independent

actors" – that is, the out-of-state medical providers prescribing mifepristone via telemedicine or mail – responded to the 2023 REMS by expanding mifepristone access to pro-life states like Louisiana in ways that were entirely predictable. On July 8, 2022, then-President Biden issued Executive Order 14076,[11] which expressly sought to protect and expand access to "*healthcare service delivery* and promote access to critical reproductive healthcare services, including abortion" in the wake of *Dobbs*. [Doc. 1-45, pp. 2-3] (emphasis added). And in a "Factsheet" issued by the White House

[11] Section 1 of EO 14076, enacted just one week after the *Dobbs* decision was issued, is entitled "Policy" and states:

> Nearly 50 years ago, *Roe* v. *Wade,* 410 U.S. 113 (1973), articulated the United States Constitution's protection of women's fundamental right to make reproductive healthcare decisions. These deeply private decisions should not be subject to government interference. Yet today, fundamental rights — to privacy, autonomy, freedom, and equality — have been denied to millions of women across the country.
>
> Eliminating the right recognized in *Roe* has already had and will continue to have devastating implications for women's health and public health more broadly. Access to reproductive healthcare services is now threatened for millions of Americans, and especially for those who live in States that are banning or severely restricting abortion care. Women's health clinics are being forced to close — including clinics that offer other preventive healthcare services such as contraception — leaving many communities without access to critical reproductive healthcare services. Women seeking abortion care — especially those in low-income, rural, and other underserved communities — now have to travel to jurisdictions where services remain legal notwithstanding the cost or risks.
>
> *In the face of this health crisis, the Federal Government is taking action to protect healthcare service delivery and promote access to critical reproductive healthcare services, including abortion.* It remains the policy of my Administration to support women's right to choose and to protect and defend reproductive rights. Doing so is essential to justice, equality, and our health, safety, and progress as a Nation.

Exec. Order No. 14,076, 88 Fed. Reg. 42,831 (July 7, 2023) (emphasis added).

on April 12, 2023, the administration touted, among other things, actions taken by FDA to "protect[] access to [abortion] care nationwide." [Doc. 1-60].

Thus, in that post-*Dobbs* regulatory environment, there is evidence that the 2023 REMS was approved without adequate consideration, at least in part, as part of an effort to circumvent anti-abortion states' ability to regulate abortion. Likewise, there is evidence that the consequences of this action were predictable – out-of-state providers and related entities would expand access to mifepristone in ways designed to reach into jurisdictions like Louisiana. These actions cause concrete and ongoing injury to Louisiana, as further discussed below.

But first, Louisiana's claimed injury must be put within the appropriate framework. The Constitution's Supremacy Clause declares that federal laws "shall be the supreme law of the land" when conflicting with state laws. U.S. CONST. art. VI, cl. 2. This includes the Food, Drug, and Cosmetic Act, 21 U.S.C. § 301, *et seq.*, and the resulting authority vested in FDA to approve and regulate drugs. Nevertheless, respect for the federal nature of our government is also paramount – "a system in which … the National Government, anxious though it may be to vindicate and protect federal rights and federal interests, always endeavors to do so in ways that will not unduly interfere with the legitimate activities of the [states]." *Younger v. Harris*, 401 U.S. 37, 44 (1971). The Supreme Court has consistently considered federalism concerns when, for example, determining the reach of federal law. *See, e.g., Sackett v. EPA*, 598 U.S. 651, 683 (2023); *U.S. Forest Serv. v. Cowpasture River Pres. Ass'n*, 590 U.S. 604, 621 (2020).

Here, Louisiana alleges that an unlawful use of federal regulatory power by an administrative agency directly undermines the enforcement of its own laws and forces it to incur additional costs.[12] *See Texas v. United States*, 809 F.3d 134, 153 (5th Cir. 2015) ("States have a sovereign interest in the power to create and enforce a legal code."). Of course, if this Court or others ultimately determine that FDA acted lawfully in its removal of the in-person dispensing requirement for mifepristone, then Louisiana would have no judicial recourse under the APA.[13] After all, this would directly implicate the Constitution's Supremacy Clause and the power vested by Congress in FDA to regulate drugs. U.S. CONST. art. VI, cl. 2; *see also GenBioPro, Inc.*, 144 F.4th at 273 (4th Cir. 2025) (finding that although state law determines whether "abortion may be performed at all," federal law "permits the FDA to regulate how mifepristone must be prescribed and dispensed *if and when* a medication abortion is performed.").

On the other hand, if FDA did not act lawfully under the APA but rather exceeded or abused the power vested in it by Congress as Plaintiffs contend, then Louisiana clearly has an interest in vindicating its sovereign prerogative under basic principles of federalism. And the Fifth Circuit has twice indicated in *Alliance II* and *Alliance III* that FDA was likely arbitrary and capricious under the APA in removing

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[12] *See supra* note 10.

[13] For the avoidance of doubt, this does not mean that medical providers would then be free to ignore the laws of the states in which they prescribe mifepristone without fear of criminal prosecution. As recently put by the Fourth Circuit Court of Appeals, "the text of the [Food, Drug and Cosmetic Act] suggests that Congress intended to create a regulatory floor, not a ceiling" on drug regulation by the states. *GenBioPro, Inc. v. Raynes*, 144 F.4th 258, 274 (4th Cir. 2025). But that issue is not before the Court here.

mifepristone's in-person dispensing requirement. *Alliance II*, 2023 WL 2913725, at *17; *Alliance III*, 78 F.4th at 241-48.

To be sure, there are factors other than the 2023 REMS that influence the arrival of mifepristone in Louisiana. For example, some states have enacted "shield laws" to protect medical practitioners in their states from extradition for prescribing and illegally shipping mifepristone into jurisdictions where it has been prohibited. *See generally What Are Shield Laws?*, CTR. FOR REPROD. RTS., (Oct. 9, 2025), https://reproductiverights.org/resources/what-are-shield-laws/; *see also, e.g.,* CAL. PENAL CODE § 847.5(b)-(c). There are also the usual practical and investigatory impediments faced by state law enforcement when engaging in drug interdiction efforts. And these may be even more significant than the 2023 REMS in influencing the accessibility of mifepristone to Louisiana residents. But there can be little doubt that the 2023 REMS is a factor, which is all that is required for Louisiana to show injury-in-fact and traceability. *See Texas v. United States*, 50 F.4th 498, 519 (5th Cir. 2022) ("DACA is not the sole cause of the State's injury, but DACA has exacerbated it. That is sufficient."). Thus, even if the 2023 REMS is not the "sole cause" of Louisiana's sovereign harms, it has surely "exacerbated" them; "that is sufficient" for standing to assert its claims. *Id.*

Furthermore, "[m]onetary costs are of course an injury" for standing purposes. *Texas*, 599 U.S. at 676. And "even one dollar's worth of harm is traditionally enough to" confer standing. *Id.* at 688 (Gorsuch, J., concurring). A state's increased medical costs, such as increased Medicaid costs due to a federal agency action, can constitute

a "pocket-book injury" sufficient to satisfy the injury-in-fact requirement of standing. *Texas v. United States*, 126 F.4th 392, 411 n.22 (5th Cir. 2025) (collecting cases).

Here, Louisiana has put forth sufficient evidence to demonstrate that it has suffered and continues to suffer pocketbook injury. Under the federal Medicaid statute, Louisiana is required to cover medical assistance for eligible pregnant women, which includes inpatient and outpatient medical services. 42 U.S.C. §§ 1396(a)(viii), (a)(1)-(2). Louisiana is required to pay a portion of the total Medicaid costs, *id.* § 1396a(a)(2), and the federal government will pay between 50 percent and 83 percent, *id.* § 1396d(b). Crucially, FDA's "own documents" show that "emergency room care is statistically certain" in mifepristone cases. *Alliance II*, 2023 WL 2913725, at *10. And according to FDA's own 2023 label, 2.9-4.6 percent of women who receive an in-person visit with a doctor, are prescribed mifepristone, and take it as directed will require an emergency room visit. [Doc. 1-9, p. 9]. Empirical evidence indicates that the emergency room visitation and hospitalization rate may be closer to ten percent for patients with an estimated gestational duration of 78-84 days. [Doc. 1-13, p. 2]; [Doc. 20-4, p. 2].[14] And rates may also be higher when mifepristone is dispensed by mail. [Doc. 1-10, pp. 34-35].

Plaintiffs further estimate that, on average, about 1,000 mifepristone-induced abortions are occurring per month in Louisiana. [Doc. 20-2, p. 36]; [Doc. 20-22, pp. 1-2]. And, according to Plaintiffs' expert, many of these women obtaining abortions are likely to be on Medicaid. [Doc. 20-22, pp. 2-3]. In support of this

[14] *See* https://www.contraceptionjournal.org/article/S0010-7824(25)00308-7/abstract for the complete study.

contention, Plaintiffs have supplied evidence from the Louisiana Department of Health identifying more than $92,000 in Medicaid costs incurred for emergency room care and hospitalizations required because of two mifepristone-induced abortions in 2025 in which the drugs were received from out-of-state prescribers. [Doc. 20-20, pp. 4-5, ¶¶ 11-12]. These two incidents alone are sufficient to establish Louisiana's standing, but it is likely that many more Medicaid patients have required similar care due to complications from mifepristone. [*Id.*, pp. 4-5, ¶¶ 10, 13-15]; [Doc. 20-19, pp. 3-4, ¶¶ 7-8]; [Doc. 20-23, p. 4, ¶¶ 14-16].

And regardless of whether Louisiana's financial harm is the $92,000 previously discussed or far more than that, Louisiana's harm is more than zero. *See Texas*, 50 F.4th at 517-18 ("The record does not indicate precisely what portion of all costs for illegal aliens is spent on DACA recipients, but no one disputes that some are."). Accordingly, because "even one dollar's worth of harm" is sufficient, Louisiana has put forth sufficient evidence to demonstrate a substantial likelihood of success in proving it has suffered financial injury for standing purposes. *Texas*, 599 U.S. at 688 (Gorsuch, J., concurring).

For all of these reasons, Louisiana has established injury that is traceable to FDA's actions and redressable, at least in part, by the relief requested herein. Louisiana therefore has standing to challenge the 2023 REMS on the record before the Court.[15]

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[15] Because the Court determines that the State of Louisiana has standing, it need not consider standing for Markezich. *Biden v. Nebraska*, 600 U.S. 477, 489 (2023) ("If at least one plaintiff has standing, the suit may proceed."), *citing Rumsfeld v. Forum for Acad. & Institutional Rts., Inc.*, 547 U.S. 47, 52 n.2 (2006).

III. Analysis Under Rule 65

With standing established for these purposes, the Court next considers whether Plaintiffs have carried their burden under the Rule 65 framework applicable to the Plaintiffs' requested § 705 relief.[16]

A. Likelihood of Success on the Merits

"The exact quantum of evidence that a plaintiff must present to satisfy the likelihood-of-success factor varies from case to case." *League of United Latin Am. Citizens v. Abbott*, 809 F. Supp. 3d 502, 546 (W.D. Tex. 2025), *citing Jefferson Cmty. Health Care Ctrs., Inc. v. Jefferson Par. Gov't*, 849 F.3d 615, 626 (5th Cir. 2017) ("[T]here is no particular degree of likelihood of success that is required in every case. …"). "The Fifth Circuit applies a 'sliding scale' approach, whereby a plaintiff who makes a strong showing on the other three preliminary injunction factors bears a lesser burden on the likelihood-of-success requirement (and vice versa)." *Id.*, *citing TitleMax of Texas, Inc v. City of Dallas*, 142 F.4th 322, 328 (5th Cir. 2025). Thus, "[w]here the other factors are strong," the movant need only show "some likelihood of success on the merits" to obtain a preliminary injunction. *Id.*

As discussed above, in *Alliance III*, the Fifth Circuit found that FDA, in promulgating the 2021 Nonenforcement Decision, had based its decision on the absence of data that it had only five years previously intentionally eliminated – finding that "considerable evidence shows that FAERS data is insufficient to draw

[16] The Plaintiffs do not squarely address in their briefing the application of the Rule 65 factors as they apply to Plaintiff Markezich. The Court therefore limits its analysis to Plaintiff Louisiana.

general conclusions about adverse events." *Alliance III*, 78 F.4th at 249. The Court also found that FDA had "relied on various literature relating to remote prescription of mifepristone – despite FDA's admission that the literature did not affirmatively support its position." *Id.* at 250.

To be sure, the 2023 REMS had not yet been put into effect when suit was filed in *Alliance I*. Therefore, those plaintiffs did not specifically challenge the 2023 REMS, as the Plaintiffs do here. But the Fifth Circuit's analysis in *Alliance III* found fault with both the 2016 Amendments and the 2021 Nonenforcement Decision – and included in its discussion that "in January 2023, FDA amended mifepristone's REMS … formalizing the change" rendered in the 2021 Nonenforcement Decision. *Id.* at 247. Likewise, in rejecting a mootness challenge by FDA, the *Alliance III* court described the 2023 REMS as merely a "final form of a previous, identical policy," removing mifepristone's in-person dispensing requirement. *Id.* at 248-49.

Accordingly, Plaintiffs' challenge to the 2023 REMS focuses on the very same failure to engage in reasoned decision-making under the APA when FDA modified the mifepristone regulatory regime. *Id.* at 245, 255. And the Supreme Court, in vacating the Fifth Circuit's opinion in *Alliance III*, addressed only those plaintiffs' lack of Article III standing to bring an APA challenge. *Alliance IV*, 602 U.S. at 396-97. The *Alliance III* court's reasoning is therefore due strong consideration in weighing Plaintiffs' likelihood of success on the merits.

Further, HHS Secretary Kennedy and FDA Commissioner Makary essentially acknowledged APA procedural deficits with respect to mifepristone in their September 19, 2025, letter, stating that FDA's intention to review the mifepristone

regulatory framework was precipitated by "the lack of adequate consideration underlying the prior REMS approvals" and recent safety concerns. [Doc. 1-110]. Thus, the Court concludes that Plaintiffs are likely to succeed on the merits of their 2023 REMS challenge.

B. Irreparable Injury

The Court has already found that Louisiana demonstrated an injury-in-fact, and those same facts establish irreparable harm. An irreparable harm is one that has "no adequate remedy at law." *Louisiana v. Biden*, 55 F.4th 1017, 1033-34 (5th Cir. 2022). Here, the 2023 REMS operates, arguably, in derogation of Louisiana law and interferes with Louisiana's ability to enforce its laws and implement the policy choices of its citizens. *Louisiana v. EEOC*, 705 F. Supp. 3d 643, 653 (W.D. La. 2024).

No remedy at law can redress that sovereign harm. By permitting medical providers to prescribe mifepristone remotely, the 2023 REMS facilitates the distribution of mifepristone into Louisiana notwithstanding contrary law. Louisiana suffers sovereign harm each time those laws are circumvented. And Louisiana has also demonstrated financial injury that cannot be "remedied where, as here, the defendant is entitled to sovereign immunity." *Alliance III*, 78 F.4th at 251.

C. Balance of Harms/Public Interest

No one disputes that "[a]bortion presents a profound moral issue." *Dobbs*, 597 U.S. at 223; s*ee also Alliance IV*, 602 U.S. at 376, 396 (noting both the longstanding controversy surrounding mifepristone and plaintiffs' "sincere legal, moral, ideological, and policy objections"). But this Court is not a forum for resolving moral or policy disagreements. Its task is to apply established legal standards to the record

before it. That inquiry turns on legally cognizable harms to the parties and the public interest, not on the weight of competing moral views. And where, as here, the issues implicate scientific and medical judgments committed by Congress to an agency with specialized knowledge, that limitation carries particular force.

Having previously discussed the ongoing harm suffered by Plaintiff Louisiana, the Court starts its analysis by looking at the interests of the Government. First, the Court notes that "anytime the Government is enjoined … 'it suffers a form of irreparable injury.'" *Alliance III*, 78 F.4th at 251, *quoting Maryland v. King*, 567 U.S. 1301, 1303 (2012) (Roberts, C.J., in chambers). Specific to this matter, FDA is charged with implementing federal statutes governing the safety and efficacy of drugs through an evidence-based administrative rule-making process. *Alliance IV*, 602 U.S. at 374-75.

In carrying out that mandate, the agency evaluates scientific and clinical data, makes factual findings based on the administrative record, and, where appropriate, considers public comments. *See Weinberger v. Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609, 617 (1973) (explaining that FDA approval requires adequate, well-controlled clinical investigations by qualified experts, not anecdotal or uncontrolled data). The agency must also "articulate a satisfactory explanation for its action including a rational connection between the facts found and the choice made." *Motor Vehicle Mfrs. Ass'n of the United States, Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983). This science-based regime derives from and is limited to the confines of its Congressional mandate.

And FDA, being a component of the Executive Branch, operates as an agency ultimately accountable to the President. The public interest in the proper function of FDA and its scientifically grounded, congressionally authorized protocol is substantial. The Intervenors also have a substantial financial interest in this matter. Any change in the current regulatory regime governing the prescription of mifepristone, which has now been in place for five years, would affect their profit margins and compliance costs.

No doubt Louisiana has a great interest in this issue as well. *Dobbs* returned the issue of abortion to the people of the States and their elected representatives, including regulation of abortion methods, procedures, and the use of related drugs. 597 U.S. at 302. The 2023 REMS clearly facilitates easier access to mifepristone for Louisiana residents. But the Court must also take into consideration that any interim relief ordered by this Court would not relieve Louisiana of its duty to enforce its own laws. In practice, even with the remedy requested herein, mifepristone would likely continue to reach those who seek it, as our country's decades of experience with the war on illegal drugs clearly and painfully demonstrates.[17] Meanwhile, Louisiana retains many meaningful, boots-on-the-ground law enforcement mechanisms to mitigate its sovereign and financial harms while FDA completes its ongoing review.

The Court next turns to the public interest and begins with the premise, as recognized by the *Alliance III* court, that "[t]here is generally no public interest in the

[17] In 2025, for instance, cocaine production reached record levels despite fifty-five years of counter-narcotics enforcement efforts by the United States and other nations. *World Drug Report 2025*, UNITED NATIONS OFF. ON DRUGS & CRIME (June 13, 2025).

perpetuation of unlawful agency action." *Louisiana,* 55 F.4th at 1035. But the Court also notes that the Supreme Court fully stayed the preliminary injunction issued by the *Alliance I* district court, as affirmed in part by the Fifth Circuit in *Alliance II*, (including its injunction of the 2021 Nonenforcement Decision). *Danco Lab'ys, LLC*, 143 S. Ct. 1075. This effectively allowed the challenged FDA actions with respect to mifepristone to continue throughout the course of the appeal. And, of course, that injunction was ultimately vacated for lack of standing. *Alliance IV*, 602 U.S. at 396-97.

Here, unlike in the *Alliance* cases, FDA does not defend its decision-making on the merits but instead acknowledges deficits and requests a stay to complete a fulsome review of the merits of Plaintiffs' claims – a review that was announced before this lawsuit was filed and has already been initiated. [Doc. 1-110]. FDA also has the authority to take interim actions to ensure drug safety if new information is discovered during the pendency of its review. *See generally* [Doc. 250].

Also weighing on its analysis is the Court's understanding that this case arises amid multiple parallel lawsuits across the country addressing the same regulatory issues surrounding access to mifepristone, creating a substantial risk of inconsistent judicial outcomes on a question of nationwide importance.[18] Although not styled as

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[18] *See Mifepristone Litigation and Federal Action Tracker*, UCLA LAW CTR. ON REPROD. HEALTH, LAW, & POLICY (last updated Apr. 2026), https://law.ucla.edu/academics/centers/center-reproductive-health-law-and-policy/mifepristone-litigation-and-federal-action-tracker.

At the time of the parties' briefing, five other states are challenging either the approval of mifepristone or subsequent actions easing restrictions. *See Missouri v. FDA*, No. 4:25-cv-1580-CMS (E.D. Mo.) (Missouri, Idaho, and Kansas challenging actions easing REMS restrictions); *Florida v. FDA*, No. 7:25-cv-126-O (N.D. Tex.) (Florida and Texas challenging

a universal injunction, the relief sought by Plaintiffs would, as a practical matter, have a nationwide effect. As the Supreme Court recently observed, such sweeping relief creates asymmetry because a plaintiff "must win just one suit to secure sweeping relief," whereas the Government "must win everywhere" to avoid it. *Trump v. CASA, Inc.*, 606 U.S. 831, 855 (2025). It also risks "rushed, high-stakes, [and] low-information" decision-making in consequential cases. *Id.* at 855-56, *quoting Labrador v. Poe ex rel. Poe*, 144 S. Ct. 921, 927 (2024) (Gorsuch, J., concurring).

These concerns are reinforced by settled limits on equitable relief, which require that remedies be tailored to the plaintiff's injury and may not be "more burdensome … than necessary." *Texas*, 599 U.S. at 702 (Gorsuch, J., concurring), *quoting Califano v. Yamasaki*, 442 U.S. 682, 702 (1979) (internal quotation marks omitted). "Faithful application of those principles suggests that an extraordinary remedy like vacatur would demand truly extraordinary circumstances to justify it." *Id.* at 702 (Gorsuch, J., concurring).

This is because, like "universal injunctions, vacatur can stymie the orderly review of important questions, lead to forum shopping … and facilitate efforts to evade the APA's normal rulemaking processes." *Id.* at 703 (Gorsuch, J., concurring). "Vacatur can also sweep up nonparties who may not wish to receive the benefit of the

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approval of mifepristone and actions easing REMS restrictions). Other plaintiffs have challenged FDA's restrictions as too burdensome. *See Purcell v. Kennedy*, 2025 WL 3101785 (D. Haw. Oct. 30, 2025) (finding that FDA violated the APA by failing to provide a reasoned explanation for its burdensome conditions on the prescription of mifepristone, which that court determined appeared to be unwarranted relative to the drug's safety); *Washington v. FDA*, No. 1:23-cv-3026-TOR, 2025 WL 1888794 (E.D. Wash. 2025) (plaintiffs challenge REMS as too restrictive); *Whole Woman's Health All. v. FDA*, No. 3:23-cv-19 (W.D. Va.) (same). This list does not include a multitude of citizen petitions.

court's decision," which, here, would include the 18 states and other amici that filed briefs urging denial of Plaintiffs' Motion. *Id.* (Gorsuch, J., concurring); *see also, e.g., supra* note 2. As a result, vacatur improperly applied, "strains our separation of powers" because "it exaggerates the role of the Judiciary in our constitutional order, allowing individual judges to act more like a legislature by decreeing the rights and duties of people nationwide." *Id.* (Gorsuch, J., concurring). All told, although federal courts are vested with much authority, the Constitution does not establish, nor does this Court condone, "government by lawsuit." *Id.* at 704, *quoting* ROBERT H. JACKSON, THE STRUGGLE FOR JUDICIAL SUPREMACY 286-87 (1941).

Next, the Court finds it appropriate to look at the substance of the alleged deficiencies pointed to by Plaintiffs in weighing the equities of issuing interim relief. No doubt, the State has shown evidence of ongoing harm owing to the 2023 REMS. But the APA deficiencies pointed to by the Plaintiffs and found by the Fifth Circuit in *Alliance III* show only that the 2023 REMS was "taken without sufficient consideration of the effects those changes would have on patients" due to a lack of underlying data. *Alliance III*, 78 F.4th at 253. Those same deficiencies likewise prevent this Court from determining whether FDA's in-person dispensing requirement is scientifically necessary to ensure mifepristone is "safe" and "effective." *Id.* at 245; *see also* 21 U.S.C. § 355(b)(1)(i).

On the one hand, a proper science-driven evaluation may lead FDA to conclude that the in-person dispensing requirement is necessary to comply with FDA's mandate to ensure that mifepristone is "safe and effective" for use, 21 U.S.C. § 355(b)(1)(i), and Plaintiffs offer substantial evidence supporting that possibility. On

the other hand, FDA may determine, after a thorough and scientifically-driven process, that such a requirement is not required. This Court is ill-equipped to make this determination, particularly where FDA has thus far failed to even collect the data necessary to comply with the APA's requirement that it "examine the relevant data and articulate a satisfactory explanation for its action including a 'rational connection between the facts found and the choice made.'" *Alliance III*, 78 F.4th at 245, *quoting Motor Vehicle Mfrs.*, 463 U.S. at 43. And ultimately it is FDA, not this Court, that possesses the expertise to evaluate scientific evidence and make public health judgments.[19]

At bottom, the APA does not charge the judiciary with the task of supplanting the role of federal agencies in promulgating regulations. *See Prometheus Radio Project*, 592 U.S. at 423. Rather, it is quite simply meant to be "a check" upon administrators to ensure that they are doing their job as directed by Congress. *Morton Salt Co.*, 338 U.S. at 644 (1950). Here, FDA has acknowledged its own deficits and has initiated an ongoing review of mifepristone.

Finally, this Court finds that prudence in issuing injunctive relief is warranted here because the 2023 REMS has governed a nationally integrated regulatory scheme

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[19] *See, e.g.*, *FDA,* 141 S. Ct. at 578-79 (Roberts, C.J., concurring in grant of application for stay) ("[C]ourts owe significant deference to the politically accountable entities with the 'background, competence, and expertise to assess public health.'"); *Cytori Therapeutics, Inc.* v. *Food & Drug Admin.*, 715 F.3d 922, 927 (D.C. Cir. 2013) (Kavanaugh, J.) ("A court is ill-equipped to second-guess that kind of agency scientific judgment under the guise of the APA's arbitrary and capricious standard."); *Otsuka Pharm. Co.* v. *Burwell*, 302 F. Supp. 3d 375, 403 (D.D.C. 2016) (Jackson, J.) ("To begin with, the FDA is an expert agency charged with making precisely these sorts of highly technical determinations, and its interpretation … is premised on 'the agency's evaluations of scientific data within its area of expertise.'"), *aff'd sub nom. Otsuka Pharm. Co.* v. *Price*, 869 F.3d 987 (D.C. Cir. 2017).

for five years (since the promulgation of the 2021 Nonenforcement Decision), and imposing sweeping relief now risks the "patchwork" of judicial remedy the Court has warned against. *CASA*, 606 U.S. at 872 (Kavanaugh, J., concurring). There are now at least five other lawsuits in federal courts around the nation addressing issues similar to those before the Court. *See supra* note 18. And again, FDA's ongoing review of the mifepristone REMS indicates both responsiveness to Congress's directive that drugs be "safe and effective," 21 U.S.C. § 355, as well as accountability to the public. *See DHS v. Regents of the Univ. of California*, 591 U.S. 1, 16 (2020), *quoting Franklin v. Massachusetts*, 505 U.S. 788, 796 (1992) ("The APA 'sets forth the procedures by which federal agencies are accountable to the public and their actions subject to review by the courts.'"). FDA's review should be conducted and completed free from judicial interference.

Therefore, for the reasons discussed, the Court declines to grant the Plaintiffs § 705 relief at this time. Given the length of time the 2023 REMS has been in effect, reliance interests on that scheme throughout the nation, the sweeping effect any remedy would have across states with differing abortion laws, and most importantly, FDA's recognition of its own shortcomings in regulating mifepristone and ongoing fulsome review of the mifepristone REMS, the Court will afford the agency a time-limited period of deference to complete its review and carry out the responsibilities assigned to it by Congress. This case will therefore be stayed.

But the stay granted to FDA will not remain open-ended. FDA has an obligation to act with all deliberate speed to review its past actions and complete a thorough analysis that addresses the deficiencies it has acknowledged. The parties

and the American public deserve nothing less. Should the agency fail to complete its review and make any necessary revisions to the REMS within a reasonable timeframe, the Court's analysis – and the weight accorded to these factors – will inevitably change.

CONCLUSION

Considering the foregoing,

IT IS HEREBY ORDERED that Defendants' MOTION TO STAY THE CASE [Doc. 50] is GRANTED, and this matter is STAYED pending completion of FDA's ongoing review of the mifepristone REMS and issuance of any resulting agency decision.

IT IS FURTHER ORDERED that Plaintiffs' MOTION FOR PRELIMINARY RELIEF UNDER 5 U.S.C. § 705 [Doc. 20] is DENIED WITHOUT PREJUDICE and with permission to refile, as appropriate, following completion of FDA's review or upon a lifting of the stay upon a material change in circumstances.

IT IS FURTHER ORDERED, pursuant to Plaintiffs' request at the motions hearing on February 24, 2026, that FDA produce the entirety of the administrative record to Plaintiffs' counsel within sixty (60) days.

IT IS FURTHER ORDERED that Danco's MOTION TO DISMISS [Doc. 230] and GenBioPro's MOTION TO DISMISS [Doc. 232] are hereby DENIED WITHOUT PREJUDICE and with permission to refile, as appropriate, following completion of FDA's review or upon a lifting of the stay upon a material change in circumstances.

IT IS FURTHER ORDERED that FDA shall file a report on or before six (6) months from the date of this Order providing the Court with the status of its review in terms of process and any updated timeframe for completion of review. Within

fourteen (14) days after FDA completes its REMS review, FDA shall file a brief advising the Court of any agency action and proposing a schedule for further proceedings, if necessary.

THUS, DONE AND SIGNED in Chambers on this 7th day of April 2026.

DAVID C. JOSEPH
UNITED STATES DISTRICT JUDGE

EXHIBIT B

09:29:03

UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF LOUISIANA
LAFAYETTE DIVISION

****

STATE OF LOUISIANA ET AL	CASE NO. 6:25-cv-01491
VERSUS	JUDGE DAVID C. JOSEPH
U.S. FOOD & DRUG ADMINISTRATION ET AL	MAGISTRATE JUDGE DAVID J. AYO

****

TRANSCRIPT OF MOTION HEARING PROCEEDINGS
HEARD BEFORE THE HONORABLE DAVID C. JOSEPH
UNITED STATES DISTRICT JUDGE
FEBRUARY 24, 2026

APPEARANCES:

FOR THE PLAINTIFF STATE OF LOUISIANA AND ROSALIE MARKEZICH:	LA DEPARTMENT OF JUSTICE 1885 N. Third Street Baton Rouge, LA 70802 (BY: J. BENJAMIN AGUINAGA, Esquire) (BY: CAITLIN A. HUETTEMANN, Esquire) ALLIANCE DEFENDING FREEDOM 44180 Riverside Parkway Lansdowne, VA 20176 (BY: ERIN M. HAWLEY, Esquire)
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FOR THE MOVANT DANCO LABORATORIES LLC:	HOGAN LOVELLS 555 13th Street NW Washington, DC 20004 (BY: ALEXANDER V. SVERDLOV, Esquire) (BY: JESSICA L. ELLSWORTH, Esquire) MOST & ASSOCIATES 201 St. Charles Avenue Suite 2500 #9685 New Orleans, LA 70170 (BY: WILLIAM B. MOST, Esquire)

APPEARANCES:

FOR THE MOVANT GENBIOPRO INC.:	ARNOLD & PORTER 601 Massachusetts Avenue NW Washington, DC 20001 (BY: DAPHNE O'CONNOR, Esquire) (BY: ROBERT J. KATERBERG, Esquire)
	ADCOCK LAW 8131 Oak Street Unit 100 New Orleans, LA 70118 (BY: JOHN N. ADCOCK, Esquire)
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PROCEEDINGS RECORDED BY MECHANICAL STENOGRAPHY. TRANSCRIPT PRODUCED BY COMPUTER.

COURT PROCEEDINGS

(Court is called to order.)

THE COURT: Thank you. Please be seated.

Okay. Good morning, everybody. We're on the record now in 25-cv-1491, *State of Louisiana versus The Food & Drug Administration.*

Counsel, please make your appearances.

MR. AGUINAGA: Good morning, Your Honor. Benjamin Aguinaga on behalf of the State.

THE COURT: Good morning.

MS. HAWLEY: Good morning, Your Honor. Erin Morrow Hawley on behalf of the State and Ms. Markezich.

MS. MURRILL: Good morning, Your Honor. Liz Murrill, Attorney General for the State of Louisiana.

THE COURT: Good morning to each of you.

MR. BAPTIST: Good morning, Your Honor. Erik Baptist on behalf of the State of Louisiana and Ms. Markezich.

MS. MCINTYRE: Good morning, Your Honor. Gabriella McIntyre on behalf of the State and Ms. Markezich.

MS. HUETTEMANN: Good morning, Your Honor. Caitlin Huettemann on behalf of the State of Louisiana.

MR. FAIRCLOTH: Good morning, Your Honor. Zach Faircloth on behalf of the State.

MR. BASGALL: Good morning, Your Honor. Frank Basgall on behalf of the State and Ms. Markezich.

10:00:54 **MR. KATZEN:** Good morning, Your Honor. Noah Katzen on
10:00:56 behalf of federal defendants.
10:00:58 **THE COURT:** You're all by yourself, Mr. Katzen?
10:01:00 **MR. KATZEN:** All by myself.
10:01:06 **THE COURT:** Okay.
10:01:06 **MS. ELLSWORTH:** Good morning, Your Honor. Jessica
10:01:06 Ellsworth on behalf of Danco Laboratories.
10:01:11 **MS. SVERDLOV:** Good morning, Your Honor. Alexander
10:01:11 Sverdlov on behalf of Danco Laboratories.
10:01:15 **MR. MOST:** William Most for the same plaintiff -- for the
10:01:17 same party. Thank you.
10:01:21 **MR. KATERBURG:** Good morning, Your Honor. Robert
10:01:22 Katerberg for intervener defendant GenBioPro.
10:01:22 **MS. O'CONNOR:** Good morning, Your Honor. Daphne O'Connor
10:01:22 on behalf of GenBioPro.
10:01:26 **MR. ADCOCK:** Good morning. John Adcock on behalf of the
10:01:29 intervener GenBioPro.
10:01:29 **THE COURT:** Good morning to each of you, as well. I
10:01:32 think the way we should proceed today -- we're here on plaintiffs'
10:01:36 motion for a preliminary injunction of the 2023 REMS. We have two
10:01:42 proposed interveners who have filed motions to intervene. My
10:01:47 understanding is that those motions are not opposed; is that
10:01:51 correct?
10:01:51 **MR. AGUINAGA:** That's correct, Your Honor.
10:01:52 **MR. KATZEN:** That's correct.

10:01:54 **THE COURT:** And that's as of right? That's a motion to
10:01:58 intervene as a right because they have a financial interest in the
10:02:02 litigation?
10:02:02 **MR. AGUINAGA:** That's correct, Your Honor.
10:02:03 **MR. KATZEN:** We have taken no position on that.
10:02:06 **THE COURT:** I think so. Because I think that they have a
10:02:10 right to intervene, I will allow them time today to address the
10:02:15 preliminary injunction. So I think the way we're going to proceed
10:02:20 is I will allow the plaintiffs 30 minutes to present their case. I
10:02:24 understand you're going to split your time. Is that right, Mr.
10:02:28 Aguinaga?
10:02:28 **MR. AGUINAGA:** That's correct, Your Honor.
10:02:31 **THE COURT:** And then the defendants will have -- well, is
10:02:33 20 minutes enough for you?
10:02:36 **MR. KATZEN:** I believe it should be, Your Honor.
10:02:37 **THE COURT:** Okay. And then 20 minutes for the --
10:02:39 collectively among the interveners, split however you would like to
10:02:42 do so, and then ten minutes for rebuttal by the plaintiffs because
10:02:47 the plaintiffs have the burden of proof. Does that sound
10:02:49 reasonable to everybody?
10:02:49 **MR. AGUINAGA:** Sounds good.
10:02:50 **THE COURT:** No one has to use all of their time. With
10:02:55 that, I think we should proceed. Please proceed, Mr. Aguinaga.
10:03:03 **MR. AGUINAGA:** Well, thank you, Judge Joseph, and may it
10:03:06 please the Court. Benjamin Aguinaga on behalf of the State.

10:03:10 As we explained and as we've just discussed, I'm going to try to open the first half of the 30 minutes on Article III standing, and then my colleague Ms. Hawley will address the remaining preliminary relief and stay factors.

I begin with Article III standing because we do think that in light of the Fifth Circuit's *Alliance* decisions that Article III standing is really the ultimate question in this case. That question is whether we, as plaintiffs, have standing to sue. We do, and I think the best way to approach that issue is to start with three points of common ground that I understand to be common ground among the parties:

One is there is no dispute that approximately a thousand abortions are occurring every month in Louisiana by mail-order drugs;

Two, there is no dispute that each of those abortions is an independent violation of Louisiana law, which is sort of the classic sovereign harm;

And three, there's no dispute that flowing from each of those abortions are classic pocketbook injuries that the State is suffering.

I think those are facts that we can start with just in terms of the Article III standing analysis, and that's why I think the analysis itself becomes so easy, because the next question is: Well, is there an injury in fact? And as I take the other side to dispute, really the dispute comes down to causation and

redressability, not really whether these pocketbook injuries and the violations of our laws are classic pocketbook injuries in fact and classic sovereign harms. So I think the injury in fact question in this case is actually quite straightforward because nobody really raises a strong argument otherwise. And so I think ultimately, at the end of the day, what you've got is a question about whether the 2023 REMS is the cause of those harms. And that's where you get to Step 2 of the standing analysis.

As we lay out in the reply brief, Your Honor --

THE COURT: Traceability.

MR. AGUINAGA: Traceability, Your Honor.

As we lay out in the reply brief, I do think the way to frame that question is the way the Court, the Supreme Court in the *Alliance* case framed it, which is to say traceability and redressability are flip sides of the same coin. At the end of the day, what you're asking is: Would granting the plaintiffs the relief they seek -- here, ultimately vacatur of the 2023 REMS -- redress the harm that they are asserting as the injury in fact at Step 1 of the standing analysis? And that I think is where page 117 of the Supreme Court's *Diamond Alternative Energy* opinion comes into play because that's the page where the Court says: If by design a regulation is intended to produce an effect, then ordinarily that means that vacating that regulation will have the effect of reducing the intended effect.

And that's squarely on point here because if the

10:05:50 1 historical record is clear about anything, it is that when
10:05:52 2 President Biden saw the *Dobbs* decision come down, the same day he
10:05:56 3 issued a directive to all of his agency heads to say: Find me a
10:05:59 4 way to send mail order mifepristone into states that are now
10:06:04 5 attempting to restrict and ban abortion. That, I think, is what
10:06:08 6 makes this case an easy one for standing.
10:06:10 7 You know, the *Diamond* case is helpful in a lot of ways.
10:06:13 8 One of the ways it's helpful is it repeats the common line in the
10:06:15 9 Supreme Court's cases that say that courts and parties often make
10:06:18 10 the standing analysis more difficult than it has to be. This is
10:06:21 11 one of those cases because we've got a clear historical record that
10:06:26 12 the valid purpose of the 2023 REMS and removing the in-person
10:06:30 13 dispensing requirement is to produce exactly the injuries that we
10:06:34 14 are suffering today. That, I think, sets aside all of the parade
10:06:38 15 of horribles that you see from the other side on if you find
10:06:41 16 standing for us in this case, then every state has standing to
10:06:44 17 challenge every agency action in the future. Most, if not all, of
10:06:48 18 those cases are going to fail at the standing stage because they
10:06:51 19 don't have the historical record.
10:06:54 20 And I will slow down -- I'm so sorry -- for the court
10:06:54 21 reporter.
10:06:55 22 They don't have the historical record that we have in
10:06:59 23 this case. And that's, I think, something that is undisputed
10:07:03 24 because, of course, those words came from the President himself and
10:07:06 25 from his Secretary of Health and Human Services. And that's, I

10:07:10 think, why you see parties like GenBioPro coming in and trying to
10:07:15 rewrite that historical record. Because once you accept what those
10:07:18 statements say on their face, once you accept as fact the intended
10:07:22 consequences that we're suffering today of the 2023 REMS, then this
10:07:26 is basically *Diamond* itself. This is *Monsanto*. We're the alfalfa
10:07:32 farmers in *Monsanto* who say: We don't want genetically modified
10:07:37 alfalfa from the farm next door intruding into our farms where
10:07:38 we're trying to grow alfalfa that is pure.
10:07:43 That's exactly what we've done here. We closed our
10:07:44 market to abortion altogether. That includes mail-order abortion
10:07:48 drugs. And yet, because of the 2023 REMS, you see a thousand
10:07:53 abortions a month occurring in the state.
10:07:56 That's why we think this case is straightforward on
10:07:59 standing, Your Honor. And I think at the end of the day, at this
10:08:01 preliminary stage, what we're asking you to do is enter relief that
10:08:05 would redress that injury, which is exactly the same relief that
10:08:10 the *Alliance* two Fifth Circuit panel recognized was appropriate,
10:08:12 which is a stay of the REMS. And what the Fifth Circuit said in
10:08:18 *Alliance* two is that a stay of the REMS means that the in-person
10:08:19 dispensing requirement would remain in effect. And there is no
10:08:22 argument on the other side that that would not redress our
10:08:25 injuries.
10:08:26 In a way, Your Honor, I think the best amici in this case
10:08:29 are actually FDA's amici because what they tell you with one voice
10:08:34 is that if you grant us the relief we request, then mifepristone

10:08:38 cannot be mailed. And lo and behold, that's exactly what redress
10:08:43 our harm, which is the mailing of mifepristone into the state.
10:08:46 Let me start -- let me end, actually, with just one thing
10:08:49 about chain of causation, because there's a line in the
10:08:52 Government's brief that says that the State is not in the chain.
10:08:56 And I think that's a reference to the *Diamond* case which referred
10:09:00 to basically a manufacturing chain, a product that would go through
10:09:04 a manufacturing chain. The chain that the Supreme Court was
10:09:07 referring to in *Diamond* and that it referred to in *Alliance* -- if
10:09:12 you look at page -- or, like, around page 385 of *Alliance*, what the
10:09:15 Supreme Court was referring to is a chain of predictable events.
10:09:20 What *Alliance* says -- the Supreme Court says, is a
10:09:22 plaintiff has to show a chain of predictable events starting with
10:09:26 the Government action and ending with the asserted injury. And if
10:09:31 there's anything clear about what's happened here is that not just
10:09:34 the predictable effects, but the intended effects of the 2023 REMS
10:09:39 have played out exactly how they were intended to play out. Like,
10:09:42 this is just a textbook -- like, a textbook example of predictable
10:09:46 chain of events because we know, in fact, that they have occurred.
10:09:50 Your Honor, that's standing. We don't think there is a
10:09:54 difficult question there. And I think, you know, once you resolve
10:09:56 that question, then the Fifth Circuit has decided all the other
10:09:59 questions.
10:10:00 And at this point, unless the Court has questions about
10:10:02 standing, I'm happy to invite my colleague Ms. Hawley up to talk

about the remaining factors.

THE COURT: On standing -- in this case, because of the regulatory history, we don't know how many medication abortions would occur in Louisiana if not for the 2023 REMS because before that, you had the 2021 COVID relief, allowing for mailing of this drug; 2022 *Dobbs* happened; 2023 this regulation came out, as you say, in response to the *Dobbs* decision. So we don't know how many would occur if not for this 2023 REMS; correct?

MR. AGUINAGA: Not with scientific certainty, Your Honor. What we do know -- and if you haven't had a chance to look at the #WeCount PowerPoint slides --

THE COURT: Seen it.

MR. AGUINAGA: Yeah. The chart spikes, right, after *Dobbs.* Now, of course, I think the compilation of those numbers began in earnest after *Dobbs* because then everybody realized we need to assess how effective the 2023 REMS is in actually injecting mail-order drugs into those states that ban abortion. So I think that's part of the reason why you see the spike in those charts.

And at least at this point, as I say, I don't think there is any dispute among the parties that that data, the best available data we've got says at least a thousand abortions a month in the state. And to be clear, Your Honor, I think this is a difficult case insofar as what you see from states like New York and California are overt attempts to conceal what's happening so that when we get a drug within our state -- and I don't know if you have

10:11:31 seen the pill bottles. We have seen the pill bottles that don't
10:11:36 have a doctor's name, don't have a pharmacy name, don't have a
10:11:39 practice name. The only thing we know is, like, a FedEx shipping
10:11:43 label from California. That's what shows up in our state.
10:11:44 And so it's going to be very, very difficult to come up
10:11:45 with firmer evidence about the rate of abortions in states like
10:11:49 Louisiana. So that's why I think we lean so heavily on that
10:11:53 #WeCount data because that is abortion providers' own data that
10:11:57 they're submitting to that organization, and that's really the best
10:12:01 we've got to go on. And I think the good thing for us, at least at
10:12:04 this preliminary stage, is nobody disputes that that number is a
10:12:09 fact.
10:12:09 **THE COURT:** Would you agree that if the Court were to
10:12:11 grant a preliminary injunction, as you request, that it would not
10:12:16 solve the problem with this drug being sent into Louisiana? Do you
10:12:22 agree there would still be that drug being sent into Louisiana?
10:12:25 **MR. AGUINAGA:** Well, Your Honor, I think there is
10:12:26 certainly a possibility that a bad actor in California could say,
10:12:32 "Notwithstanding the reinstatement of the federal in-person
10:12:36 dispensing requirement, I'm going to violate my certifications to
10:12:39 the manufacturers or whomever and still send the drug into the
10:12:42 state." That's certainly a possibility.
10:12:44 What the Supreme Court said in *Department of Commerce*
10:12:46 *versus New York* is that traditionally you don't base the Article
10:12:51 III standing analysis on speculation about future unlawful

10:12:55 behavior. And so I think that's always going it to be a
10:12:58 possibility, but at the end of the day, the burden we have is to
10:13:01 show that it would at least partially alleviate our injury. And I
10:13:03 think that's why it referenced FDA's amici. Everybody's saying,
10:13:06 like, the world is going to fall if we can't mail mifepristone.
10:13:11 Well, if that's what everybody understands to be the natural
10:13:14 consequence of the relief we're seeking, then that, for sure, is at
10:13:16 least partial relief, if not total relief, Your Honor.
10:13:18 **THE COURT:** Yeah. There would still be demand in the
10:13:21 state; right? There would still be the same demand? These drugs
10:13:24 are being mailed at the request of Louisiana citizens; right?
10:13:28 **MR. AGUINAGA:** Allegedly, Your Honor. And, again, a lot
10:13:29 of this is anonymous. Yes, anybody in Louisiana can go on that
10:13:34 website, like aidaccess.org, fill out a five-minute form, and
10:13:38 request drugs to be mailed to a Louisiana address. So no doubt
10:13:40 that can continue to happen. The question is: Is there at least a
10:13:45 plausible argument that removing the in-person dispensing
10:13:49 requirement will at least stop some of that activity, if not all of
10:13:51 it? And I think what you see from everybody in this case is, like,
10:13:53 yes, that is the natural consequence of the relief we're seeking.
10:13:56 **THE COURT:** I mean, the war on drugs has been going on 50
10:13:59 years now, and just this past year there's more cocaine produced
10:14:02 than any year before. Okay?
10:14:04 **MR. AGUINAGA:** Yeah. No doubt, Your Honor. No doubt.
10:14:06 **THE COURT:** If there's a demand, there's going to be

supply. That's the point. So I mean, I'm not directly contesting what you're saying here, that it might ameliorate some of the, at least, obvious violation of Louisiana law; but I don't know that ultimately it would make any difference.

MR. AGUINAGA: Well, I think it will make a difference, Your Honor, and that's why you should take groups like the ACLU at their word. We've given you that quote in the reply brief, where everybody knows on the other side of the aisle in this case that if the in-person dispensing requirement is back in place, then if not eliminating the problem entirely, it will at least eliminate the bulk of the problem, which is the actors in states like California and New York who are attempting to send mifepristone into the state.

And just think about it, Judge Joseph. I mean, I think -- you know, I cited to you the *Department of Commerce versus New York* case that says you don't speculate about future unlawful activity. I mean, think about the rationale that --

THE COURT: It's already unlawful activity. It's already unlawful activity. The doctors that are shipping it already know that they're violating Louisiana law when they do it.

MR. AGUINAGA: That's correct. Under state law, it's unlawful, Your Honor. The reason they think they can do it with impunity is because they're doing it from states that have, themselves, enacted these so-called shield laws that try to immunize them from state law liability. They don't have immunity

10:15:29 from federal liability. And what we're talking about here when
10:15:31 we're talking about the in-person dispensing requirement is the
10:15:34 requirement that they have to certify to their manufacturers, to
10:15:38 the drug manufacturers and others, that they are complying with
10:15:41 that requirement. If they can't certify that or if they certify
10:15:45 that and break their oath, then what they're doing is basically
10:15:49 placing their own practice in jeopardy. And that's what I think is
10:15:52 more than sufficient for standing purposes here.

10:15:55 **THE COURT:** And I don't know who wants to address this
10:15:57 issue, because I do have questions about remedy, and then also, I
10:16:00 guess, one question that deals primarily with standing. What
10:16:04 efforts, other than this lawsuit, is Louisiana taking to try to
10:16:08 interdict these drugs? What other efforts are going on? Because,
10:16:11 I mean, we have a direct comparison. You know, this country has
10:16:16 banned certain substances, both by state and at the federal level,
10:16:21 for many, many years; and there are techniques that have been
10:16:25 developed by the DEA, the FBI, all other manner of law enforcement
10:16:29 agencies to try to interdict these drugs and prohibit them from
10:16:35 coming into the state. What else is Louisiana doing besides this
10:16:38 lawsuit? Because, again, I think there's -- you know, it may
10:16:40 change the method; but ultimately, if the demand is there, it's not
10:16:43 going to change the result.

10:16:45 **MR. AGUINAGA:** Your Honor, respectfully, if it were not
10:16:46 going to change the result, then nobody would care about this case.
10:16:49 You wouldn't see like millions of amicus briefs being filed in the

docket. I think that's a tell that this case matters, and it matters to the State, and it matters to the parties, and it matters to the people outside who are participating as amicus.

THE COURT: I certainly think there's lots of vested interest in this issue and there has been ever since *Roe v. Wade*.

MR. AGUINAGA: For sure. And to answer your question directly, so all those drug interdiction efforts where you've got federal and state collaboration, it must be nice to be able to work with the federal government hand in hand to combat a drug problem within your state. We don't have that luxury. What we do have, and what we've tried so far -- and you can see this in the Toner Declaration as well as our complaint, is we have identified a couple of names of doctors who are repeat offenders in the state. We have issued arrest warrants for them, indicted them, have extradition requests out for them, and we're going to pursue those avenues, as well. At the end of the day, because there are so many bad actors, that sort of technique is not going to solve our problem across the board. And that's why I think this case is so important, because when you talk about chain of causation and traceability, doesn't it make sense to start with the very first logical step in the analysis, which is: What is the first cause of this harm? It's the 2023 REMS taking away that requirement. If it had never done that, then prescribers in California and New York could have never been able to lawfully under federal law send mifepristone into the state.

10:18:13 **THE COURT:** As far as remedy, who wants to address
10:18:16 remedy?
10:18:16 **MR. AGUINAGA:** I'm happy to talk about it. I know Ms.
10:18:20 Hawley is primed for it, too. Why don't I defer to her.
10:18:25 **THE COURT:** All right.
10:18:26 **MR. AGUINAGA:** Thank you, Your Honor.
10:18:28 **MS. HAWLEY:** Thank you, Your Honor. May it please the
10:18:36 Court.
10:18:38 FDA does not defend the 2023 REMS on the merits. It
10:18:44 instead concedes that the 2023 REMS were, quote, informed by a lack
10:18:49 of adequate consideration that necessitates a new review. That
10:18:55 lack of adequate consideration is what caused two separate Fifth
10:18:59 Circuit panels to conclude that the 2023 REMS were inadequate,
10:19:04 defective, and deeply troubling. Those REMS remain so today.
10:19:10 Louisiana is entitled to preliminary relief because there
10:19:13 is no question it has a likelihood of success on the merits. As my
10:19:18 colleague explained, it's also suffering irreparable harm. Each
10:19:21 and every day, Louisiana gets flooded with mifepristone crossing
10:19:25 state lines, endangering women who are forced to take a black box
10:19:31 drug all alone without ever seeing a doctor who might advise them
10:19:35 if they have an ectopic pregnancy or are further along in their
10:19:39 gestational age than they thought. It takes the lives of tens of
10:19:41 thousands of unborn Louisiana children. It injures the State's
10:19:46 sovereign interest. Louisiana's pro-life law, it's democratically
10:19:49 pro-life law is basically unenforceable after the 2023 REMS, and it

causes unquestionable economic harm every time a woman harmed by mifepristone enters a Louisiana emergency room.

As the Fifth Circuit held in *Alliance*, there simply is no public interest. Neither the public nor the FDA have an interest in an unlawful regulation by an agency, nor is there a public interest in an especially risky drug being on the market without adequate protections.

With respect to the FDA's -- what it looked at in 2023, it looked at primarily two sources of information. One is the FAERS data. It called that data unreliable on its own website. I would point Your Honor to ECF 1-52, pages 3 and 5. On those pages, it says that the FAERS data cannot be used to assess the safety profile of a drug. It goes on to say that the FAERS data cannot be used to calculate the incidents of an adverse event. That's precisely what FDA used that data for in 2023. That's at ECF 1-50, 64. It looked at the time period before, with enforcement and without. It compared those data. That's precisely the prohibited purpose.

Now, GenBioPro and Danco attempt to wave away the problem with the FAERS data by pointing to their own requirement as sponsors to report adverse events. The problem with that analysis, Your Honor, is that the abortion providers have the exact same responsibility to report that data to sponsors as they do to FDA. That's precisely zero. That's why Commissioner Makary recently called self-reporting data in mifepristone, quote, not very good.

10:21:33 The reason is, when you have self-reported data a lot of the data
10:21:36 is not going to be recovered.
10:21:38 In fact, in the *Alliance* decision, the Fifth Circuit
10:21:41 quotes a doctor's testimony, saying that it takes at least 30
10:21:45 minutes to file every FAERS report. She tries to do it routinely.
10:21:50 There's a 48-page document that explains how to file a FAERS
10:21:54 report. It takes these doctors inordinate amounts of time. No one
10:21:59 does them.
10:22:00 And to be honest, Professor -- or, excuse me,
10:22:00 Commissioner Makary's statement saying the data is not really very
10:22:04 good is probably a vast understatement. In the time period the FDA
10:22:08 looked at from January 2020 to September 2021, there were only 8
10:22:13 cases identified by the FAERS data. That was the same data that
10:22:16 the sponsors identified. And if you look at Table 2 of the current
10:22:21 FDA label, you will see that there should have been at least 20,000
10:22:25 women who went to the emergency room after taking mifepristone.
10:22:29 This would be nationwide. These would be adverse events. But we
10:22:33 get 8 cases. The idea that that's a reliable indicator of adverse
10:22:40 events is simply laughable.
10:22:42 The second thing, and I'll hurry along here, Your Honor,
10:22:45 that the FDA looked at was the literature review. At 180 of ECF
10:22:52 1-50 it called that data, quote, not adequate on its own to justify
10:22:56 removing the safety protections. Instead it said that it was
10:22:58 merely not inconsistent with the FDA's apparently predetermined
10:23:03 conclusion that taking away mifepristone -- or the in-person visit

for mifepristone was safe. That's why the Fifth Circuit in two different panels called reliance on that literature unreasonable.

The last thing I'll note with respect to the literature, Your Honor, is that the problems with the FAERS data were of the FDA's own making. As the stay panel noted, in 2016 FDA took away the requirement that abortion providers report adverse events. In 2021 and 2023, it then relied on that absence of data to find the drug safe.

THE COURT: The stay panel, you're talking about the second procuring opinion by the Fifth Circuit?

MS. HAWLEY: The first --

THE COURT: *Alliance* one? Or *Alliance* two?

MS. HAWLEY: *Alliance* one, Your Honor, yes. And that said, it was basically an ostrich's head in the sand approach to first say: You don't need to report data, and then since there's no data, we're going to find it safe.

THE COURT: Right.

MS. HAWLEY: Your Honor, I believe, had some questions about remedy.

THE COURT: Right. Well, thank you. And first -- I do have a question about remedy, but first, a couple of points.

So what percentage, on average, of Medicaid does the State pay?

MS. HAWLEY: So I'm not sure. My colleague might know that, but the reality is that under cases like *Uzuegbunam* and

10:24:24 others, a single dollar of expense is enough for standing purposes.
10:24:28 There are many women on Medicaid in Louisiana, and there are
10:24:34 specific examples in the record. The State has paid out tens of
10:24:38 thousands of dollars in only two documented cases.
10:24:42 **THE COURT:** Right. And a lot of that is federal money,
10:24:44 is my point.
10:24:45 **MS. HAWLEY:** Certainly, some of it is. I'm not specific
10:24:47 of the proportion. I'm sure my colleague will know that, but a
10:24:51 substantial portion is paid by Louisiana. And, again, Your Honor,
10:24:54 as you know, a dollar is enough for standing purposes.
10:24:59 **THE COURT:** So here, let's talk about the remedy that the
10:25:02 State is asking for. There are seven other cases, by my count,
10:25:07 pending in federal court dealing with this drug and the authorized
10:25:13 use of this drug. Is there a way that you could see to limit any
10:25:16 relief just to the parties of this case?
10:25:19 **MS. HAWLEY:** So I don't think so, Your Honor, for two
10:25:21 reasons. One, we think Section 705 of the Administrative Procedure
10:25:27 Act is directing relief against the agency action. Of course, the
10:25:32 text of that statute says to postpone the effective date.
10:25:36 **THE COURT:** Right. I think the statute is written in the
10:25:39 anticipation that it's filed before the regulation comes in effect.
10:25:43 I mean, that's clearly what the drafters intended.
10:25:46 **MS. HAWLEY:** I don't think that's true, Your Honor,
10:25:49 because if you look at Section 705, it's addressed in two parts.
10:25:52 One part is addressed to the agency, and the agency can stay its

own process before it comes into play; but the Court is instead empowered to provide any appropriate and necessary relief to stay the effective date.

As the Fifth Circuit said in *White Lions*, as well as *Alliance*, it doesn't matter whether the effective date has passed because there's the power in Section 05 [SIC] to stay in order to preserve status or rights.

The Government and intervener suggest that the status quo is the situation on the ground now. That's simply untrue. Again, under cases like *White Lions*, *Alliance*, *Texas versus EPA*, even going all the way back to the Supreme Court's decision in *Ken*, what has been clear is the status quo -- even Wright & Miller says that the status quo was the last uncontested state of affairs. So the status quo is what was in place before the contested agency action.

So it's clear under the text of Section 705 that this Court is empowered to put in place a stay, as happened in *Texas versus EPA*, it's happened in *White Lion*, it's happened in *Alliance* to stay that effective date.

THE COURT: Let's not talk about what the Court is empowered to do. Let's talk about what the Court should do in light of the seven other cases around the country that are pending that may result in conflicting injunctions.

MS. HAWLEY: Certainly, Your Honor. So two responses to that. So one, to get back to your question about, you know, the practicalities, whether it would be possible to do relief only to

Louisiana, I guess theoretically the Court could do something, like fashion a REMS to say you can mail the drugs everywhere except Louisiana; but I think, to be honest, that would look more like an injunction. It would require FDA to do something, and it seems a lot more intrusive. Other than stopping short of doing something like that, it is hard -- the issue is out-of-state providers mailing into Louisiana, so it is difficult to foresee how a Louisiana-specific remedy could take care of those out-of-state providers.

With respect to the other pending cases, Your Honor, I think only one of them is in any -- that's the West -- excuse me, the Virginia case -- has any imminent chance of coming to the contrary conclusion. But even if it did -- so we think that the merits are so strong here, the Court should not come to that conclusion; but even if it does, as the Court explained in the *Alliance* decision, itself, that's really the job of the Supreme Court to iron out those sorts of differences. And the fact that a district judge might disagree in another case is not reason for this Court to stay its hand.

THE COURT: Setting aside the possible application of the Comstock Act to this, to this REMS -- and I think we need to clearly separate these issues. Number one is standing, and that's, you know, what the harm is and what the sovereign interest of Louisiana is. But the only substantive claim Louisiana has is that the procedure that the FDA took to implement this regulation,

again, setting aside the Comstock Act and possible conflict with the law, but that that's not valid. And then if the procedure was valid and they still came to the same conclusion, what would Louisiana do?

MS. HAWLEY: So I think that's partially correct, Your Honor. The Fifth Circuit held, and we believe, that the 2023 REMS is not only unreasonably explained but unreasonable. So Your Honor is correct that in some situation it might be possible. If the study showed something vastly different than they show, maybe the FDA could come to the conclusion it did in 2023. But even if that were to happen with this pending review, that would have nothing to do with the unlawfulness of the 2023 action. Under *State Farm* and more recent cases, the Supreme Court has been clear that an agency action is evaluated at the time that action was taken based on the rationale before the Court. So we think FDA is simply incorrect to suggest that its review might preclude this Court's. Again, nothing FDA can do will make the 2023 REMS lawful.

And in the meantime, Your Honor, what FDA and interveners are asking for is to leave in place a concededly unlawful REMS that is risking, even taking the lives of thousands of Louisiana children so the FDA can spend an indefinite amount of time to study and possibly come to the same or different results. Louisiana is suffering irreparable harm. It meets the factors for preliminary relief.

THE COURT: It seems that the decision to file the

10:30:45 preliminary injunction motion that we're here on today was due, at
10:30:49 least in part, to an anonymous report in the media that the FDA was
10:30:55 waiting until after the election to do anything on this REMS; is
10:31:01 that right?
10:31:01 **MS. HAWLEY:** So I think --
10:31:03 **THE COURT:** The case had been pending for a while before
10:31:05 this motion was filed.
10:31:07 **MS. HAWLEY:** So I think what can be said, Your Honor, is
10:31:11 that the MPI motion was filed as soon as we could. So we got the
10:31:15 complaint on file and I think the MPI was filed two months later,
10:31:20 which is not as quick as we would have liked, but it's certainly
10:31:23 not an inordinate delay.
10:31:24 The standard for delay, of course, is reasonable
10:31:27 diligence. The Court has found even up to a year is fine for an
10:31:31 MPI to be filed, especially where, as in this case, there is
10:31:34 irreparable harm. In fact, neither FDA nor the interveners have
10:31:38 cited a single case finding that delay should matter where there is
10:31:43 ongoing irreparable harm and a likelihood of success on the merits.
10:31:46 **THE COURT:** Right. I think the commissioner denies that
10:31:48 this is the case on the record; is that right?
10:31:51 **MS. HAWLEY:** I'm sorry. I'm not sure what you're saying,
10:31:53 sir.
10:31:53 **THE COURT:** The reason I know this is because it's
10:31:55 included in your brief.
10:31:56 **MS. HAWLEY:** So the commissioner denies what, Your Honor?

10:31:58 **THE COURT:** Denies that they are waiting until after the
10:32:00 midterms to conduct the review.
10:32:02 **MS. HAWLEY:** So I think that was --
10:32:06 **THE COURT:** I'm saying, the reason I know that it was
10:32:08 based on an anonymous report in the media about waiting until after
10:32:10 the midterms is because you put it in your brief.
10:32:12 **MS. HAWLEY:** Oh, sure, Your Honor.
10:32:12 **THE COURT:** That's how I know that.
10:32:14 **MS. HAWLEY:** Sure, Your Honor. But to be clear, we know
10:32:16 this won't take place before the midterms because of the timeline
10:32:20 that FDA has, itself, laid out. So if you look at what they
10:32:24 represent in their brief, as far as we're aware, there is no
10:32:28 evidence that they have even requested the data yet. Maybe our
10:32:32 friends can enlighten us on that. But even if they've requested
10:32:36 the data, even if they've received the data, they say it will take
10:32:38 a year or more but they hope to be sooner than that. In addition
10:32:42 to that, Your Honor, it will take at least six months for the
10:32:47 administrative process to run through its course after that study
10:32:50 is analyzed. So that puts us out to 2027, very best case scenario.
10:32:55 Again, I'm not even sure FDA has the data.
10:32:58 **THE COURT:** All right. Thank you very much.
10:33:00 **MS. HAWLEY:** Thank you, sir.
10:33:17 **MR. KATZEN:** Good morning, again, Your Honor.
10:33:20 FDA is conducting a review of the mifepristone REMS that
10:33:24 could, depending upon the outcome, result in plaintiffs' challenge

10:33:28 to the 2023 REMS modification becoming moot. Women's safety is an
10:33:34 important public health objective, and Congress entrusted the
10:33:38 agency with the responsibility, in particular, to ensure drug
10:33:41 safety. The best way for the agency to pursue that objective is
10:33:46 through an orderly review process that enables the agency to meet
10:33:50 its statutory responsibilities and apply gold-standard science.
10:33:55 Science, rather than political considerations, are what drives
10:33:59 FDA's review.

10:34:00 This Court should not reach the merits, let alone award
10:34:04 preliminary relief, without the full benefit of FDA's input
10:34:08 following its review. Instead, the Court should do what the
10:34:12 *Purcell* court did during the 2021 to 2023 period in which FDA last
10:34:17 reviewed the REMS: Stay its hand until the review is complete.
10:34:21 Put simply, the parties should not litigate, and this Court should
10:34:26 not decide, the complex issues of drug safety raised here at the
10:34:32 very moment that the agency charged with drug safety is considering
10:34:36 those issues.

10:34:37 Plaintiffs' request for judicial intervention at this
10:34:42 point also raises the specter of FDA having to potentially defend
10:34:45 against and maybe navigate conflicting injunctions and review
10:34:49 supplemental applications while its review is ongoing. Judicial
10:34:55 tug-of-war and regulatory whiplash are not conducive to orderly
10:35:00 agency proceeding. If Louisiana could wait nearly three years to
10:35:04 bring this suit, it does not need preliminary relief while the
10:35:09 agency is undertaking its review. Indeed, in its reply brief

10:35:15 Louisiana admits that it has long believed that its interests were
10:35:18 adequately represented by other state litigants in, for example,
10:35:24 the *Alliance for Hippocratic Medicine* case despite the fact that
10:35:26 those state plaintiffs never sought preliminary relief.
10:35:30 Our point about Section 705, since Your Honor raised
10:35:34 that, is that it underscores that the longer a plaintiff waits, the
10:35:40 less appropriate it is to award preliminary relief. Section 705
10:35:45 uses two verbs, postpone and preserve. It's talking about
10:35:50 postponing the effective date of agency action and preserving the
10:35:53 relative status of the parties while the Court adjudicates the
10:35:58 merits. And the preliminary relief in general is aimed at
10:36:02 preserving the relative position of the parties. I think the
10:36:04 Supreme Court in *Starbucks versus McKinney* recently said that is
10:36:07 the sole purpose of preliminary relief.
10:36:10 Three years after the agency action took effect is too
10:36:15 long for plaintiffs to claim, come to court, claiming that they
10:36:18 need instantaneous relief, especially given the pendency of the
10:36:25 ongoing agency review. But even if the Court does not stay
10:36:27 proceedings, it should at least deny preliminary relief for the
10:36:31 fundamental reason that plaintiffs lack standing. Both of the
10:36:34 theories of standing that Louisiana presses at this stage were
10:36:39 rejected squarely by the Ninth Circuit in *Washington versus FDA*,
10:36:46 and this Court should do the same here.
10:36:46 I'll start with sovereign harm. Courts have held that
10:36:50 states have standing to vindicate their authority to create and

10:36:55 enforce a legal code. There has been no injury to Louisiana in
10:37:00 that interest. Louisiana's authority to create and enforce laws
10:37:06 regulating abortion remains precisely the same now as it did before
10:37:11 the 2023 REMS modification. The State identifies no case, and
10:37:17 we're aware of none, in which a state was found to suffer an injury
10:37:21 to this sovereign interest absent a conflict between state and
10:37:27 federal law.

10:37:28 Now, that conflict can take several forms. It can be
10:37:33 where the federal law preempts the state law or supersedes the
10:37:36 state law. It can be, as in Your Honor's case in *Louisiana versus*
10:37:40 *EOC*, where the federal agency action directs the state to do
10:37:44 something that the state otherwise wouldn't do or that's contrary
10:37:47 to the state's laws or policies. Or it can be where the federal
10:37:51 action applies some kind of pressure to the state to change its
10:37:55 laws, as was held to be the case in the *DAPA* case. Or as in the
10:37:59 *Texas versus Becerra* EMTALA case, it could be where the federal
10:38:03 government effectively -- is held to have effectively decreed that
10:38:07 it is unlawful as a matter of federal law for third parties to
10:38:12 follow a state law. The 2023 REMS modification poses no conflict
10:38:16 of that time with Louisiana state law.

10:38:19 Louisiana today --

10:38:20 **THE COURT:** What about -- I think the main point -- I
10:38:24 mean, there's two main points of Louisiana. Number one, that this
10:38:27 agency action was actually directed by the FDA, undermining
10:38:32 Louisiana and other states' laws. So it was not directed for any

health purposes. It was directed to undermine, you know, states that have restrictions on abortion.

MR. KATZEN: I don't think Your Honor needs to reach that issue because they failed to demonstrate an injury in fact, right. They present that issue as relevant to the causation prong, but they haven't demonstrated the sovereign injury in fact that could even give rise to this theory of standing.

Now, they point to their allegation that actual violations of Louisiana law are occurring when those drugs are mailed into the state. The *Harrison versus Jefferson Parish School Board* case, cited I think in the interveners' briefs, makes clear that there is a distinction between the states' interest in compliance with its laws that is ordinarily good enough to get the state to be able to, you know, bring a suit, criminal or civil, in its own courts, and the sovereign interest that's needed for Article III in the authority to make and enforce the legal code. And there has been no injury to the State's authority to make and enforce its laws relating to abortion, so I don't think we need to get to that causation analysis.

But the point about this *Diamond* theory of causation, too, is if you look at the cases that talk about what it means to be the object of regulation, they're using object to refer to the party who is, in essence, the regulated party. And we don't need to speculate about who the regulated party is in the case of mifepristone regulation because the Supreme Court told us in

10:40:10 *Alliance for Hippocratic Medicine*. The Supreme Court said that the
10:40:16 regulated party when it comes to the REMS are those who are
10:40:19 required to do or prohibited to do something by the REMS, in other
10:40:23 words, the sponsors, doctors who prescribe mifepristone, and women
10:40:30 who use mifepristone. Louisiana is none of those.
10:40:35 And if Louisiana's theory were valid, it's hard to
10:40:40 imagine any easing of federal restrictions or federal regulations
10:40:45 that wouldn't result in a sovereign injury to the State. And we
10:40:50 don't have to get very far from this case. Let's just take an
10:40:55 ordinary FDA drug approval decision.
10:40:57 The legal effect when FDA approves a drug is that it
10:41:01 lifts the FDCA's bar on introducing that drug into interstate
10:41:08 commerce. When, as is typical, FDA approves a drug without
10:41:13 imposing an in-person dispensing requirement, that will mean that
10:41:17 prescribers, as far as the FDCA is concerned, can mail that drug
10:41:21 into the state. And it could be that some of those prescribers --
10:41:26 those doctors' prescriptions will not comport with that state's
10:41:30 laws regulating the practice of medicine. Under Louisiana's
10:41:34 theory, it's difficult to see why the State wouldn't suffer an
10:41:38 injury every time that happens and so in connection with every
10:41:42 single FDA drug-approval decision.
10:41:46 Perhaps sensing that its sovereign harm theory might
10:41:52 stretch the concept too far, Louisiana tries to recharacterize that
10:41:58 injury as a pocketbook injury by pointing to the expenses that the
10:42:01 State incurs to enforce its laws. That doesn't work, either.

10:42:03 Under *Clapper*, a plaintiff's expenses are a -- satisfy
10:42:09 Article III only if they're necessary to avoid another injury that
10:42:13 would, itself, satisfy Article III. Since their sovereign harm
10:42:17 theory fails to satisfy Article III, the expenses Louisiana incurs
10:42:23 to avoid that alleged harm or mitigate that alleged harm also
10:42:28 necessarily fail Article III under *Clapper*.
10:42:33 That leaves only Louisiana's Medicaid payor theory. Not
10:42:36 only did the Ninth Circuit reject that theory, so in effect did the
10:42:41 Supreme Court. Contrary to what Louisiana says in their reply
10:42:44 brief, the opinion in *Alliance for Hippocratic Medicine* did not
10:42:50 begin and end with the conscience injury that's discussed in Part
10:42:53 2(B)(1) of that opinion. In Part 2(B)(2), the Court goes on to
10:42:58 hold that doctors do not have standing to challenge the loosening
10:43:02 of public health regulations on the theory that they might be
10:43:05 burdened with more patients. That chain of causation, the Court
10:43:10 said, was just too attenuated and it necessarily follows from that;
10:43:15 that those same -- that when those same doctors with their
10:43:16 attenuated injury pass that attenuated injury on to the State by
10:43:23 billing Medicaid, that chain remains too attenuated.
10:43:28 In short, given FDA's ongoing review, the benefits of
10:43:31 waiting for the completion of that review, the disruptive effects
10:43:34 of judicial intervention, and Louisiana's delay, the Court should
10:43:36 stay this case and deny the motion for preliminary relief. But
10:43:39 even if the Court does not agree that it should stay the case, it
10:43:43 should at least deny preliminary relief because plaintiffs lack

10:43:47 standing. Thank you.

10:43:49 **THE COURT:** How long will the review of the 2023 REMS
10:43:53 last?

10:43:54 **MR. KATZEN:** I don't have a timeline I can give Your
10:43:57 Honor. I think the current plan is for FDA to try to complete the
10:44:01 study it's undertaking in less than -- in sooner than a year, but I
10:44:06 can't put a timeframe on the review as a whole.

10:44:08 **THE COURT:** So that was announced last September, is that
10:44:15 right, by the secretary?

10:44:15 **MR. KATZEN:** It was confirmed last September. It may
10:44:17 have been mentioned publicly before that, as well, but it was
10:44:21 certainly stated in the September --

10:44:23 **THE COURT:** So by this September, you think the review
10:44:26 would be complete?

10:44:27 **MR. KATZEN:** By this September?

10:44:30 **THE COURT:** Right.

10:44:30 **MR. KATZEN:** I can't make any representations about the
10:44:32 time --

10:44:32 **THE COURT:** You said within a year and it was announced
10:44:35 last September.

10:44:36 **MR. KATZEN:** I'm sorry. I'm sorry. In January of this
10:44:37 year, FDA said on its website that it expects to have the study
10:44:44 that it's doing, which is part of the review -- it's not the whole
10:44:48 review itself -- have the study complete in sooner than a year.
10:44:52 That's the current plan of the agency. But the review itself, I

10:44:57 don't have a timeframe to put on that.

10:44:59 **THE COURT:** So the review has begun? It began last

10:45:02 month?

10:45:03 **MR. KATZEN:** The study is part of the review, and they're

10:45:05 in the data collection phase of the study. FDA, yes. FDA is

10:45:09 beginning its review -- begun its review.

10:45:11 **THE COURT:** What are they currently doing as part of

10:45:15 their review?

10:45:16 **MR. KATZEN:** I can't talk specifically about what they

10:45:18 are doing. I can say there's three different kind of work streams.

10:45:22 One is the study. Well, maybe four different work streams. The

10:45:24 study, there's just the review of all evidence before --

10:45:26 **THE COURT:** Why can't you talk specifically about it?

10:45:28 Because you don't know? Or because you're not supposed to talk

10:45:30 about it?

10:45:31 **MR. KATZEN:** No, no. This is my understanding of what,

10:45:33 in general, the agency is doing. I can't review all their

10:45:37 deliberative processes. I can't, you know, get ahead of the agency

10:45:42 on anything; but I can tell you --

10:45:43 **THE COURT:** Well, you can say generally what they're

10:45:46 doing. You're telling me to defer to the agency process. I'm

10:45:49 asking you: What are they doing?

10:45:52 **MR. KATZEN:** Yeah, I think I am going to answer this

10:45:54 question. They are conducting a study. They are reviewing all

10:45:59 evidence before the agency. They are reviewing citizen petitions

10:46:05 that have requested various forms of action on the REMS and all the
10:46:11 material appended to those citizen petitions. And they are
10:46:15 reviewing, also, the issues identified in the *Purcell* remand that
10:46:22 was issued last October.
10:46:25 **THE COURT:** What's DOJ's position on the application of
10:46:31 the Comstock Act to the 2023 REMS? That wasn't addressed, I don't
10:46:35 think, in your brief.
10:46:35 **MR. KATZEN:** We're not taking a position on any merits
10:46:37 issue with respect to this motion.
10:46:40 **THE COURT:** Has the FDA produced the full administrative
10:46:44 record from the 2023 REMS to the plaintiffs in this case?
10:46:48 **MR. KATZEN:** We have not, Your Honor.
10:46:50 **THE COURT:** Have they asked for it?
10:46:52 **MR. KATZEN:** They have not asked for it.
10:46:55 **THE COURT:** Do the plaintiffs want the administrative
10:46:57 record?
10:46:58 **MR. AGUINAGA:** Absolutely, Your Honor.
10:47:01 **THE COURT:** All right. Thank you, sir. I appreciate
10:47:03 your argument. And we'll hear from the interveners now.
10:47:09 **MR. KATZEN:** Thank you, Your Honor.
10:47:09 **MS. ELLSWORTH:** Good morning, Your Honor. Jessica
10:47:17 Ellsworth on behalf of Danco Laboratories. And the two interveners
10:47:22 have conferred to try and split up the argument, similar to the way
10:47:25 the plaintiffs did. So I'm going to address standing and if you
10:47:29 have questions about any other procedural issues, and then Mr.

Katerberg is going to address the merits, the remedies, the other PI factors.

THE COURT: Okay.

MS. ELLSWORTH: And I will try to also streamline based on the Government's argument which also addressed standing.

Louisiana comes to this Court lacking a cognizable injury in fact that is caused by Louisiana's 2023 REMS. The Supreme Court addressed standing to challenge the mifepristone REMS just two years ago, and it unanimously held that plaintiff doctors in that case lacked standing for three, I think, primary reasons that are relevant here:

The first is that FDA's regulation of mifepristone did not require the plaintiffs to do or refrain from doing anything. That's true here, as well;

The second is that Article III standing does not flow from a plaintiff's desire, however genuine it is, that FDA make a drug less available to individuals who want to take it. That's also true here;

And the third is that because the plaintiff's claims of injury were attenuated and not a predictable result of the mifepristone REMS, they flowed from discretionary decisions of third parties. That same shortcoming is here -- is true here, as well.

The 2023 REMS does not require or forbid Louisiana to do anything. In fact, it doesn't regulate Louisiana's conduct at all.

10:48:55 Louisiana can and does have its own additional state law
10:48:59 restrictions on mifepristone, and the 2023 REMS doesn't override,
10:49:03 preclude, or otherwise invalidate those state law restrictions.
10:49:08 Louisiana's claim is an equally attenuated chain of
10:49:15 healthcare decisions made by independent actors and not a
10:49:17 predictable result of the REMS. It is fairly traceable to
10:49:21 discretionary decisions by several layers of independent actors,
10:49:25 including other states who have taken a different policy approach
10:49:29 and providers in those states. The net result of this is Louisiana
10:49:33 lacks what the Supreme Court has called a personal stake in whether
10:49:42 federal law imposes an in-person dispensing requirement through the
10:49:44 mifepristone REMS.
10:49:45 As the Supreme Court recognized in the *Alliance* case,
10:49:48 when a plaintiff is challenging the Government's decision not -- to
10:49:52 regulate or not regulate someone other than the plaintiff, it is,
10:49:56 to quote the Supreme Court, ordinarily substantially more difficult
10:50:00 to establish standing. To be sure, Louisiana has strong views on
10:50:05 the availability of mifepristone, so did the *Alliance* doctors; but
10:50:10 the Supreme Court emphasized, with all nine justices speaking
10:50:14 together on this point, that legal, moral, ideological, and policy
10:50:18 objections to a particular government action are insufficient to
10:50:21 create standing.
10:50:22 Louisiana asserts two injuries in fact here. And the
10:50:27 first is their sovereign harms. And I want to note that I believe
10:50:31 I heard Louisiana's counsel say that there was not a challenge to

10:50:35 whether this was a cognizable injury in fact. They also say that
10:50:40 in their reply brief. We certainly challenge that is a cognizable
10:50:45 injury in fact. You can see it in our PI response at pages 5 and
10:50:50 6. It's right in the headers.
10:50:52 Louisiana asserts that it has a sovereign interest in
10:50:55 being able to enforce Louisiana law and that the 2023 REMS makes
10:51:01 mifepristone use harder to detect. This is exactly what the Ninth
10:51:07 Circuit rejected when Idaho made this same argument in a REMS
10:51:11 challenge just last year. Like Idaho, Louisiana does not argue
10:51:14 that the 2023 REMS preempts or otherwise interferes with the
10:51:18 State's ability to enact or enforce restrictions on its own laws
10:51:23 within its own boundaries. The reality is that Louisiana can have
10:51:28 whatever laws it wants to have, just like other states can have
10:51:32 whatever laws they want to have. Nothing in the 2023 REMS speaks
10:51:35 to any of that.
10:51:36 Louisiana's argument appears to be that it suffered a
10:51:41 sovereign injury because enforcing its laws has required them to
10:51:46 expend state resources. But expending state resources to enforce
10:51:51 state law is the norm in our system of government, where there is a
10:51:55 layer of federal law and there are layers of state law. No court,
10:52:00 and Louisiana can't point to any, has ever held that a state has a
10:52:04 sovereign interest in federal regulation aligning with the state's
10:52:10 legal priorities so that the state can save money on its own
10:52:13 enforcement actions, nor would that make any sense because there
10:52:17 are 50 states who can have 50 different sets of enforcement

priorities and enforcement actions, and there is simply no possible way that federal law could be required to advance all of those individual state interests.

Let's talk about the financial harms. Louisiana asserts two financial harms. One is what we have been talking about related to enforcement. The other are the Medicaid expenditures. Louisiana's Medicaid expenditure theory is the same attenuated downstream economic injury that the doctors offered in the *Alliance* case, except they've added an additional layer because now they say it's about who pays the doctors, who, themselves, don't have an Article III injury in fact because those doctors are at the end of an already too attenuated chain of healthcare decisions.

Louisiana doesn't grapple in its papers, and I didn't hear it talk today about the fact *Alliance* addressed this issue. What Louisiana does do is rely on the same basic assertion about complication rates that the doctors in the *Alliance* case pointed to, as well. But the Supreme Court forcefully rejected the argument that there could be this novel view that doctors got some special Article III standing authority because they might someday encounter someone who had been injured by some product that was out there. As the Court said, that would open floodgates; it was unprincipled; it was virtually limitless. And the same is true here. If a state or presumably any health insurance provider could sue, had Article III standing to sue, anytime that it thought a product should be regulated differently, that would -- what the

10:54:03 Ninth Circuit said, that would make a mockery of Article III. It
10:54:08 would open the floodgates to the same sort of novel standing
10:54:12 argument that the Supreme Court unanimously rejected for doctors.
10:54:15 And you can see this in part because the Supreme Court's
10:54:18 decision walks through a series of hypotheticals to show how novel
10:54:22 and unprincipled this theory would be, talking about what happens
10:54:27 when the government rolls back EPA emissions. What if a Louisiana
10:54:33 Medicaid enrollee then develops asthma? Does that give Louisiana
10:54:38 standing to challenge the EPA's rollback? What about when there is
10:54:42 a gun restriction that's appealed? The Supreme Court went through
10:54:46 hypothetical after hypothetical and then said, quite simply, the
10:54:49 answer is no. The chain of causation is simply too attenuated. It
10:54:55 would be unprecedented and a limitless approach that would allow
10:54:58 standing to exist to challenge almost any policy affecting public
10:55:03 health. That's at page 391.
10:55:04 In addition to this *Alliance*-based problem, the Supreme
10:55:07 Court has also cautioned against allowing state standing based on
10:55:11 federal policy that has some indirect effect on state revenue.
10:55:16 This is the *United States versus Texas* case. And the Court in that
10:55:20 case -- you can see it in Footnote 3 -- talked about indirect
10:55:23 effects being a common occurrence from federal government policies
10:55:29 and that it is too attenuated to constitute injury in fact.
10:55:34 That leaves us with the enforcement spending that I was
10:55:37 talking a little bit about earlier. The enforcement difficulty
10:55:40 here is not caused by FDA's action. It flows from independent

10:55:45 discretionary actions first of other states who have enacted a
10:55:49 different set of policies, as *Dobbs* told them that they were
10:55:53 entitled to do. It flows from actors, providers in those other
10:55:58 states who have chosen not to comply with Louisiana law, whether
10:56:03 because of the state laws where they practice or for other reasons.
10:56:08 And that also is layered on top of the enforcement challenges
10:56:13 coming at the end of this already attenuated chain of independent
10:56:17 third-party decisions, starting with someone in Louisiana reaching
10:56:20 out and requesting these drugs be mailed to them.
10:56:24 I think that I heard counsel on the other side say that
10:56:31 it was very clear that the 2023 REMS were directed at states like
10:56:36 Louisiana and that the harms in Louisiana, the mailing of drugs
10:56:41 into Louisiana, was queued to this 2023 REMS decision. And that is
10:56:47 flat wrong and inconsistent with the record that the plaintiffs
10:56:52 themselves have put before the Court. You can see this most
10:56:55 principally in the chart that's on page 1 of their principle --
10:56:59 their PI brief. That chart shows that the rise of medication
10:57:04 abortions in Louisiana in 2023 coincided with shield laws being
10:57:10 enacted by other states, not with *Dobbs* and not with the 2023 REMS.
10:57:15 You can see it's a little, light-blue dotted line between June and
10:57:19 July of 2023. And the #WeCount data, the #WeCount report that they
10:57:24 rely on says the same thing. You can see that at ECF 20-2 at page
10:57:29 9 and in their complaint at paragraph 85.
10:57:34 So in other words, the spike did not begin after *Dobbs*,
10:57:38 as Louisiana told you.

10:57:40 **THE COURT:** Is the shield law subject to any litigation
10:57:42 that you're aware of?
10:57:44 **MS. ELLSWORTH:** I believe that there is some litigation
10:57:46 or at least some -- I think there is some litigation between some
10:57:50 of the states about questions like extradition. I'm not involved
10:57:54 in any of that, but I have read about some of it.
10:57:54 **THE COURT:** All right.
10:57:59 **MS. ELLSWORTH:** This, I think, dovetails with Louisiana's
10:58:01 argument that somehow it was the object of the 2023 REMS. And,
10:58:08 Your Honor, the simplest way I think to know that's not true is to
10:58:10 just look at the timeline. The 2023 REMS formalized a policy that
10:58:14 FDA put in place in early 2021 and directed be formalized as a
10:58:20 permanent REMS change also in 2021. So that was before *Dobbs* came
10:58:25 down. It was before any of the statements that they're pointing to
10:58:29 from non-FDA officials. And their complaint in paragraph 64
10:58:35 specifically says that the 2023 REMS -- this is a quote -- imported
10:58:40 FDA's 2021 rationale when it implemented the 2023 changes.
10:58:45 **THE COURT:** You're saying the process to implement the
10:58:48 2023 REMS started in 2021?
10:58:51 **MS. ELLSWORTH:** Yes, Your Honor. In 2021, FDA first --
10:58:54 **THE COURT:** You're saying, basically, that after *Dobbs*
10:58:57 maybe some politicians tried to capitalize on that?
10:59:00 **MS. ELLSWORTH:** That's exactly right, Your Honor. But
10:59:03 that had already been put in place. It had been put in motion back
10:59:06 in 2021. The SNDA -- it's the Supplemental New Drug Application

that was approved, that is what the challenge is to here, was submitted to the agency also before *Dobbs* was decided so that the argument here that the 2023 REMS was directed at Louisiana state law just doesn't work on the reality of the timeline.

I have just two other points I want to make, Your Honor, cognizant of time.

I think I heard Louisiana talk about the first cause of the harm being an indication that this Court should find causation and redressability and that the first cause of the harm is this 2023 REMS approval. With all due respect, this first cause theory, or what they call in their brief the indispensable ingredient theory, is not how courts approach Article III standing. It's not how courts approach causation. And you know that because when courts are looking at causation, they're looking at two things. They're looking at whether something is fairly traceable to the government action, and they're looking at whether and how independent actors and their discretionary decisions play a role in it. And all of that would be cut out if you just said, "Well, the first step is that FDA had to approve this drug." So anything else, no matter how speculative, no matter how attenuated, no matter how predictable, you just don't pay any attention to that. That is not how the law has worked.

The last point on standing I want to make, Your Honor, is to address Louisiana's lack of standing on Count 2, which is the one that addresses the Comstock Act. In this count, Louisiana

11:00:51 seeks to force FDA to incorporate the Comstock Act restrictions
11:00:56 into the 2023 REMS and thus to compel FDA to enforce Louisiana's
11:01:00 reading of that criminal statute.

11:01:03 The Supreme Court has rejected that a state can use the
11:01:07 APA to force the federal government to exercise enforcement of a
11:01:12 criminal statute in a particular way. That is the *United States*
11:01:16 *versus Texas* case where Texas claimed a Custom and Border Patrol
11:01:22 policy violated the APA because it was contrary to a different
11:01:27 federal statute that had an arrest mandate.

11:01:29 Louisiana, likewise, is claiming that the REMS violates
11:01:31 the APA because it is contrary to a criminal prohibition. That
11:01:36 conflicts with the principle holding of *U.S. v. Texas*, which is
11:01:41 that a state does not have a judicially cognizable Article III
11:01:46 injury -- interest in whether or how the federal government
11:01:48 enforces a federal criminal statute.

11:01:51 **THE COURT:** Well, I don't think that's the position,
11:01:52 though. Their position is: We have standing, A; and, B, because
11:01:56 we have standing, we can challenge under the APA whether this
11:02:01 conflicts with the law. And I tried to make that point earlier.
11:02:05 What do you have to say? Do you have a response to that?

11:02:06 **MS. ELLSWORTH:** So, Your Honor, in order to show -- they
11:02:09 have to show standing for each claim, as I think Your Honor knows.

11:02:15 **THE COURT:** They have to show standing that they can
11:02:17 contest the lawfulness of the regulation under the APA, period.
11:02:20 And then they have to show that the regulation violates the APA.

11:02:25 **MS. ELLSWORTH:** Yes, I do agree. It's a two-step inquiry
11:02:28 just like that. But in order to have standing to challenge the
11:02:32 fact that they say the REMS doesn't incorporate the Comstock Act
11:02:38 prohibitions, you know, first of all, the REMS statute specifically
11:02:40 tells FDA what it can and cannot consider. But I think even more
11:02:45 problematic for Louisiana is the statement in *United States versus*
11:02:48 *Texas* which is that a state does not have a judicially cognizable
11:02:54 injury in fact in how the federal government enforces federal
11:02:57 criminal law.
11:02:58 **THE COURT:** I have read that case.
11:02:59 **MS. ELLSWORTH:** So if Your Honor has further questions
11:03:01 about standing, I'm happy to address them; otherwise, I will turn
11:03:04 the mic over.
11:03:06 **THE COURT:** Thank you.
11:03:08 **MS. ELLSWORTH:** Thank you very much, Your Honor.
11:03:08 **MR. KATERBURG:** Thank you, Your Honor. Rob Katerberg for
11:03:21 GenBioPro.
11:03:21 So the threshold issues you've heard about already from
11:03:25 Ms. Ellsworth, Mr. Katzen. Those are one reason why plaintiffs
11:03:28 can't show a likelihood of success which is necessary for any
11:03:31 interim relief to issue. But it's important to note, even if
11:03:33 plaintiffs could overcome those threshold issues, that would just
11:03:37 get them in the door. They'd still obviously have to show that
11:03:40 they are likely to be able to prove their case ultimately,
11:03:42 factually, and legally to the point of being entitled to a final

judgment. And that's either on their arbitrary and capricious claim or on their unlawfulness claim.

Now, two points on that that are very important to keep in mind: The first is that the relevant FDA action here is a very narrow, technical one that calls for essentially an empirical exercise, scientific findings and judgments under a highly specialized statute. So we're looking at 21, U.S.C., 355-1, Risk Evaluation and Mitigation Strategies for Drugs. And the issue is: What set of special conditions, if any, is necessary to address particular risk situations with a drug without going overboard and impeding access to the drug?

And so that's the balancing that FDA had to do in finding that in-person dispensation is not necessary for safety, while adding here, as they did in the 2023 REMS, a new requirement for pharmacy certification as an additional guardrail. So that's an important thing to keep in mind, is FDA's very niche function to conduct a balancing under this very technical statute. It's not a political act. It's a judgment about what conditions are necessary to assure safe use of a drug.

The second, which was alluded to earlier, is that FDA conducted that balancing and found in-person dispensation unnecessary on an administrative record. And you heard it just a few moments ago. The plaintiffs haven't even asked for the administrative record, which is quite surprising to me, given that APA review by definition is on an administrative record. The

11:05:19 Court's not supposed to consider anything outside the
11:05:22 administrative record, just like an appellate court hearing an
11:05:25 appeal of a district court judgment focuses its review on the
11:05:29 record before the district court.
11:05:30 The administrative record, which is massive, by the way
11:05:33 -- I understand it's been produced in a Washington -- a litigation
11:05:36 in Washington for the 2023 REMS. It's not before the Court. And
11:05:41 that alone, we would submit, is enough reason for the Court to deny
11:05:46 relief. I don't know how the Court could conclude that plaintiffs
11:05:48 are likely to succeed on a claim that FDA's action is not supported
11:05:54 by the administrative record without having the administrative
11:05:56 record to consult.
11:05:58 But, Your Honor, just from the bits and pieces of the
11:06:00 administrative record that have come into the Court, record through
11:06:04 the parties' filings, because there are parts of it here and there
11:06:09 -- for example, you do have the FDA's explanation of its decision
11:06:09 at ECF 10 -- excuse me, 1-50. It's clear, Your Honor, the evidence
11:06:16 is overwhelming to support the FDA's finding that in-person
11:06:20 dispensation is not necessary to ensure safety.
11:06:24 FDA didn't just rely on one thing. They relied on
11:06:27 multiple types of evidence to reach that conclusion. First, their
11:06:31 own REMS assessment data. So when they put into place a REMS for a
11:06:36 drug, what that involves is they're automatically engaged in
11:06:40 monitoring to see how the REMS is working. They considered that as
11:06:43 part of their analysis. And that's at ECF 1-50 at pages 60 to 62.

That's the -- I'm referring to the pagination in the ECF strip at the top of the page.

Secondly, Your Honor, FDA's own vast body of data on adverse events compared periods when the in-person dispensation requirement was being enforced and periods when it was not being enforced. So there was a natural experiment there from the period during COVID-19, when FDA was under a court injunction not to require in-person dispensal. And that is at pages 62 to 64 of ECF 1-50. And FDA concluded there does not appear to be a difference in adverse events between periods when the in-person dispensing requirement was being enforced and periods when it was not being enforced.

Now, Ms. Hawley has a criticism of that.

THE COURT: Didn't the Fifth Circuit point out that that's because that data wasn't requested by the FDA?

MR. KATERBURG: Your Honor, that's a misunderstanding. So there was a limited 2016 change in mandatory reporting by prescribers of adverse events. But let me be very clear about something. GenBioPro and Danco have always had extremely rigorous requirements to report all adverse events that come into their knowledge or possession about their drugs to FDA. There's an elaborate set of regulations governing this. It's 21 CFR 314.80. And I commend to you the amicus brief of the former FDA commissioners that provides a lot of informed background on that.

But as a general matter, drug adverse event reporting is

11:08:24 mandatory for drug companies but permitted, not mandatory,
11:08:28 permitted, encouraged for prescribers.
11:08:32 Mifepristone is subject to heightened requirements and
11:08:35 continues to be under the current REMS because prescribers are
11:08:39 required to report fatal adverse events. What the 2016 change that
11:08:44 plaintiffs put so much weight on and the Fifth Circuit referred to,
11:08:48 all it did was to change from prescribers having to report all
11:08:52 mandatory adverse events to just having to report fatal adverse
11:08:55 events.
11:08:57 And Your Honor, Justice Kavanaugh in his opinion in *AHM*
11:09:00 actually went out of his way to mention this. He said even post
11:09:04 the 2016 changes, mifepristone continued to have a prescriber
11:09:07 reporting requirement that was still more stringent than the
11:09:13 requirements for most other drugs. That's 602 U.S. at 376.
11:09:18 So there's really zero evidence that that change actually
11:09:24 affected at all the quality --
11:09:24 **THE COURT:** That's in the background factual section of
11:09:27 the opinion you're talking about?
11:09:28 **MR. KATERBURG:** That's right, Your Honor. That issue
11:09:32 wasn't really necessary. It didn't feed into the standing
11:09:35 analysis, but that makes it all the more significant that he really
11:09:38 went out of his way to make that observation.
11:09:41 And the former FDA commissioner's brief explains that FDA
11:09:44 uses that database, the FAERS database as a key analytical tool for
11:09:50 drugs across the board when the vast majority of drugs that FDA

11:09:55 regulates don't have any mandatory prescriber reporting requirement
11:09:57 at all.
11:09:58 Your Honor, just one other point on this. The periods,
11:10:02 the two periods being compared, so the period when in-person
11:10:07 dispensal was being enforced versus when it was not, they were both
11:10:10 well after this 2016 tweak. So they were in 2020 and 2021. The
11:10:16 specific periods compared are laid out in the FDA's analysis down
11:10:21 to the day. So you can look at that at page 62 of ECF 1-50. So my
11:10:26 point here is the comparison was apples to apples. So it's not as
11:10:30 if one of the periods being compared was subject to the earlier
11:10:33 reporting regime and the other was subject to a later reporting
11:10:37 regime, where, like, the conclusion might be skewed because they
11:10:39 were looking at two different data sources. The data source was
11:10:42 exactly the same, and what FDA concluded was that there was simply
11:10:46 no difference in the adverse events that were reported.
11:10:50 In addition to that, Your Honor, there was a literature
11:10:52 review. FDA analyzed numerous studies and came to the conclusion
11:10:57 that those studies essentially corroborated the conclusion based on
11:11:02 the adverse event reporting. Now, we've heard from my friends on
11:11:07 the other side that the FDA acknowledged limitations in those
11:11:11 studies. And we would respectfully submit that's good science. It
11:11:15 shows that they're taking a nuanced, thoughtful approach and
11:11:19 acknowledging, you know, that no one study is perfect. They all
11:11:22 have limitations. But when you look at them all together,
11:11:25 essentially a metaanalysis, they do support the underlying

11:11:28 conclusion.

11:11:31 So for example, the 2021 Chong study, the conclusion that
11:11:36 was reached is that the direct-to-patient telemedicine service was
11:11:42 safe, effective, and acceptable and supports the claim that there
11:11:45 is no medical reason for mifepristone to be dispensed in clinics as
11:11:49 required by the FDA at the time prior to the change that was first
11:11:53 made in 2021. And then the Aiken study, also -- all these studies,
11:11:57 by the way, are in the record as exhibits to our, GenBioPro's,
11:12:02 opposition to the motion for preliminary injunction. The Aiken
11:12:07 study, which was a study in the UK that involved some 50,000
11:12:11 patients, 50,000 observations, concluded that a telemedicine hybrid
11:12:15 model for medical abortion without an ultrasound is effective,
11:12:19 safe, and acceptable and improves access to care.

11:12:22 Your Honor, I would like to say a few words about the
11:12:25 balancing of the harms and the public interest considerations that
11:12:29 are also a part of the preliminary injunction analysis. The relief
11:12:34 that the plaintiffs are seeking here would have dramatic impact,
11:12:39 reaching far beyond Louisiana. Now, obviously, for my client,
11:12:43 GenBioPro, and for Danco, there are huge operational impacts on
11:12:47 both of the companies. And those impacts are detailed in
11:12:49 declarations that both companies submitted. Revamping a
11:12:52 distribution system is essentially like relaunching a product. But
11:12:56 that goes -- that's just the beginning of it. The impacts go far
11:12:58 beyond the upheaval operation of these companies.

11:13:02 And one thing that weighs particularly heavily in the

balancing here is the huge impact that granting the relief would have on millions of Americans outside of Louisiana, states where abortion is legal and that in some cases have policies to maintain and expand access. And we'd urge Your Honor to take a close look at the amicus briefs submitted by New York and 19 other states who go into those profound nationwide effects. Those are effects that sweep far and wide across the many states that allow abortion, and they would be vastly disproportionate to the interests that Louisiana invokes to support its standing here.

One thing, Judge, that I think bears noting about the interest that Louisiana is asserting here. Your Honor noted earlier that there is a number of different pending litigations involving these REMS. Louisiana is actually just one of six states asserting all the exact same interests and harms across three different lawsuits against FDA over the same issues as here; and yet, Louisiana, in addition to sitting on its hands for years before filing, stands alone among its similarly motivated sister states as an outlier in seeking this extraordinary preliminary injunctive relief. None of the other states have done that. And the relief that they are seeking, as I noted, would cause turmoil and disruption in numerous other states that have different policies.

There is collateral damage to those other states. There's collateral damage to millions of Americans, including people in rural communities, low-income communities, disabled,

11:14:38 domestic violence victims, who often don't have in-person dispensal
11:14:45 options. All those are detailed in the amicus briefs, and we
11:14:50 believe that they also would need to weigh heavily in this Court's
11:14:52 exercise of equitable powers. Even at the permanent injunction
11:14:54 stage, but doubly so in the current issue, is interim provisional
11:14:59 relief -- relief that, by definition, may be rescinded when the
11:15:02 case further progresses.
11:15:03 So for all these reasons, we ask that the Court deny the
11:15:07 motion for preliminary injunction. And since plaintiffs lack
11:15:10 Article III standing, we believe the Court should dismiss the case
11:15:14 for lack of jurisdiction, as well.
11:15:16 **THE COURT:** Okay. Thank you, Counsel.
11:15:20 Before any rebuttal, I do have a couple more questions
11:15:25 for the FDA. I asked plaintiffs' counsel if she could conceive of
11:15:31 any remedy limited to the parties of this case, Rule 65 remedy.
11:15:37 Can you think of any?
11:15:39 **MR. KATZEN:** We aren't proposing any narrowing of relief.
11:15:42 We've made an argument there's no relief should be granted, but
11:15:44 we're not proposing any way of narrowing the relief that they've
11:15:47 sought.
11:15:47 **THE COURT:** All right. I'm asking you: Can you think of
11:15:50 any way, as a technical matter, to do that in this case?
11:15:52 **MR. KATZEN:** I can't, Your Honor.
11:15:53 **THE COURT:** Secondly, is there a mechanism within the FDA
11:15:56 if during its review process, if it sees a public health issue with

11:16:06 the 2023 REMS -- particularly the dispensing of the in-person
11:16:12 dispensing requirement -- is there a way for the FDA to take
11:16:17 immediate action to change it, to restore it, or to alter the 2023
11:16:28 REMS to meet the public health concern?
11:16:31 **MR. KATZEN:** So the way the REMS modification works is
11:16:35 that FDA doesn't, itself, change the REMS. It has to direct the
11:16:38 sponsors to submit supplemental applications that if approved would
11:16:43 modify the REMS. And there are statutory timeframes that govern
11:16:49 that period.
11:16:50 **THE COURT:** Is there a way to act on an emergent basis to
11:16:55 do that? is my question. Is there a way that they can do that
11:16:57 based on what they're seeing in an emergent basis during the period
11:17:01 of review?
11:17:02 **MR. KATZEN:** I don't want to make representation about
11:17:05 what they can do practically. Under the regulation -- under the
11:17:13 statute, the sponsors have 120 days, or such reasonable time as FDA
11:17:19 directs, to submit the supplemental application; and then FDA has
11:17:23 180 days, by statute, to review that application once it's
11:17:28 received. There is also an administrative review process that the
11:17:31 sponsors could take advantage of if they're directed to submit --
11:17:32 **THE COURT:** Why don't you file a brief on that within
11:17:35 seven days of the hearing. I don't think that's the answer. There
11:17:38 has been many cases where a drug is being used in a particular way
11:17:41 based on approval from the FDA that later comes to the attention of
11:17:45 the FDA that this drug is causing outside harm to the proposed

benefit, and they do something quickly. So I need to know that.

MR. KATZEN: So the question that you want me to brief is whether there's anything FDA could do on an emergent basis --

THE COURT: If during the course of their review, they see a public health concern with a portion of 2023 REMS. Yes, that's my question.

MR. KATZEN: Okay.

THE COURT: All right. Thank you. All right.

MR. AGUINAGA: Your Honor, I'll be quick. Would it be possible for Ms. Hawley to offer a couple of thoughts right after me?

THE COURT: Okay.

MR. AGUINAGA: Thank you, Your Honor. I think just five brief points.

First, my friends on the other side love the *Washington versus FDA* case from the Ninth Circuit, which, of course, is not binding here. I think the most important thing to take away from that decision, if you look, I think it's around page 1174, the premise and the preface of the whole decision by that Court is they're dealing with a complaint, they have no evidence, and, in fact, that decision came out before we have all of the #WeCount data that we have in our case. And of course, in that case the Ninth Circuit didn't have receipts like the Medicaid receipts that we have in this case. So all of that is to say that when you read that opinion, it's -- I think virtually every paragraph has the

word of speculation because that was the way the Ninth Circuit got rid of Idaho's arguments in that case, was to say this is all speculative, which is not the case here.

The second thing I'd say is just turning to the harms that we have asserted. If you haven't had a chance to look at *Texas versus Becerra*, which we cite at pages 6 and 7 of our reply brief -- that's Judge Hendrick's decision. And I think it's a helpful decision because he does two things there. One thing he says is that, of course, encouraging a violation of state law is a sovereign harm, but separate and apart from that, the increased regulatory burden that a state incurs to enforce basically criminal law against those violations is, itself, a cognizable harm. Those two things squarely apply here, and I think that's a helpful decision for sort of assessing the sovereign harm in conjunction with the economic harms associated with enforcement.

The other thing I'd say regarding Medicaid costs: You didn't hear anything from my friends on the other side about the *Texas versus United States* decisions from the Fifth Circuit that we cite at pages 20 to 22 of our opening brief. Those are decisions before and after the *United States versus Texas* Supreme Court case, *Alliance for Hippocratic Medicine*, those decisions. And if you look at the 2025 case from the Fifth Circuit which goes into detail about Footnote 3 that my friends love so much from *United States versus Texas*, a resounding rejection by the Fifth Circuit with --

THE COURT: *United States versus Texas*, what was the

11:20:30 subject matter of that? There's a lot of those cases, so which one
11:20:33 are you referring to?
11:20:33 **MR. AGUINAGA:** Right. This is one of the docket cases.
11:20:35 And I'll give you a pincite, Your Honor. 126 F.4th at 410. That's
11:20:39 the Fifth Circuit's express address and rejection of this sort of
11:20:44 argument.
11:20:44 **THE COURT:** What was the subject matter of that case? I
11:20:47 guess is my question.
11:20:47 **MR. AGUINAGA:** Right. The question was whether the
11:20:49 docket issue imposed harms on the State of Texas. And what the
11:20:53 Court reiterated after the *United States versus Texas* from the
11:20:57 Supreme Court, after *Alliance for Hippocratic Medicine*, is that the
11:21:01 exact sort of Medicaid costs that we're raising here were
11:21:04 cognizable injuries for the State of Texas in that litigation. And
11:21:07 so I think everything you hear from my friends on the other side
11:21:10 you have to filter through. The Fifth Circuit's already talked
11:21:13 about those express arguments.
11:21:13 **THE COURT:** About the traceability issues; correct? That
11:21:16 would be where it would leave us; right? With traceability?
11:21:19 **MR. AGUINAGA:** Right, right. And for all the reasons we
11:21:21 discussed earlier, we think we win that analysis. But just in
11:21:25 terms of whether at the injury in fact part of the first part of
11:21:27 the standing analysis, whether Medicaid costs are, like, cognizable
11:21:32 Article III injuries, the Fifth Circuit has said time and again,
11:21:35 even after all the decisions they lacked from the Supreme Court,

11:21:38 the answer is yes.

11:21:39 My friend from -- representing Danco said that this is
11:21:43 not the fault of the 2023 REMS; this is all the shield laws' fault.
11:21:49 And, like, respectfully, that's not true. That's not how causation
11:21:53 works in the Article III standing context. Look at pages -- and
11:21:56 these are really great pages on our opening brief -- pages 20 to
11:22:00 22. What we say there, one of the citations we give you is the
11:22:03 Fifth Circuit saying there is no sole cause standard under Article
11:22:08 III, which is we don't have a burden to say that the 2023 REMS was
11:22:11 the only cause of our harms. What we're saying, and what the Fifth
11:22:16 Circuit allows us to say, is it was one of two indispensable
11:22:20 ingredients. Yes, on the one hand, you've got prescribers who are
11:22:22 chomping at the bit to send mifepristone into Louisiana; but on the
11:22:26 other hand, the only reason that they are able to do that in the
11:22:29 first place is because HHS specifically lifted the in-person
11:22:33 dispensing requirement to allow that to happen. That's why we meet
11:22:37 our burden on causation under Article III.

11:22:41 The last thing I'll leave the Court with is just if
11:22:44 you're looking at a way to frame up your Article III standing
11:22:47 analysis and conclude it, I highly commend to you page 125 of the
11:22:51 Supreme Court's decision in *Diamond Alternative Energy* because
11:22:54 that's where the Supreme Court says, like, look, if the Government
11:22:56 sets out to target a person through regulation, they can't then
11:23:01 turn around and try to avoid lawsuits on the ground that the
11:23:06 targets are unaffected bystanders.

11:23:09 **THE COURT:** All right. What do you have? What do you
11:23:10 say in response to the interveners' argument that actually this
11:23:11 process of making the 2021 changes permanent started in 2021?
11:23:17 **MR. AGUINAGA:** Well, Your Honor, that's only half of the
11:23:20 story. Look at around paragraph 56 of our complaint where we give
11:23:24 you the background on how the 2023 REMS came to be. The date that
11:23:28 FDA decided to make it permanent in 2021, just after the oral
11:23:33 argument in *Dobbs* when it was clear to everybody where the Supreme
11:23:37 Court was going to go in *Dobbs*. And then over the next course of
11:23:40 the year, we give you the timeline on how the Biden Administration
11:23:43 carried out that plan.
11:23:44 So, yes, they can say, as a technical matter, it began
11:23:47 before 2023; but the driving force all along was a recognition by
11:23:53 the Biden Administration that they needed a way to inject
11:23:56 medication abortion drugs into states that were going to ban or
11:24:00 heavily restrict abortion. That's common sense. And I want to
11:24:03 zoom out to say when the Supreme Court says, at the end of the day,
11:24:04 that this is all about common sense, let's use common sense here.
11:24:08 All of this is the intended and predictable consequence of the 2023
11:24:12 REMS because that's how it was designed.
11:24:14 With that, Your Honor, I'm happy to submit and let Ms.
11:24:18 Hawley take over.
11:24:19 **THE COURT:** Thank you.
11:24:20 **MS. HAWLEY:** Thank you, Your Honor. Just a few quick
11:24:27 points.

First, in response to your question regarding Medicaid, the State of Louisiana is on the hook for approximately 25 percent of those costs. That's at Exhibit 20 to our MPI, paragraph 7.

Second, Your Honor, with respect to the stay, I think with your dialogue with FDA what that revealed is that we have an indefinite timeframe. Under decisions like *Wedgeworth*, stays are inappropriate when there is no sort of definitive time when relief might occur. Here, we don't know if the data has been acquired. We don't know if the study has started. In our best guess, it will take at least six months after the study is completed. I think the best that can be said is maybe that was started in January, but I'm not sure even that is true. So it would be January plus a year, plus at least six months.

THE COURT: Well, Counsel's represented to me that they have started it in January.

MS. HAWLEY: I'm not sure he said that they started the study, Your Honor. I think they have to have the data before they start the study. I don't know if they have the data.

THE COURT: They started the process, is what he told me.

MS. HAWLEY: Yes. Yes, sir.

With respect to Section 706 and the administrative record, Section 706 says that a Court can issue relief based on parts of the administrative record cited by the parties. That part of the administration is at ECF Section 1-50. That is the decisional document from 2023. That's all this Court needs to

decide on the merits, which, again, the Fifth Circuit has already found a likelihood of success.

And really briefly, Your Honor, with respect to the FAERS data, my friend on the other side representing GenBioPro said that they report all of the information that, quote, comes into their possession. With respect, they are not anywhere near the emergency rooms that are treating women harmed by mifepristone. Again, in the time period, a $1^{1}/_{2}$-year time period assessed by the FDA, there were only 8 reported FAERS incidents. GenBioPro, in its brief, touts a study -- actually one that FDA discounted and did not rely on, but it touts a study with adverse event incidents of 0.9. If you take the 1.5 million -- that's a conservative number from Guttmacher's -- that occurred -- 1.5 million abortions during that $1^{3}/_{4}$ of the year, we come away with tens of thousands of adverse events, not 8. Again, Commissioner Makary's estimate of that data is, quote, not very good, is, if anything, an understatement.

They also rely on the Aiken study. Not even the FDA relied on the Aiken study because they found that study to be wholly unreliable and ungeneralizable to the United States' population, precisely because it didn't include serious adverse events, things like infections without sepsis, hemorrhaging without transfusions, hospitalizations without subsequent procedures. So that study, even the FDA did not rely on. FDA, in fact, relied on only four studies, not the 15 suggested by GenBioPro. And as the Fifth Circuit found, even the reliance on those studies was

11:27:31 unreliable.

11:27:32 One thing on sort of the harms to GenBioPro and Danco. I
11:27:38 would point Your Honor to paragraph 15 of the Long Declaration
11:27:41 attached to Danco's MPI -- motion in response to the MPI. And that
11:27:47 clarifies that all of the steps that might have been necessary in
11:27:52 the Woodcock Declaration for the *AHM* case would not, in fact, be
11:27:55 necessary in this case. If there was a stay issued of the 2023
11:27:59 REMS, the last remaining REMS would automatically come into effect.
11:28:03 There would be no need for an SDNA. In addition, all GenBioPro and
11:28:09 Danco would need to do would be to notify their prescribers to
11:28:17 recertify. That's a short process. It's at ECF 1-50, page 30,
11:28:22 about a page-and-a-half long. The FDA, again, called it minimally
11:28:27 burdensome. And that can certainly happen in a very short time
11:28:31 period.

11:28:31 In conclusion, Your Honor, Louisiana does not believe
11:28:34 there is any public interest in leaving a risky and unsafe drug on
11:28:38 the market, one that the FDA in 2020 called the in-person visit
11:28:41 necessary to mitigate those risk profiles. Thank you.

11:28:45 **THE COURT:** One more question. So after the 2023 REMS --
11:28:52 I know there was litigation that's actually still pending now in
11:28:56 Missouri. But a stay was issued of the REMS by a colleague of mine
11:29:03 in Texas, and then the Fifth Circuit, I think, affirmed that, and I
11:29:06 have read the rulings on those. So how long was the stay in
11:29:14 effect?

11:29:14 **MS. HAWLEY:** So not very long, Your Honor.

11:29:16 **THE COURT:** Supreme Court vacated those? Is that what happened?

11:29:20 **MS. HAWLEY:** Yes, sir.

11:29:20 **THE COURT:** So basically the data is, since 2023 this has fairly consistently been the law of the land, so to speak?

11:29:21 **MS. HAWLEY:** Yes, Your Honor.

11:29:27 **THE COURT:** All right. I appreciate it, Counsel. The case is submitted. Court's adjourned.

11:29:28 (Whereupon the proceedings concluded at 11:29 a.m.)

11:29:32 * * *

11:29:39 **REPORTER'S CERTIFICATE**

I, Beth Delatte, Registered Professional Reporter, Certified Court Reporter in and for the State of Louisiana, Official Court Reporter for the United States District Court, Western District of Louisiana, do hereby certify that the foregoing is a true and correct transcript, to the best of my ability and understanding, from the record of the proceedings in the above-entitled and numbered matter.

/s/Beth Delatte
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No. 26-30203

IN THE UNITED STATES COURT OF APPEALS FOR THE FIFTH CIRCUIT

STATE OF LOUISIANA, by & through its ATTORNEY GENERAL, LIZ MURRILL; ROSALIE MARKEZICH,

Plaintiffs-Appellants,

v.

FOOD & DRUG ADMINISTRATION; MARTY MAKARY, COMMISSIONER, U.S. FOOD AND DRUG ADMINISTRATION; TRACY BETH HØEG, in her official capacity as ACTING DIRECTOR, CENTER FOR DRUG EVALUATION & RESEARCH, U.S. FOOD & DRUG ADMINISTRATION; UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES; ROBERT F. KENNEDY, JR., SECRETARY, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES,

Defendants-Appellees,

v.

DANCO LABORATORIES, L.L.C.; GENBIOPRO, INCORPORATED,

Intervenors-Appellees.

On Appeal from the United States District Court
for the Western District of Louisiana

RESPONSE TO PLAINTIFFS' MOTION FOR § 705 STAY OR INJUNCTION PENDING APPEAL

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CERTIFICATE OF INTERESTED PERSONS

Louisiana v. FDA

A certificate of interested persons is not required, under Fifth Circuit Rule 28.2.1, as appellees are all governmental parties.

/s/ Daniel Winik
Daniel Winik

TABLE OF CONTENTS

Page

INTRODUCTION 1

STATEMENT 5

ARGUMENT 10

I. Plaintiffs Failed To Comply With Rule 8 11

II. Plaintiffs' Appeal Is Likely To Fail 13

A. The District Court's Assessment Of The Equities Was Well Within Its Discretion 13

B. Plaintiffs Lack Standing 17

III. The Equitable Factors Disfavor An Injunction Pending Appeal 25

CONCLUSION 26

CERTIFICATE OF COMPLIANCE

INTRODUCTION

Protecting the health and safety of pregnant women is profoundly important. To that end, in September 2025, the Secretary of Health and Human Services and the Commissioner of Food and Drugs announced that the Food and Drug Administration (FDA) is reviewing the Risk Evaluation and Mitigation Strategy (REMS) for mifepristone, a drug approved for medical abortion. Dkt. 1-110. The announcement stated that this review is "informed by the lack of adequate consideration underlying the prior REMS approvals," including a 2023 approval of a modification that removed the in-person dispensing requirement. *Id.* at 1. It expressed FDA's commitment "to protecting the health and safety of pregnant women" and "ensur[ing] … decisions are grounded in Gold Standard Science and rigorous, transparent, and objective evidence." *Id.* at 2. And it is consistent with this Court's criticism of the reasoning FDA employed in calling for the removal of the in-person dispensing requirement in 2021. *See Alliance for Hippocratic Med. v. FDA*, 78 F.4th 210, 249-251 (5th Cir. 2023), *rev'd on other grounds*, 602 U.S. 367 (2024).

In undertaking this review, FDA recognized that the validity of its mifepristone restrictions is hotly contested. Five other States are challenging the approval of mifepristone or subsequent actions easing restrictions. *See*

Missouri v. FDA, No. 25-cv-1580 (E.D. Mo.); *Florida v. FDA*, No. 25-cv-126 (N.D. Tex.). Other plaintiffs have challenged FDA's restrictions as too burdensome. *Purcell v. Kennedy*, 2025 WL 3101785 (D. Haw. Oct. 30, 2025); *Washington v. FDA*, 2025 WL 1888794 (E.D. Wash. July 8, 2025); *Whole Woman's Health All. v. FDA*, No. 23-cv-19 (W.D. Va.). And numerous citizen petitions are pending before FDA, seeking relief in both directions.

Given this complexity, FDA concluded that the best path forward is to review the mifepristone REMS based on all the evidence before it, including a new study it is undertaking. FDA, *Questions and Answers on Mifepristone for Medical Termination of Pregnancy Through Ten Weeks Gestation* (No. 37).[1] FDA is actively "work[ing] on the collection of the robust and timely data that is necessary for a well-controlled study with adequate statistical power." *Id.* Although such studies "often take approximately a year or more to conduct," FDA's "current … plan" is to complete the study "sooner." *Id.* And once FDA has analyzed the data from that study (as well as all other

[1] https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/questions-and-answers-mifepristone-medical-termination-pregnancy-through-ten-weeks-gestation (visited Apr. 22, 2026).

evidence before it), it will decide whether "substantive changes to the REMS" are "warranted." *Id.*

Plaintiffs waited nearly three years after the 2023 REMS modification to bring this challenge to the modification, and waited another two and a half months before asking the district court to pretermit FDA's review and impose an immediate stay of the modification. Instead of granting that request, the district court chose to exercise its broad discretion "to control the disposition of the causes on its docket with economy of time and effort," *Landis v. North Am. Co.*, 299 U.S. 248, 254 (1936), by granting a "time-limited" stay of the litigation to allow FDA "to complete its review and carry out the responsibilities assigned to it by Congress," Op. 35. The district court's ruling is reviewable only for abuse of discretion. Indeed, it would not have been reviewable, except by mandamus, had the district court simply held plaintiffs' motion in abeyance during the stay. That would have been functionally equivalent to the court's actual ruling, which denied plaintiffs' motion without prejudice to its renewal upon the lifting of the stay.

The district court's ruling, far from an abuse of its discretion, was a sound exercise of it. As the court observed, the relief plaintiffs seek not only would disrupt FDA's ongoing review, and usurp FDA's scientific role, but

also would threaten chaos if (as is likely) it prompted plaintiffs elsewhere to seek a conflicting injunction. This is not a theoretical risk: In 2023, minutes after the district court in *Alliance* stayed FDA's approval of mifepristone, another district court in another Circuit issued a contrary edict. *Washington v. FDA*, 668 F. Supp. 3d 1125, 1144 (E.D. Wash. 2023), *vacated*, 2025 WL 1888794 (E.D. Wash. July 8, 2025). There is no need to intervene in this precipitous way, particularly given plaintiffs' long delay in bringing this suit and given Louisiana's freedom in the interim to make and enforce pro-life policies under *Dobbs v. Jackson Women's Health Org.*, 597 U.S. 215 (2022).

Having failed to persuade the district court, plaintiffs now ask this Court to grant immediate injunctive relief, or an equivalent stay of the 2023 REMS modification under 5 U.S.C. § 705, while they appeal. But they cannot satisfy the demanding standard for that extraordinary relief. To start, plaintiffs failed to comply with Federal Rule of Appellate Procedure 8(a)(1)'s requirement that they "move first in the district court for" the relief. Plaintiffs also cannot show "'a strong likelihood of success on the merits,'" *Vapor Tech. Ass'n v. Graham*, 167 F.4th 302, 305 (5th Cir. 2026), because there is no basis to conclude that the district court abused its equitable discretion and because plaintiffs lack standing. Plaintiffs' lack of standing means they cannot

establish "'irreparable injury in the absence of an injunction,'" *id.* And for the same reasons it was appropriate for the district court to stay the litigation, plaintiffs cannot establish "'that the balance of hardships weighs in their favor'" or "'that the public interest favors'" the relief they seek, *id.* Plaintiffs' motion should be denied.

STATEMENT

1. The Federal Food, Drug, and Cosmetic Act generally prohibits introducing a "new drug" into interstate commerce without FDA approval. 21 U.S.C. § 355(a). In 2007, Congress codified and expanded FDA's regulatory regime by authorizing FDA to require a "risk evaluation and mitigation strategy," or REMS, when necessary to ensure that a drug's benefits outweigh its risks. *Id.* § 355-1. Under the REMS framework, FDA's approval of a drug may include "elements to assure safe use," like a requirement that a drug be dispensed only in certain settings. *Id.* § 355-1(f)(3).

In 2000, FDA approved mifepristone for medical abortion, subject to restrictions to assure safe use. *See FDA v. Alliance for Hippocratic Med.*, 602 U.S. 367, 376 (2024).[2] Since 2008, those restrictions—previously imposed

[2] FDA has separately approved another manufacturer's mifepristone product, Korlym, for Cushing's syndrome. It is not at issue here.

under another regulatory framework—have been part of a REMS. *See* 73 Fed. Reg. 16313, 16314 (Mar. 27, 2008).

For most of the drug's history, mifepristone's restrictions included an "in-person dispensing requirement," ensuring that the drug could be dispensed only in "clinics, medical offices, and hospitals, by or under the supervision of a certified prescriber." Dkt. 20-16 (2021 REMS). In July 2020, a district court enjoined enforcement of that requirement during the COVID-19 pandemic. *American Coll. of Obstetricians & Gynecologists v. FDA*, 472 F. Supp. 3d 183, 233 (D. Md. 2020). The Supreme Court stayed that injunction pending appeal in January 2021. *FDA v. American Coll. of Obstetricians & Gynecologists*, 141 S. Ct. 578 (2021). But in April 2021, FDA announced that it would not enforce the in-person dispensing requirement during the COVID-19 public health emergency, and the following month it announced it would review the REMS. *See* Dkt. 1-10 at 5, 6 n.10.

In December 2021, FDA directed mifepristone's sponsors to submit supplemental applications proposing to remove the in-person dispensing requirement. *See* Dkt. 1 ¶ 56; 21 U.S.C. § 355-1(g)(4)(B). The sponsors submitted those applications, and FDA approved them in January 2023.

As noted above, FDA is now conducting a new review of the mifepristone REMS. In announcing the review in a letter, the Secretary and Commissioner explained that, "to determine whether modifications [to the REMS] are necessary," FDA will consider evidence relating to "real-world outcomes" and conduct "a study of the safety of the current REMS." Dkt. 1-110 at 1. FDA will also comply with the *Purcell* court's order to reassess the REMS, 2025 WL 3101785, at *28, and address numerous pending citizen petitions.

2. On the day the Secretary and Commissioner issued their letter, plaintiffs here—Louisiana and Rosalie Markezich—sought to intervene in *Missouri v. FDA*, No. 22-cv-223 (N.D. Tex.), after the Supreme Court had held that the original plaintiffs in that case (then styled *Alliance for Hippocratic Medicine v. FDA*) lacked standing. The district court denied plaintiffs' motion to intervene and transferred that case to Missouri. *Missouri v. FDA*, 2025 WL 2825980, at *13 (N.D. Tex. Sept. 30, 2025).

A week later, plaintiffs brought this challenge to the 2023 REMS modification. Two and a half months later, and nearly three years after the challenged REMS modification, they moved for a stay of the REMS modification under 5 U.S.C. § 705 or a preliminary injunction. Two mifepristone

manufacturers intervened and moved to dismiss. The government moved to stay the case pending FDA's review of the mifepristone REMS.

3. The district court granted the government's motion and denied plaintiffs' motion (as well as intervenors' motions to dismiss) without prejudice to the refiling of those motions upon the lifting of the stay.

The court determined that Louisiana has standing on the theory that the 2023 REMS modification has the "predictable" effect of leading third parties to "expand access to mifepristone in ways designed to reach into jurisdictions like Louisiana," causing "sovereign harm[]" to Louisiana's interest in enforcing its laws and "pocketbook injury" to its Medicaid program. Op. 21, 23-24. The court also concluded that Louisiana is likely to prevail in its challenge to the REMS modification, Op. 26-28, and that the "same facts" that establish its standing also "establish irreparable harm," Op. 28.

But the court determined that the balance-of-harms and public-interest factors weighed against preliminary relief. Op. 28-35. The court identified three factors bearing on its equitable discretion.

First, the court explained that this case "implicate[s] scientific and medical judgments committed by Congress to an agency with specialized knowledge"—one that is "accountable to the President" and thus to the

political process—and that "[t]he public interest in the proper function of FDA and its scientifically grounded, congressionally authorized protocol is substantial." Op. 29-30. The court noted that it was "ill-equipped" "to evaluate scientific evidence and make" the sorts of "public health judgments" that Congress vested in the agency. Op. 34.

Second, the court noted that the requested relief "would, as a practical matter, have a nationwide effect," Op. 32, and thus implicated the concerns animating *Trump v. CASA, Inc.*, 606 U.S. 831 (2025). Those concerns are particularly acute, the court explained, given the need for a "nationally integrated regulatory scheme" and the "substantial risk of inconsistent judicial outcomes" created by the "multiple parallel lawsuits across the country addressing the same regulatory issues surrounding access to mifepristone." Op. 31, 34.

Finally, the court explained that even if the requested relief were granted, "mifepristone would likely continue to reach those" in Louisiana "who seek it," and that "Louisiana retains many meaningful, boots-on-the-ground law enforcement mechanisms to mitigate its sovereign and financial harms while FDA completes its ongoing review." Op. 30.

The court accordingly stayed the case to "afford the agency a time-limited period of deference to complete its review and carry out the responsibilities assigned to it by Congress." Op. 35. The court stated that its analysis would "change" if FDA did not "complete its review and make any necessary revisions to the REMS within a reasonable timeframe." Op. 36. The court therefore denied plaintiffs' motion "with permission to refile, as appropriate, following completion of FDA's review or upon a lifting of the stay upon a material change in circumstances." *Id.* It ordered a status report in six months. *Id.*

ARGUMENT

To obtain "an injunction pending appeal," "[t]he movant must show '(1) a strong likelihood of success on the merits; (2) irreparable injury in the absence of an injunction; (3) that the balance of hardships weighs in their favor if injunctive relief is granted; and (4) that the public interest favors such relief.'" *Vapor Tech. Ass'n v. Graham*, 167 F.4th 302, 305 (5th Cir. 2026). The same factors apply to § 705 stays pending review. *Wages & White Lion Invs., LLC v. FDA*, 16 F.4th 1130, 1135 (5th Cir. 2021).

Plaintiffs invoke the "'sliding-scale' approach" (Mot. 8), under which "'a showing of some likelihood of success on the merits'" may "'justify

temporary injunctive relief'" in the district court if the movant's showing on "'the other factors'" of the preliminary-injunction standard is "'strong,'" *TitleMax of Tex., Inc v. City of Dallas*, 142 F.4th 322, 328 (5th Cir. 2025). But this Court has rejected the proposition that something less than a likelihood of success can justify an injunction pending appeal if "'the balance of equities weighs heavily in favor of'" the movant. *Vapor Tech.*, 167 F.4th at 305 n.10.

Plaintiffs therefore must satisfy all four elements of the standard, and they have not come close. Nor did they comply with the requirement to "move first in the district court," Fed. R. App. P. 8(a)(1).

I. Plaintiffs Failed To Comply With Rule 8

At the threshold, this Court can and should deny plaintiffs' motion because plaintiffs failed to "move first in the district court" for the relief they seek, as Federal Rule of Appellate Procedure 8(a)(1)(C) requires. That requirement does not apply when "moving first in the district court would be impracticable," Fed. R. App. P. 8(a)(2)(A)(i), but there is no basis for any assertion of impracticability here. Plaintiffs waited ten days to file their motion in this Court (on April 17) after the district court ruled (on April 7), and they rightly did not characterize their motion here as an emergency; they sought relief only by May 11. They could easily have used some of the time between

the district court's ruling and their filing of this motion to file a similar motion in the district court and allow that court to rule.

Plaintiffs make no effort to argue that "moving first in the district court would [have been] impracticable," Fed. R. App. P. 8(a)(2)(A)(i). They argue, citing out-of-Circuit cases, that it would have been "futile." Mot. 1. But the rule sets impracticability, not futility, as the standard, and in any event, *this* Court has explained that "[i]t does not follow from" a district court's "refusal to grant a preliminary injunction … that the district court would refuse injunctive relief pending an appeal." *Bayless v. Martine*, 430 F.2d 873, 879 n.4 (5th Cir. 1970); *see Whole Woman's Health v. Paxton*, 972 F.3d 649, 654 (5th Cir. 2020) (citing *Bayless* for the proposition that "it would not be" "'pointless' to move first" for a stay in a district court that previously rejected the movant's argument). If a movant's prediction that the district court would deny the motion required by Rule 8(a)(1)(C) were an excuse for bypassing that requirement, the rule would be a nullity.

A movant's "failure to show the impracticability of moving first in the district court is sufficient grounds to deny its motion" for a stay or injunction pending appeal in this Court. *Whole Woman's Health*, 972 F.3d at 654 (stay); *see Brantley v. University of Tex. at Austin*, 2026 U.S. App. LEXIS 2874 (5th Cir.

Jan. 30, 2026) (per curiam) (unpublished) (injunction); *Brown v. Cain*, 546 F. App'x 471, 477 (5th Cir. 2013) (per curiam) (unpublished) (injunction); *Jenoriki v. U.S. Postal Inspection Serv.*, 24 F.3d 240 (5th Cir. 1994) (per curiam) (unpublished) (injunction); *Cullum v. Attorney Gen.*, 5 F.3d 1495 (5th Cir. 1993) (unpublished) (injunction).

II. Plaintiffs' Appeal Is Likely To Fail

Plaintiffs' motion also fails because plaintiffs are unlikely to prevail in this appeal. They cannot show that the district court's assessment of the equities was an abuse of its discretion, and they lack standing.

A. The District Court's Assessment Of The Equities Was Well Within Its Discretion

"'The decision to grant or deny a preliminary injunction … may be reversed on appeal only by a showing of abuse of discretion.'" *AbbVie, Inc. v. Fitch*, 152 F.4th 635, 642 (5th Cir. 2025) (per curiam). The same is true of a district court's exercise of its equitable power to stay proceedings. *See GATX Aircraft Corp. v. M/V Courtney Leigh*, 768 F.2d 711, 716 (5th Cir. 1985); *see also Landis*, 299 U.S. at 254 (discussing the power). And here, the district court acted well within its discretion by staying the litigation rather than granting plaintiffs' request for preliminary relief. As the district court explained,

there are at least three reasons the balance-of-equities and public-interest factors weighed in favor of that outcome.

First, this case "implicate[s] scientific and medical judgments committed by Congress to an agency with specialized knowledge"—judgments that courts are "ill-equipped" to make. Op. 29, 34. Of course, courts sometimes must address scientific and medical issues in reviewing agency actions under the deferential standards of the Administrative Procedure Act (APA), *see* 5 U.S.C. § 706(2). But the district court reasonably determined that it would be imprudent to do so when FDA is conducting a review that could moot this case, obviating the need for judicial intervention, or bring FDA's expertise to bear in a way that would illuminate subsequent judicial review.

Second, the district court recognized that the requested relief—which "would, as a practical matter, have a nationwide effect," Op. 32—would create a "substantial risk of inconsistent judicial outcomes" given the "multiple parallel lawsuits across the country addressing the same regulatory issues surrounding access to mifepristone." Op. 31. As noted above, an injunction in plaintiffs' favor, from the district court or this Court, could well lead one of the courts presiding over related litigation to enter a dueling injunction forbidding any greater restrictions on mifepristone (or perhaps any REMS

restrictions at all). That is what happened immediately after the district court's § 705 stay in *Alliance*. *See supra* p. 4.

As plaintiffs note (Mot. 22), courts do entertain challenges to agency action where the requested relief would have nationwide implications, and there is sometimes no way to avoid the possibility of conflicting decisions that could occasion the need for Supreme Court review. But, like plaintiffs' point that courts must sometimes consider scientific issues in conducting APA review (Mot. 21), that is non-responsive to the district court's equitable reasoning. The court's point was not that it *could* not consider plaintiffs' request but that it *should* not do so precipitously, when allowing FDA's review to unfold could lead to a more orderly and efficient disposition.

Finally, the district court explained that "Louisiana retains many meaningful, boots-on-the-ground law enforcement mechanisms to mitigate its" asserted "sovereign and financial harms while FDA completes its ongoing review." Op. 30. That is consistent with plaintiffs' having waited three years after the 2023 REMS modification (and a year and a half after the Supreme Court's *Alliance* decision) to challenge the modification in this case—a delay that itself weighs against plaintiffs' request for interim relief, *see, e.g.*, *Benisek v. Lamone*, 585 U.S. 155, 159-160 (2018).

At bottom, plaintiffs' insistence that they are entitled to an injunction fails to acknowledge the "extraordinary" nature of interim equitable relief, *Winter v. Natural Res. Def. Council, Inc.*, 555 U.S. 7, 24 (2008). Such relief is "never awarded as of right," *id.*, even assuming the movant is likely to prevail on the merits. It requires courts to "'balance the competing claims of injury,'" to "'consider the effect on each party of the granting or withholding of the requested relief,'" and to "'pay particular regard for the public consequences in employing the extraordinary remedy.'" *Id.* In conducting that assessment, moreover, courts must consider that the purpose of preliminary relief is "to preserve" the parties' existing positions and thus "'prevent irreparable harm'" during the litigation, not to upend the status quo. *City of Dallas v. Delta Air Lines, Inc.*, 847 F.3d 279, 285 (5th Cir. 2017).[3]

The district court was sensitive to plaintiffs' concerns. It emphasized the "time-limited" nature of the "deference" it was affording FDA and stated that its analysis would "change" if FDA does not "complete its review and

[3] Indeed, it is doubtful that § 705 *can* be employed to "postpone" the effective date of an agency action that has already taken effect. We raise this point only to preserve it, since the Court has employed § 705 in this fashion, *see Career Colleges & Schs. of Texas v. U.S. Dep't of Educ.*, 98 F.4th 220 (5th Cir. 2024), *cert. granted*, 145 S. Ct. 1039 (2025), *and dismissed*, 146 S. Ct. 59 (2025).

make any necessary revisions to the REMS within a reasonable timeframe." Op. 35-36. And it allowed plaintiffs to refile their motion, "as appropriate, following completion of FDA's review or upon a lifting of the stay upon a material change in circumstances." Op. 36. There is no basis to disturb its assessment of the equities.

B. Plaintiffs Lack Standing

Plaintiffs are also unlikely to succeed because they lack standing.

Standing "'is ordinarily substantially more difficult to establish'" where, as here, "a plaintiff challenges the government's 'unlawful regulation (or lack of regulation) of *someone else*'" than where the plaintiff is regulated. *Alliance*, 602 U.S. at 382. "That is often because unregulated parties may have more difficulty establishing causation—that is, linking their asserted injuries to the government's regulation (or lack of regulation) of someone else." *Id.* An unregulated party's showing of causation generally must rest on the proposition that "third parties" who are directly affected by the government's regulatory choices "will likely react in predictable ways that in turn will likely injure the plaintiffs." *Id.* at 383 (quotation marks omitted). But "[t]he causation requirement precludes" both "speculative links … , where it is not sufficiently predictable how third parties would react to government

action or cause downstream injury to plaintiffs," and "attenuated links … , where the government action is" too "far removed from its distant (even if predictable) ripple effects." *Id.*

Plaintiffs' motion does not argue that Ms. Markezich has standing, and the district court made no such determination. The district court did conclude that Louisiana has standing. But that was error: Neither of Louisiana's two theories of standing can surmount the hurdles discussed above.

1. Start with Louisiana's assertion of harm to its "'sovereign interest in the power to create and enforce a legal code'" (Mot. 12).

Plaintiffs' motion does not suggest that the 2023 REMS modification affects Louisiana's power to "regulate abortion for legitimate reasons," including "respect for and preservation of prenatal life at all stages of development," *Dobbs*, 597 U.S. at 300-301. *See GenBioPro, Inc. v. Raynes*, 144 F.4th 258, 274 (4th Cir. 2025) (correctly holding that the REMS establishes "a regulatory floor, not a ceiling"). So there is no doubt that Louisiana can "'create'" (Mot. 12) a prohibition against abortion.

Louisiana argues (Mot. 12-13) that the removal of the in-person dispensing requirement undermines its ability to "'enforce'" that prohibition because it facilitates mailing mifepristone into the State. But Louisiana's

laws apply to abortions conducted using mifepristone delivered from out of state just as they do to abortions by other means. Louisiana appears to suggest (Mot. 13) that violations of its laws themselves constitute sovereign injuries. But this Court rejected Louisiana's assertion of that argument in another case, explaining that "[v]iolating the law is different from hindering its enforcement" and that, "when speaking about the sovereign's interest in enforcing its laws, the Supreme Court has spoken about the state's interest in the *enforceability* of its laws." *Harrison v. Jefferson Parish Sch. Bd.*, 78 F.4th 765, 772 (5th Cir. 2023).

Louisiana's argument must boil down, then, to the proposition that it is "more difficult to police" violations of its laws when mifepristone can be mailed into the State, *Washington v. FDA*, 108 F.4th 1163, 1177 (9th Cir. 2024). But this sort of "logistical burden on law enforcement" cannot suffice to establish standing, or else States would have "standing to challenge any federal action"—for example, any loosening of regulations relating to firearms, the environment, or banking—that they can allege would "increase[] crime or disorder, or impose[] indirect compliance costs for state law enforcement." *Id.* That sort of "attenuated link[]" cannot establish the requisite

nexus between a challenged action and a harm allegedly flowing from it. *Alliance*, 602 U.S. at 383.

Indeed, the Supreme Court rejected precisely such a theory of state standing in the Term before *Alliance*. In *United States v. Texas*, 599 U.S. 670 (2023), the district court had concluded that Texas established standing to challenge federal immigration-enforcement guidelines partly on the ground that they led to the "commi[ssion]" of "more crimes" within the State. *Texas v. United States*, 606 F. Supp. 3d 437, 467 (S.D. Tex. 2022). But the Supreme Court held that "none of the" plaintiffs' "various theories of standing" could establish an Article III controversy. 599 U.S. at 680 n.3.

2. Louisiana's remaining theory—that it suffers a "monetary injury" because some women who take mifepristone will require emergency care covered by its Medicaid program (Mot. 13-14)—is no more persuasive.

Again, that is clear from the Supreme Court's *Texas* decision. The state plaintiffs there asserted standing to challenge the guidelines on the theory that they "impose[d] costs on the States," such as by requiring them to "continue to incarcerate or supply social services … to noncitizens who should [have been] (but [were] not being) arrested by the Federal Government." 599 U.S. at 674. The district court accepted that theory, *id.* at 675, but the

Supreme Court reversed. In doing so, it described as "attenuated" theories of state standing resting on claims that a federal policy "has produced only" "indirect effects on state revenues or state spending." *Id.* at 680 n.3. And "attenuated links" cannot establish the causation element of standing. *Alliance*, 602 U.S. at 383.

As the Ninth Circuit explained in applying these decisions to a claim like this, "an alleged uptick in Medicaid costs" from the elimination of the in-person dispensing requirement, leading to greater mifepristone use within a State's borders, "is exactly the kind of 'indirect effect[] on … state spending'" that the Supreme Court has made clear is insufficient for standing. *Washington*, 108 F.4th at 1176. And accepting it would have radical consequences. "[V]irtually all drugs come with complications, risks, and side effects," and "[a]pproval of a new drug may therefore yield more visits to doctors"—some of which will be reimbursable by Medicaid—"to treat complications or side effects." *Alliance*, 602 U.S. at 392. Allowing Louisiana to challenge the 2023 REMS modification based on downstream Medicaid costs would thus allow States—and even private entities "that provide[] health insurance or subsidized medical care"—"'to challenge any FDA decision approving a new drug'" or loosening restrictions on one. *Washington*, 108 F.4th

at 1176. And the theory would extend beyond FDA actions. All sorts of other federal actions—"roll[ing] back emissions standards for power plants," "increas[ing] a speed limit from 65 to 80 miles per hour," or rescinding "certain restrictions on guns," *Alliance*, 602 U.S. at 391—could likewise be challenged by a State, or a private healthcare payor, on the theory that they would increase the need for reimbursable medical care. This sort of "boundless theory of standing," "in which all peripheral costs imposed on States" by federal actions can allow the States to challenge the actions in federal court, "'would make a mockery … of the constitutional requirement of case or controversy.'" *Arizona v. Biden*, 40 F.4th 375, 386 (6th Cir. 2022).

In accepting Louisiana's theory, the district court cited *Texas v. United States*, 126 F.4th 392, 411 n.22 (5th Cir. 2025), for the proposition that "[a] state's increased medical costs, such as increased Medicaid costs due to a federal agency action, can constitute a 'pocket-book injury' sufficient to satisfy the injury-in-fact requirement of standing." Op. 23-24. But no one disputes that Medicaid costs constitute an Article III injury. The relevant question is whether they are, with sufficient certainty and proximity, *caused* by the challenged federal action. And on that question, the *Texas* decision sheds little light. The question there was whether the plaintiff States had standing

to challenge the Deferred Action for Childhood Arrivals (DACA) program, which led *directly* to the continued presence of noncitizens for whom the States bore monetary support obligations. The Court had previously held that those costs allowed States to challenge DACA, *see Texas v. United States*, 50 F.4th 498, 517-520 (5th Cir. 2022), so the relevant question was whether the Supreme Court's intervening decision in the immigration-priorities case (*United States v. Texas*) had abrogated that decision with the clarity required to overcome the "rule of orderliness," 126 F.4th at 409. The Court's determination that the immigration-priorities decision did not abrogate its prior DACA holding, *id.* at 409-411, has little bearing here given the far more attenuated connection between the challenged federal action and the costs that Louisiana asserts.

3. In defense of its standing theories, Louisiana invokes *Diamond Alternative Energy, LLC v. EPA*, 606 U.S. 100 (2025), and *Bost v. Illinois State Board of Elections*, 146 S. Ct. 513 (2026), for the proposition that the government cannot "'target a [State] through stringent and allegedly unlawful regulation, and then evade the resulting lawsuit[] by claiming that the target[] of its regulation should be locked out of court as [an] unaffected bystander[].'" Mot. 15-16 (quoting *Diamond*, 606 U.S. at 125). But in both cases,

the challenged actions "'target[ed]'" the plaintiffs (*id.*) in a manner plainly absent here.

In *Diamond*, fuel producers challenged the federal approval of state regulations requiring automakers to "manufacture more electric vehicles and fewer gasoline-powered vehicles," and the Supreme Court held that they had standing based on one of the established doctrines discussed in *Alliance*: the proposition that regulating one participant in an economic chain "'may cause downstream or upstream economic injuries to others in the chain.'" *Diamond*, 606 U.S. at 116-117 (quoting *Alliance*, 602 U.S. at 384). Louisiana experiences no such "commonsense economic" consequence, *id.*, from the action challenged here.

Bost is just as far afield. It involved no claim of standing by an unregulated party. Rather, the Court held that a political candidate had standing to "challenge[] Illinois's procedure for counting mail-in ballots received after election day" because "an unlawful extension of vote counting deprives candidates of the opportunity to compete for election under the Constitution and laws of the United States." 146 S. Ct. at 518, 521. That is a direct harm, not a derivative one.

Finally, Louisiana argues (Mot. 16) that it "need not show that the 2023 REMS is *solely* responsible for [its] harms, or that vacating the REMS would *completely* eliminate [its] harms," to establish standing. We agree. But Louisiana must show, among other things, that the challenged action is *a* sufficiently non-speculative, non-attenuated cause of its harms. It has not.

III. The Equitable Factors Disfavor An Injunction Pending Appeal

Finally, for the same reasons plaintiffs are unlikely to prevail in this appeal, they cannot satisfy the equitable factors of the injunction-pending-appeal standard. They cannot show "'irreparable injury in the absence of an injunction,'" *Vapor Tech.*, 167 F.4th at 305, because they have not established any Article III injury bearing the requisite connection to the challenged action. And they cannot show "'that the balance of hardships weighs in their favor,'" or "'that the public interest favors'" relief, *id.*, for the same reasons they are unlikely to persuade this Court to disturb the district court's contrary assessment.

CONCLUSION

Plaintiffs' motion should be denied.

Respectfully submitted,

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CERTIFICATE OF COMPLIANCE

I certify that this response complies with Federal Rule of Appellate Procedure 27(d)(1)(E) because it has been prepared in 14-point Book Antiqua, a proportionally spaced font, and that it complies with the type-volume limitation of Federal Rule of Appellate Procedure 27(d)(2)(A) because it contains 5,199 words, according to Microsoft Word.

/s/ Daniel Winik
Daniel Winik

No. 26-30203

In the United States Court of Appeals for the Fifth Circuit

STATE OF LOUISIANA, BY AND THROUGH ITS ATTORNEY GENERAL, LIZ MURRILL; ROSALIE MARKEZICH,
Plaintiffs-Appellants

v.

FOOD & DRUG ADMINISTRATION; MARTY MAKARY, COMMISSIONER, U.S. FOOD AND DRUG ADMINISTRATION; RICHARD PAZDUR, IN HIS OFFICIAL CAPACITY AS DIRECTOR, CENTER FOR DRUG EVALUATION & RESEARCH, U.S. FOOD & DRUG ADMINISTRATION; UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES; ROBERT F. KENNEDY, JR., SECRETARY, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES,
Defendants-Appellees

v.

DANCO LABORATORIES, L.L.C.; GENBIOPRO, INCORPORATED,
Intervenors-Appellees

On Appeal from the United States District Court
for the Western District of Louisiana
No. 6:25-cv-01491-DCJ-DJA, Hon. David C. Joseph

REPLY IN SUPPORT OF MOTION FOR § 705 STAY OR INJUNCTION PENDING APPEAL

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TABLE OF CONTENTS

TABLE OF AUTHORITIES ii

REPLY 1

ARGUMENT 2

I. THERE IS NO RULE 8 ISSUE. 2

II. THE PRELIMINARY-RELIEF FACTORS WARRANT A § 705 STAY. 4

A. FDA's "Equities" Analysis Is Non-Existent. 5

B. Louisiana Has Standing and Is Suffering Irreparable Harm. 8

CONCLUSION 13

CERTIFICATE OF SERVICE 15

CERTIFICATE OF COMPLIANCE 16

TABLE OF AUTHORITIES

Cases **Page(s)**

All. for Hippocratic Med. v. FDA (*Alliance I*),
2023 WL 2913725 (5th Cir. Apr. 12, 2023) 2, 4, 7

All. for Hippocratic Med. v. FDA (*Alliance II*),
78 F.4th 210 (5th Cir. 2023) 2, 4

Bayless v. Martine,
430 F.2d 873 (5th Cir. 1970) 3

Diamond Alt. Energy, LLC v. EPA,
606 U.S. 100 (2025) 10, 11

Dobbs v. Jackson Women's Health Organization,
597 U.S. 215 (2022) 2, 12

FDA v. Alliance for Hippocratic Medicine,
602 U.S. 367 (2024) 12, 13

Harrison v. Jefferson Parish School Board,
78 F.4th 765 (5th Cir. 2023) 9

Ruiz v. Estelle,
650 F.2d 555 (5th Cir. 1981) 3

Texas v. United States,
809 F.3d 134 (5th Cir. 2015) 8

Trump v. CASA, Inc.,
606 U.S. 831 (2025) 6

Washington v. FDA,
108 F.4th 1163 (9th Cir. 2024) 10, 11

Whole Woman's Health v. Paxton,
972 F.3d 649 (5th Cir. 2020) 3, 4

Statutes

5 U.S.C. § 705 ..... *passim*

Other Authorities

Fed R. App. P. 8 ..... 2, 3, 4

REPLY

As Danco dismissively acknowledged below, "some judges" (Dist.Ct.ECF.52-4 at 17) of this Court—namely, Chief Judge Elrod and Judges Ho, Wilson, Engelhardt, and Oldham—have already recognized that the Biden Administration's 2023 REMS is likely unlawful. The court below agreed: "Plaintiffs are likely to succeed on the merits of their 2023 REMS challenge." Dist.Ct.Op.28. The court below likewise agreed that Louisiana has "establish[ed] irreparable harm" absent a § 705 stay (or injunction against the enforcement) of the 2023 REMS. *Id.* So, a § 705 stay is warranted.

FDA's tortured opposition underscores the point. FDA professes a "profoundly important" interest in "[p]rotecting the health and safety of pregnant women." ECF.74 at 1. FDA also criticizes the 2023 REMS as "lack[ing] [] adequate consideration." *Id.* (citation omitted). But the remainder of FDA's brief is an array of half-hearted excuses for *keeping* the 2023 REMS in effect indefinitely. Never mind pregnant women like Plaintiff Rosalie Markezich who would not have been coerced to abort her baby via mailed mifepristone but for the 2023 REMS. Never mind the pregnant Louisiana women who, according to unrebutted declarations,

are arriving in emergency rooms because of mailed mifepristone authorized by the 2023 REMS. And never mind the approximately 1,000 unborn Louisiana children who are killed every month in violation of Louisiana law because of the 2023 REMS.

This was the Biden Administration's avowed goal—to nullify the each-state-can-decide-for-itself promise of *Dobbs v. Jackson Women's Health Organization*, 597 U.S. 215 (2022), by removing the in-person dispensing requirement that would otherwise prevent activists and prescribers in pro-abortion states from remotely sending illegal abortion drugs into pro-life states. Understandably, this FDA's heart is not in the fight. That is why its brief never defends the 2023 REMS. The Court should read FDA's token opposition for what it is—and enter the same § 705 stay this Court has twice upheld. *See All. for Hippocratic Med. v. FDA* (*Alliance I*), 2023 WL 2913725 (5th Cir. Apr. 12, 2023); *All. for Hippocratic Med. v. FDA* (*Alliance II*), 78 F.4th 210 (5th Cir. 2023).

ARGUMENT

I. THERE IS NO RULE 8 ISSUE.

FDA argues that Plaintiffs should have first asked the district court for a stay and complains that Plaintiffs did not recite the word

"impracticable" in explaining why they declined to request a futile stay. ECF.74 at 11. But there is nothing talismanic about the word "impracticable." And in any event, FDA does not dispute that such a request would have been futile (and therefore impracticable) because, as Louisiana explained (Mot.1), "the district court has both (a) denied the precise preliminary relief Plaintiffs now seek from this Court and (b) stayed the lawsuit, preventing any further proceedings below." Nor does FDA acknowledge that declining to credit such futility would split with the Sixth and Ninth Circuits. *See id.* (citing cases). That is sufficient to reject FDA's complaint.

FDA's own cited precedent confirms the point. *See* ECF.74 at 12 (citing *Whole Woman's Health v. Paxton*, 972 F.3d 649, 654 (5th Cir. 2020)). Rule 8 requires presentation first to the district court "unless it clearly appears that further arguments ... would be pointless in the district court." *Paxton*, 972 F.3d at 653 (quoting *Ruiz v. Estelle*, 650 F.2d 555, 567 (5th Cir. 1981)). That is the case here for the reasons just explained. *Bayless v. Martine*, 430 F.2d 873 (5th Cir. 1970) (cited at ECF.74 at 12), is inapposite because the district court there did not couple its denial of preliminary relief with a stay of proceedings—which

prevents further litigation below. Indeed, FDA never acknowledges (*see* ECF.74 at 11–13) the irony in FDA's (a) having successfully moved to stay proceedings yet (b) simultaneously claiming that Plaintiffs should have filed a "pointless" motion, *Paxton*, 972 F.3d at 653 (citation omitted). Neither Rule 8 nor this Court's precedents require such futile measures.

II. THE PRELIMINARY-RELIEF FACTORS WARRANT A § 705 STAY.

FDA's "opposition" on the preliminary-relief factors is even more puzzling because FDA never disputes that "Plaintiffs are [] likely to 'succeed on the merits of their 2023 REMS challenge.'" Mot.12.[1] Worse, FDA never acknowledges this Court's square holdings that (a) "FDA and the public will not be injured by an order staying" the 2023 REMS, and (b) "the public interest is disserved by" keeping the 2023 REMS in effect. Mot.19–20 (quoting *Alliance II*, 78 F.4th at 251–53). FDA's refusal to engage these holdings is significant because, in the ordinary case, a grant of preliminary relief plainly would be in order.

[1] To the extent that the Intervenors wish to revisit the merits, the *Alliance I* and *Alliance II* panels rejected most of those tired arguments, which are all addressed in Plaintiffs' briefing below. *See* Mot.9 n.5 (providing relevant citations).

Recognizing as much, FDA resists relief on two theories: (A) the district court correctly invoked "the balance-of-equities and public-interest factors" to deny preliminary relief; and (B) contrary to the district court's holding, Louisiana lacks both standing and irreparable harm. FDA is wrong.

A. FDA's "Equities" Analysis Is Non-Existent.

Start with the equities. *First*, FDA concedes (at 14) that courts must review the *lawfulness* of agency actions—even those "implicat[ing] scientific and medical judgments"—under the APA. ECF.74 at 14.

FDA reframes the district court's concern as one about the possibility that "FDA's expertise" and "review" may "moot this case" or "illuminate subsequent judicial review." *Id.* That is not what the district court was saying in complaining about being "ill-equipped" to "determin[e] whether FDA's in-person dispensing requirement is scientifically necessary." Dist.Ct.Op.33–34. But to the extent FDA wants to lean on its alleged review,[2] FDA does not address Louisiana's direct

[2] The Court should be aware of FDA's unmoored use (at 2) of the terms "a year" and "sooner." It remains unclear when the supposed one-year clock will begin ticking. FDA announced last September that it would conduct a study, but at the February hearing, FDA's attorney balked at the idea that FDA's review would be complete by September

response on that score: "[I]t makes no sense to *deny* preliminary relief on the grounds that agency action is *so* unlawful that the agency openly concedes a review is necessary." Mot.26.

Second, FDA concedes that courts do "entertain challenges to agency action where the requested relief [has] nationwide implications" and that sometimes there is no "way to avoid the possibility of conflicting decisions that could occasion the need for Supreme Court review." ECF.74 at 15; *see also* Mot.23–25 (giving four reasons why the district court's concern with nationwide relief is misplaced).

FDA says merely that in considering the possibility of conflicting decisions the district court appropriately exercised "equitable reasoning." ECF.74 at 15. But to avoid review because another court might disagree is not equity; it is judicial abdication. As Justice Kavanaugh has said, "determining the nationally uniform *interim* legal status ... of, say, ... mifepristone rules is a role that the American people appropriately expect ... the courts of appeals or district courts ... to fulfill." *Trump v. CASA, Inc.*, 606 U.S. 831, 877–78 (2025) (Kavanaugh, J., concurring). If

2026. Tr.33. And since FDA has again stated (at 2) that it is still collecting data, the need for preliminary relief remains stark.

conflicting lower court rulings happen to arise, the Supreme Court exists to resolve that conflict. But, as this Court has already held, the mere possibility of such a conflict offers no basis to refuse to carry out the judicial role. See Mot.22 (quoting *Alliance I*, 2023 WL 2913725, at *19).

That is the sum total of FDA's effort on the equities—and it is self-defeating. There is no plausible argument that FDA or the public would suffer any sort of harm from a § 705 stay. Given all this—and given the district court's own correct determination that Louisiana is suffering ongoing irreparable harm while the 2023 REMS remains in effect—there is no question that a § 705 stay is warranted.[3]

[3] FDA includes a throwaway sentence claiming that "'Louisiana retains many meaningful, boots-on-the-ground law enforcement mechanisms to mitigate its' asserted 'sovereign and financial harms while FDA completes its ongoing review.'" ECF.74 at 15 (quoting Dist.Ct.Op.30). That sentence does not make up for the absence of any cognizable harm on FDA's side of the ledger. That sentence also is citation-less because it is incorrect. As the district court separately acknowledged, Dist.Ct.Op.23, pro-abortion states have enacted so-called "shield laws" aimed at insulating activists and prescribers in those states from liability. Indeed, despite pro-life states' efforts, no activist or prescriber has been held to account for their conduct. That is why interim relief is so important.

B. Louisiana Has Standing and Is Suffering Irreparable Harm.

FDA next turns on the district court by disputing Louisiana's Article III standing—an issue that FDA then folds into a single paragraph on irreparable harm. ECF.74 at 25. FDA's argument is no more than a copy-and-paste of its cursory district court brief; it thus fails for all the reasons the district court and Plaintiffs explained below. Dist.Ct.Op.16–25; Mot.9 n.5 (collecting citations).

1. The injury-in-fact analysis is straightforward. FDA concedes that Louisiana's incurred "Medicaid costs constitute an Article III injury." ECF.74 at 22. FDA disputes only traceability (addressed below) and whether Louisiana's sovereign harm also qualifies as an Article III injury. *Id.* at 18. It is.

This Court has long recognized that "federal interference with the enforcement of state law" may constitute an Article III injury. *Texas v. United States*, 809 F.3d 134, 153 (5th Cir. 2015). And that is the problem here: In a world with the in-person dispensing requirement, Louisiana would be fully capable of enforcing its abortion laws—for any mine-run violator would need to be physically present in Louisiana and thus subject to apprehension within Louisiana's borders. The 2023 REMS's

removal of the in-person dispensing requirement, however, introduces a new (and now virtually exclusive) way of violating Louisiana law—namely, through out-of-state activists and prescribers who mail mifepristone into Louisiana while avoiding capture in Louisiana. Coupled with shield laws intended to protect those individuals, the 2023 REMS brings the enforcement of Louisiana's abortion laws to a halt.

As the district court correctly recognized, "the 2023 REMS operates, arguably, in derogation of Louisiana law and interferes with Louisiana's ability to enforce its laws and implement the policy choices of its citizens." Dist.Ct.Op.28. And that distinguishes FDA's passing citation (ECF.74 at 19) of *Harrison v. Jefferson Parish School Board*, 78 F.4th 765, 772 (5th Cir. 2023), which sought to distinguish between a violation of law and hindering the law's enforcement. The 2023 REMS effectively has nullified, not just hindered, the enforcement of Louisiana law by allowing activists and prescribers to launch their pro-abortion attacks outside of Louisiana's borders.

2. The only real question, then, is traceability and redressability—but FDA avoids the word "redressability." That is presumably because the redressability question ends the whole standing inquiry. Traceability

and redressability "are usually 'flip sides of the same coin'" in that, "'[i]f a defendant's action causes an injury, enjoining the action or awarding damages for the action will typically redress that injury.'" *Diamond Alt. Energy, LLC v. EPA*, 606 U.S. 100, 111 (2025).

Applied here, therefore, the question is whether vacating the 2023 REMS would, at least in part, redress Louisiana's sovereign and economic harms. Both below and here, FDA has never disputed that the answer is yes. Rightly so: As the ACLU has publicly complained, "If the court grants Louisiana's motion, [requesters] will no longer be able to fill their mifepristone prescription by mail[.]" Dist.Ct.ECF.111 at 13. Put otherwise, the 1,000 abortion drugs that are being mailed into Louisiana every month could no longer be lawfully (under federal law) mailed into Louisiana—thereby eliminating the ongoing violations of Louisiana law and the direct Medicaid costs arising out of related emergency room visits. That is textbook redressability.

FDA never acknowledges the undisputed record evidence that—as the district court recounted, Dist.Ct.Op.24–25—directly ties the Medicaid costs to mail-order mifepristone made possible by the 2023 REMS. Relatedly, FDA's invocation of *Washington v. FDA*, 108 F.4th

1163 (9th Cir. 2024), omits (among other things) the Ninth Circuit's emphasis that, unlike the court below, it was considering only "highly speculative allegations" in a complaint. *Id.* at 1175.

FDA also does not seriously dispute that the Biden Administration's targeting of pro-life states leaves no doubt that Louisiana has standing. In fact, FDA does not even acknowledge that record evidence. *See* Dist.Ct.Op.21. Instead, FDA tries (ECF.74 at 24) to limit *Diamond* to suspicious targeting of actors within the same "economic chain." But FDA is just highlighting the unremarkable fact that *Diamond* happened to arise in the business context. Nothing in *Diamond* says that where, as here, a President directs his administration to actively pursue regulations designed to undercut pro-life states' laws, the federal government can thereafter "evade the resulting lawsuits by claiming that the targets of its regulation should be locked out of court as unaffected bystanders." 606 U.S. at 125. That is preposterous. If anything, under our federalism, the *Diamond* principle applies *a fortiori* where a sovereign state is the target of federal regulation.

FDA, in addition, says next to nothing about the district court's holding that "there is evidence that the consequences of [the 2023 REMS]

were predictable—out-of-state providers and related entities would expand access to mifepristone in ways designed to reach into jurisdictions like Louisiana." Dist.Ct.Op.21. Because (a) the redressability element is clearly satisfied (and thus so is the traceability element), (b) the REMS is the product of direct targeting against pro-life states, and (c) the REMS has worked not just predictably but as intended, Louisiana, of course, has standing to challenge the REMS. Based on all the same evidence, the district court correctly concluded that Louisiana has "establish[ed] irreparable harm." Dist.Ct.Op.28.

One final point: There is extensive hyperbole in the drug manufacturers' briefs claiming that Louisiana somehow is in a *worse* position to claim standing as compared to the plaintiffs in *FDA v. Alliance for Hippocratic Medicine*, 602 U.S. 367 (2024). The exact opposite is true in at least two respects. *First*, unlike those plaintiffs, Louisiana and its sister pro-life states were the unfortunate targets of a Biden Administration that sought to undercut pro-life states' laws post-*Dobbs*. *Second*, unlike those plaintiffs, Louisiana has "offered evidence tending to suggest that FDA's deregulatory actions have both caused an increase in the number of pregnant women seeking" emergency care "*and* caused

a resulting" increase in costs to the State (not to mention the attendant sovereign harm). *Id.* at 390–91. Those key distinctions assure Louisiana's standing—and foreclose the manufacturers' hyperbolic claims about the supposed unlimited nature of Louisiana's standing theory.

CONCLUSION

The Court should stay the 2023 REMS under § 705 pending appeal or, alternatively, enjoin its enforcement pending appeal.

Dated: April 24, 2026

Respectfully submitted,

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CERTIFICATE OF SERVICE

I certify that on April 24, 2026, I filed the foregoing brief with the Court's CM/ECF system, which will automatically send an electronic notice of filing to all counsel of record.

/s/ J. Benjamin Aguiñaga
J. BENJAMIN AGUIÑAGA

CERTIFICATE OF COMPLIANCE

Pursuant to Fifth Circuit Rule 32.3, the undersigned certifies that this motion complies with:

(1) the type-volume limitations of Federal Rule of Appellate Procedure 27(d)(2) because it contains 2462 words; and

(2) the typeface requirements of Rule 32(a)(5) and the type-style requirements of Rule 32(a)(6) because it has been prepared in a proportionally spaced typeface (14-point Century Schoolbook) using Microsoft Word 2016 (the same program used to calculate the word count).

/s/ J. Benjamin Aguiñaga
J. BENJAMIN AGUIÑAGA

Dated: April 24, 2026

United States Court of Appeals for the Fifth Circuit

No. 26-30203

STATE OF LOUISIANA, *by & through its Attorney General, Liz Murrill*; ROSALIE MARKEZICH,

Plaintiffs—Appellants,

versus

FOOD & DRUG ADMINISTRATION; MARTY MAKARY, *Commissioner, U.S. Food and Drug Administration*; RICHARD PAZDUR, *in his official capacity as Director, Center for Drug Evaluation & Research, U S Food & Drug Administration*; UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES; ROBERT F. KENNEDY, JR., *Secretary, U.S. Department of Health and Human Services*,

Defendants—Appellees,

versus

DANCO LABORATORIES, L.L.C.; GENBIOPRO, INCORPORATED,

Intervenors—Appellees.

Appeal from the United States District Court
for the Western District of Louisiana
USDC No. 6:25-CV-1491

Before SOUTHWICK, DUNCAN, and ENGELHARDT, *Circuit Judges*.

STUART KYLE DUNCAN, *Circuit Judge*:

In *Dobbs v. Jackson Women's Health Organization*, 597 U.S. 215 (2022), the Supreme Court returned the regulation of abortion to the states. In response, the Biden Administration directed federal agencies to "expand access to . . . medication abortion." Exec. Order No. 14076, 87 Fed. Reg. 42053 (July 8, 2022). The next year, the Food and Drug Administration (FDA) formally altered its safety guidelines for the abortion drug mifepristone. Under the new regulation, the drug could now be prescribed online and dispensed through the mail, without any need for an in-person visit to a doctor.

In 2025, Louisiana challenged the new regulation in federal court under the Administrative Procedure Act (APA). It argued that FDA's justifications for remotely dispensing mifepristone were based on flawed or nonexistent data. It also documented how the new regulation had resulted in numerous illegal abortions in Louisiana and in Louisiana paying thousands in Medicaid bills for women harmed by mifepristone. Louisiana sought a stay of the regulation while the litigation proceeded.

In response, FDA conceded it had failed to adequately study whether remotely prescribing mifepristone is safe. But the agency resisted staying the regulation, arguing it was in the midst of a comprehensive review of mifepristone protocols. The agency, however, could not say when that review might be complete and admitted it was still collecting data.

The district court agreed that Louisiana was likely to win its challenge to the mifepristone regulation and was suffering irreparable harm from it. Nonetheless, the court declined to stay the regulation based on its balancing of the equities and the public interest. Louisiana appealed to our court and sought a stay pending appeal under 5 U.S.C. § 705.

We grant the stay.

I

We briefly describe (A) FDA's actions with respect to mifepristone, (B) prior challenges to those actions, and (C) the present suit.

A

FDA determines whether drugs are safe and effective before they can be marketed in the United States. *See* Federal Food, Drug, and Cosmetic Act, ch. 675, 52 Stat. 1040 (1938) (FDCA); *FDA v. All. for Hippocratic Med.* (*Alliance III*), 602 U.S. 367, 374–75 (2024). In that role, FDA may conclude that a drug requires enhanced guardrails—such as prescription only by "health care providers" or "in certain health care settings." 21 U.S.C. § 355-1(f)(3). Such guardrails are called Risk Evaluation and Mitigation Strategies, or REMS.

When FDA approved mifepristone in 2000, the REMS allowed only doctors to prescribe it after "three in-person visits" and directed they report serious adverse events. *Alliance III*, 602 U.S. at 375. Since then, the guardrails have been progressively lowered. In 2016, FDA announced that nurse practitioners could prescribe mifepristone after only one in-person doctor visit and that doctors needed to report only fatalities (the "2016 Amendments"). *Id.* at 375–76. In 2021, FDA stopped enforcement of the one-visit requirement, thus allowing mifepristone to be dispensed "through the mail . . . or through a mail-order pharmacy" (the "2021 Non-Enforcement Decision").[1] That "removal of the in-person dispensing requirement" was formalized in 2023 (the "2023 REMS"). *All. for Hippocratic Med. v. FDA* (*Alliance II*), 78 F.4th 210, 226 (5th Cir. 2023), *rev'd*

[1] FDA also approved GenBioPro's generic mifepristone for use in 2019. *Alliance III*, 602 U.S. at 376.

on other grounds, 602 U.S. 367 (2024); *Risk Evaluation and Mitigation Strategy (REMS) Single Shared System for Mifepristone 200 MG*, FDA (Jan. 2023), https://www.accessdata.fda.gov/drugsatfda_docs/rems/Mifepristone_2023_01_03_REMS_Full.pdf.

B

In 2022, a group of physicians providing pregnancy-related healthcare brought an APA challenge to the 2000 mifepristone approval, the 2016 Amendments, and the 2021 Non-Enforcement Decision. *See All. for Hippocratic Med. v. FDA*, 668 F. Supp. 3d 507, 560 (N.D. Tex. 2023), *vacated*, 117 F.4th 336 (5th Cir. 2024) (mem.). After the district court granted a preliminary injunction, our court affirmed in part, ruling plaintiffs were likely to win their challenge to the 2021 Non-Enforcement Decision. *See All. for Hippocratic Med. v. FDA* (*Alliance I*), No. 23-10362, 2023 WL 2913725, at *17–18, 17 n.5 (5th Cir. Apr. 12, 2023); *Alliance II*, 78 F.4th at 227, 247–51.[2] The Supreme Court reversed, however, on the grounds that the plaintiff physicians lacked standing. *Alliance III*, 602 U.S. at 396–97.

In September 2025, FDA began a comprehensive review of mifepristone, including the 2023 REMS. When announcing the review, FDA conceded the "lack of adequate consideration underlying the prior REMS approvals." The review is not complete—as of April 2026, the agency reports it is still collecting data.[3]

[2] We also explained that the 2021 Non-Enforcement Decision "remains in force" because it was formalized by the 2023 REMS. *Alliance II*, 78 F.4th at 248.

[3] *See Questions and Answers on Mifepristone for Medical Termination of Pregnancy Through Ten Weeks Gestation*, FDA, https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/questions-and-answers-mifepristone-medical-termination-pregnancy-through-ten-weeks-gestation.

C

In October 2025, the State of Louisiana and Rosalie Markezich (collectively, "Louisiana") challenged the 2023 REMS under the APA. The district court allowed mifepristone manufacturers Danco and GenBioPro (collectively, "Danco") to intervene as defendants.

Louisiana moved to preliminarily stay the 2023 REMS under 5 U.S.C. § 705. The district court declined, however. Despite finding Louisiana had standing, was likely to succeed on the merits, and was suffering irreparable harm, the court found the balance-of-the-equities and public-interest factors favored denying a stay.

As to the equities, the court reasoned that FDA has a strong interest in continuing its scientific review of mifepristone and that the intervenor companies have a "substantial financial interest" in selling the drug. While acknowledging Louisiana's "great interest" in stopping the inflow of out-of-state mifepristone, the court thought the drug would "likely continue" to reach Louisianans regardless of a stay, like other illegal drugs. It also emphasized that Louisiana retained "many meaningful, boots-on-the-ground law enforcement mechanisms to mitigate its sovereign and financial harms while FDA completes its ongoing review."

As to the public interest, the court acknowledged that the public has no interest in continuing unlawful agency action and that FDA "does not defend its decision-making [in the 2023 REMS] on the merits." Nonetheless, the agency desired "a stay [of the case] to complete a fulsome review" of mifepristone. The court also noted "multiple parallel lawsuits" challenging the 2023 REMS and worried about the "substantial risk of inconsistent judicial outcomes." Finally, while again acknowledging the "deficiencies" in the 2023 REMS, the court believed it was "ill-equipped"

to evaluate the validity of an in-person dispensing requirement, "particularly where FDA has thus far failed to even collect the data necessary" to do so.

The court therefore declined Louisiana's request to stay the 2023 REMS. Instead, the court granted FDA's request to stay the entire case so the agency could "complete its review." The court warned, though, that "FDA has an obligation to act with all deliberate speed to review its past actions and complete a thorough analysis that addresses the deficiencies it has acknowledged."

Louisiana appealed and moved for a stay of the 2023 REMS pending appeal under 5 U.S.C. § 705.

II

Under 5 U.S.C. § 705, courts may "issue all necessary and appropriate process to postpone the effective date of an agency action or to preserve status or rights pending conclusion of the review proceedings."

A party seeking a stay under § 705 must show (1) it is strongly likely to succeed on the merits; (2) it will be irreparably harmed without a stay; (3) its harm is not outweighed by harm to other parties; and (4) the public interest favors a stay. *Wages & White Lion Invs., L.L.C. v. FDA*, 16 F.4th 1130, 1135–36 (5th Cir. 2021); *Tex. League of United Latin Am. Citizens v. Hughs*, 978 F.3d 136, 143 (5th Cir. 2020). The first two factors are the most critical. *Valentine v. Collier*, 956 F.3d 797, 801 (5th Cir. 2020) (per curiam).

III

Louisiana contends the district court misapplied the § 705 stay factors. Specifically, it argues the court abused its discretion in ruling that the last two factors outweighed its successful showing on the first two. FDA's response does not address the merits—*i.e.*, whether its removal of mifepristone's in-person dispensing requirement was arbitrary and

capricious. Instead, it argues that Louisiana should have first asked the district court for a stay. It then argues, contrary to the district court's ruling, that Louisiana lacks standing. For its part, Danco argues Louisiana lacks standing, failed to administratively exhaust its claims, and fails all four stay factors.

We address each of these arguments in turn.

A

We first address the two threshold arguments that Louisiana (1) should have first asked the district court for a stay and (2) failed to administratively exhaust its claims. Both arguments fail.

1

FDA contends that, under Federal Rule of Appellate Procedure 8, Louisiana was required to first ask the district court for a stay pending appeal. *See* FED. R. APP. P. (FRAP) 8(a)(1)(A), (C). We disagree. While that it is the "ordinar[y]" practice, *see* FRAP 8(a)(1), it is not required if "moving first in the district court would be impracticable," *see id.* FRAP 8(a)(2)(A)(i). Here, it was.

Not only had the district court already denied Louisiana's motion to stay the 2023 REMS under § 705, but the court had also stayed the entire case pending completion of FDA review. Given that, it would have been "pointless" to ask the district court to stay the 2023 REMS pending appeal. *Whole Woman's Health v. Paxton*, 972 F.3d 649, 653 (5th Cir. 2020); *see also, e.g.*, *Homans v. City of Albuquerque*, 264 F.3d 1240, 1243 (10th Cir. 2001) ("[W]e have excused this requirement where another application to the district court would serve little purpose.").

Danco argues Louisiana failed to administratively exhaust its claims. "As a general rule, claims not presented to the agency may not be made for the first time to a reviewing court," *Wash. Ass'n for Television & Child. v. FCC*, 712 F.2d 677, 680 (D.C. Cir. 1983), unless "resort to administrative remedies [would be] clearly useless," *Tesoro Refin. & Mktg. Co. v. FERC*, 552 F.3d 868, 874 (D.C. Cir. 2009) (alteration in original) (quotation omitted).

Our court previously rejected this argument in *Alliance I* and *II*. *See Alliance I*, 2023 WL 2913725, at *15–16; *Alliance II*, 78 F.4th at 255. True, those decisions were reversed on standing, *see Alliance III*, 602 U.S. at 396–97, but their reasoning on exhaustion was persuasive. As they concluded, these challenges were "properly exhausted," *Alliance I*, 2023 WL 2913725, at *15, because FDA's denials of citizen petitions discussed the 2021 Non-Enforcement Decision and "show[ed] that FDA was committed to implementing these changes," *Alliance II*, 78 F.4th at 255. Danco gives us no reason to think that, today, FDA would administratively stay the 2023 REMS, which formalized the 2021 decision. *Ibid.*

Accordingly, we reject the argument that Louisiana was required to administratively exhaust its claims before bringing this suit.

B

We turn to standing. Louisiana must show it "has suffered an injury traceable to the defendant which the court's judgment would likely redress." *Deanda v. Becerra*, 96 F.4th 750, 755 (5th Cir. 2024).

On appeal, FDA and Danco dispute the district court's ruling that Louisiana has standing. Specifically, they contend that by removing mifepristone's in-person dispensing requirement, the 2023 REMS caused no injury either to Louisiana's sovereignty or its treasury. We disagree.

First, sovereign injury. Louisiana has a "sovereign interest in the power to create and enforce a legal code." *Texas v. United States*, 809 F.3d 134, 153 (5th Cir. 2015) (quotation omitted).[4]

With certain exceptions, Louisiana law bans administering, prescribing, procuring, or selling a drug like mifepristone to end the life of an unborn human being. *See* LA. STAT. ANN. § 40:1061(C) (2022) ("No person may knowingly administer to, prescribe for, or procure for, or sell to any pregnant woman any medicine, drug, or other substance with the specific intent of causing or abetting the termination of the life of an unborn human being.").[5]

An avowed purpose of the 2023 REMS was to expand access to medication abortion. *See* Exec. Order No. 14076, 87 Fed. Reg. 42053 (July 8, 2022) (in the wake of *Roe*'s overruling, directing federal agencies to "expand access to . . . medication abortion" by "protect[ing] healthcare service delivery and promot[ing] access to . . . abortion"). Predictably, the regulation has had that effect in Louisiana, despite the fact that its laws ban the practice.

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[4] *See also Alfred L. Snapp & Son, Inc. v. P.R. ex rel. Barez*, 458 U.S. 592, 601 (1982) (explaining a state's "exercise of sovereign power over individuals and entities within the relevant jurisdiction . . . involves the power to create and enforce a legal code, both civil and criminal"); *Kentucky v. Biden*, 23 F.4th 585, 599 (6th Cir. 2022) (explaining national vaccine mandate "implicates states' power to make and enforce policies and regulations, as well as states' traditional prerogative to superintend their citizens' health and safety").

[5] *See also* LA. STAT. ANN. § 14:87.1(1)(a)(i) (2022) (defining "abortion" or "induced abortion" to include "[a]dministering, prescribing, or providing any abortion-inducing drug, potion, medicine, or any other substance, device, or means to a pregnant female"); *id.* § 14:87.1(2)(a) (defining "[a]bortion-inducing drug" as "any drug or chemical, or combination of drugs or chemicals, or any other substance when used with the intent to cause an abortion"); *id.* § 14.87.1(1)(b)(i)–(v) (excluding from definition of "abortion" various procedures, including for saving unborn child's or mother's life or for removing ectopic and medically futile pregnancies).

By ending the in-person dispensing requirement, FDA opened the door for mifepristone to be remotely prescribed to Louisiana women. The record shows that the policy now facilitates nearly 1,000 illegal abortions in Louisiana per month.

This evidence also easily shows causation and redressability. As the district court explained, "out-of-state medical providers" have responded to the 2023 REMS by "expanding mifepristone access to pro-life states like Louisiana in ways that [are] entirely predictable." That should surprise no one: after all, ensuring out-of-state medical providers could prescribe mifepristone to women in states that restrict abortion was a goal of the regulation. *See, e.g.*, *First Choice Women's Res. Ctrs., Inc. v. Davenport*, No. 24-781, slip op. at 12 (U.S. Apr. 29, 2026) (confirming "courts may make 'commonsense inferences' when assessing Article III standing, including inferences about 'third party behavior'" (quoting *Diamond Alt. Energy LLC v. EPA*, 606 U.S. 100, 116 (2025))). Finally, a decision in Louisiana's favor would redress this injury because mifepristone could no longer be remotely prescribed to Louisianans.

FDA and Danco counter that the 2023 REMS only makes it "more difficult to police" violations of Louisiana law. Not so. The policy does not merely "increase[] crime or disorder, or impose[] indirect compliance costs for state law enforcement." *Washington v. FDA*, 108 F.4th 1163, 1177 (9th Cir. 2024). Rather, the 2023 REMS sanctions and facilitates conduct with the express purpose of undermining Louisiana's legal restrictions on abortion. The regulation creates an effective way for an out-of-state prescriber to place the drug in the hands of Louisianans in defiance of Louisiana law.

In sum, the agency's 2023 REMS causes "federal interference with the enforcement of [Louisiana] law," which gives Louisiana standing to

challenge it. *Texas*, 809 F.3d at 153; *see also Wyoming ex rel. Crank v. United States*, 539 F.3d 1236, 1242 (10th Cir. 2008) ("injury-in-fact" shown when federal agency's legal interpretation "interfere[d] with Wyoming's ability to enforce its legal code"); *Maine v. Taylor*, 477 U.S. 131, 137 (1986) ("[A] State clearly has a legitimate interest in the continued enforceability of its own statutes.").

2

Next, financial injury. A State's "expenditures in providing emergency medical services" constitute an injury for standing purposes. *Texas v. United States*, 50 F.4th 498, 518 (5th Cir. 2022).

Louisiana identifies $92,000 it paid in Medicaid costs from two women who needed emergency care in 2025 from complications caused by out-of-state mifepristone. Such costs will almost certainly continue because nearly 1,000 women monthly—many of whom are on Medicaid—have mifepristone-induced abortions in Louisiana.

Confirming this, FDA's 2023 mifepristone label reports that 2.9 to 4.6 percent of women prescribed mifepristone *in-person* will require emergency care. *See Alliance I*, 2023 WL 2913725, at *10 (FDA's "own documents . . . prove that emergency room care is statistically certain in hundreds of thousands of cases"). Remotely dispensing the drug will only exacerbate those risks, as the district court found. *See* DC Dkt. No. 1-10 at 35 ("[T]he literature suggests there may be more frequent ED/urgent care visits related to the use of mifepristone when dispensed by mail . . . ."). Accordingly, Louisiana has shown that it suffers financial injury caused by the 2023 REMS.

Despite acknowledging that "Medicaid costs constitute an Article III injury," FDA and Danco argue that the relation between out-of-state mifepristone and Louisiana's costs is too attenuated. Both rely on *Alliance*

III, which held that the link between the challenged regulations and plaintiff doctors' monetary injuries was "too speculative or otherwise too attenuated." 602 U.S. at 390. That case is distinguishable, however.

As the Supreme Court explained in *Alliance III*, the doctors failed to prove that FDA's deregulation of mifepristone caused them to divert time from other patients or that it produced higher insurance costs. *Id.* at 390–91. But *Alliance III* had no reason to address whether the agency's actions would cause States to pay higher Medicaid costs. *Id.* at 391. Here, Louisiana showed that they do. Unlike the doctors in *Alliance III*, Louisiana provided hard evidence linking thousands of dollars in Medicaid costs to care stemming from out-of-state mifepristone. As the district court correctly held, that "alone [is] sufficient to establish Louisiana's standing."

* * *

In sum, on either theory Louisiana has shown it has standing to challenge the 2023 REMS.[6]

C

We turn to the § 705 factors.

1

First, likelihood of success on the merits. *Nken v. Holder*, 556 U.S. 418, 434 (2009). Louisiana must make a strong showing that the 2023 REMS was not "reasonable" or "reasonably explained." *FCC v. Prometheus Radio Project*, 592 U.S. 414, 423 (2021).

[6] We therefore need not consider whether Markezich also has standing. *See Biden v. Nebraska*, 600 U.S. 477, 489 (2023) ("If at least one plaintiff has standing, the suit may proceed.").

This factor plainly favors Louisiana and FDA does not contest it. To the contrary, as the district court explained, the agency "essentially acknowledged APA procedural deficits with respect to mifepristone" by "stating that [its] intention to review the mifepristone regulatory framework was precipitated by 'the lack of adequate consideration underlying the prior REMS approvals.'"

Based on the same defects, our court has previously concluded that FDA's actions here were likely unlawful. *See Alliance II*, 78 F.4th at 249–51; *Alliance I*, 2023 WL 2913725, at *16–18. That reasoning squarely applies to the 2023 REMS and we briefly summarize it.

First, in relaxing mifepristone's in-person dispensing requirement, FDA gave "dispositive weight" to the lack of adverse-event data in a reporting system (known as "FAERS"). *Alliance II*, 78 F.4th at 249. The problem? FDA had previously eliminated the requirement to report mifepristone's adverse events to FAERS. *Ibid.* Obviously, "[i]t's unreasonable for an agency to eliminate a reporting requirement for a thing and then use the resulting absence of data to support its decision." *Ibid.* (quoting *Alliance I*, 2023 WL 2913725, at *17).[7]

Second, FDA "relied on various literature relating to remote prescription of mifepristone—despite FDA's admission that the literature did not affirmatively support its position." *Alliance II*, 78 F.4th at 250. The

[7] Danco points out that federal law requires manufacturers report to FDA known adverse events. *See* 21 U.S.C. § 355(k)(1); 21 C.F.R. §§ 314.80, 314.81. We rejected this argument in *Alliance II*. *See* 78 F.4th at 247, 249–50. In short, Danco's reporting requirements are "significantly different than the ones that were removed," insofar as Danco "had no direct relationship with Mifeprex patients and little ability to track [adverse] events." *Id.* at 247. As *Alliance II* concluded, "Danco's residual reporting requirements do not cure this APA violation." *Ibid.*; *see also id.* at 250 (explaining that "Danco's data was exactly the same as the data FDA obtained from FAERS").

agency explained the literature was "not adequate on [its] own to establish the safety of the model of dispensing mifepristone by mail." *Ibid.* (quotation omitted). This is a textbook example of arbitrary and capricious agency action. *See, e.g.*, *Motor Vehicle Mfrs. Ass'n of the U.S., Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 52 (1983) ("The agency must explain the evidence which is available, and must offer a 'rational connection between the facts found and the choice made.'" (quoting *Burlington Truck Lines, Inc. v. United States*, 371 U.S. 156, 168 (1962))).

Accordingly, like the district court, we conclude Louisiana has strongly shown a likelihood of winning its APA challenge to the 2023 REMS.

2

Second, irreparable harm. *See Nken*, 556 U.S. at 434; *Louisiana v. Biden*, 55 F.4th 1017, 1033–34 (5th Cir. 2022).

We agree with the district court that Louisiana has shown it is suffering irreparable harm, largely for the same reasons Louisiana has shown injury for standing purposes.

As discussed, the 2023 REMS injures Louisiana by undermining its laws protecting unborn human life and also by causing it to spend Medicaid funds on emergency care for women harmed by mifepristone. Both injuries are irreparable.

Every abortion facilitated by FDA's action cancels Louisiana's ban on medical abortions and undermines its policy that "every unborn child is human being from the moment of conception and is, therefore, a legal person." LA. STAT. ANN. § 40:1061.1(A)(1) (2022). Once lost, that sovereign prerogative of protecting unborn life cannot be regained by legal

remedy. And because FDA "is entitled to sovereign immunity," *Alliance II*, 78 F.4th at 251, Louisiana's financial harms are also irremediable.

FDA's only response is that Louisiana cannot prevail on this factor because it lacks any "Article III injury." We have already rejected that argument, however.[8]

Accordingly, like the district court, we conclude that Louisiana has shown that it is irreparably harmed without a stay.

3

We turn to the balance-of-harms and public interest factors. *Nken*, 556 U.S. at 434. These factors "merge when the government opposes" a stay. *Airlines for Am. v. Dep't of Transp.*, 110 F.4th 672, 677 (5th Cir. 2024) (quotation omitted).

Louisiana argues the district court erred by finding its irreparable harms are outweighed by FDA's interest in continuing its review and Danco's financial interests in selling mifepristone. We agree.

Once again, our court has spoken persuasively to this point before. "[N]either the FDA nor the public has any interest in enforcing a regulation that violates federal law." *Alliance II*, 78 F4th at 251 (citing *Louisiana*, 55 F.4th at 1035). We have now three times found that the agency's progressive relaxation of mifepristone's guardrails likely lacked a basis in data and scientific literature. FDA itself now concedes the regulations were marred by "procedural deficits" and a "lack of adequate consideration." The public

[8] Danco argues Louisiana waited too long to sue and seek a stay. That is beside the point. Louisiana has shown the 2023 REMS causes it daily irreparable harm by undermining its laws and costing it irremediable Medicaid funds. "Those costs are ongoing . . . and more than sufficient to satisfy the irreparable harm standard in this circuit." *Career Colleges & Schs. of Tex. v. Dep't of Educ.*, 98 F.4th 220, 237 (5th Cir. 2024).

interest is not served by perpetuating a medical practice whose safety the agency admits was inadequately studied. Indeed, the public interest demands the opposite. *See Alliance II*, 78 F.4th at 253 (explaining "the public interest is disserved by a drug that does not afford adequate protections to its users"); *see also Hill Dermaceuticals, Inc. v. FDA*, 524 F. Supp. 2d 5, 12 (D.D.C. 2007) ("[T]he public interest weighs strongly in favor of preventing unsafe drugs from entering the market.").

For its part, Danco points to a stay's effect on its compliance costs and mifepristone profits. While we acknowledge a stay would impose costs on Danco, *cf. Alliance II*, 78 F.4th at 252, the company exaggerates by predicting a stay would destroy any "valid legal framework for distributing" the drug. To the contrary, a stay would only pause a method of prescribing mifepristone that began five years ago and was formally approved only three years ago. *Cf. Alliance I*, 2023 WL 2913725, at *20 (doubting that post-2016 deregulation was "so critical to the public given that the Nation operated—and mifepristone was administered to millions of women—without them for sixteen years following the 2000 Approval"). And, in any event, Danco's potential financial losses pale beside Louisiana's sovereign interest in its laws protecting the unborn and the public's interest in not exposing women to unsafe medical procedures.

The district court raised various concerns about the equities and public interest. We do not find that any of them tip the balance against Louisiana, however.

First, the district court cautioned it was "not a forum for resolving moral or policy disagreements" nor for adjudicating "scientific and medical judgments committed by Congress to an agency with specialized knowledge." All quite true. This case, however, does not ask courts to resolve such matters. Despite dealing with the charged subject of abortion, at

bottom the case is an APA challenge to a regulation, a task courts routinely undertake. *See, e.g.*, *Sw. Elec. Power Co. v. EPA*, 920 F.3d 999, 1013 (5th Cir. 2019) (explaining that, while courts may not second-guess an agency's "evaluation of complex scientific data," they must "ensure that the agency examined the relevant data and articulated a satisfactory explanation for its action" (quotations omitted)).

Second, the district court emphasized the importance of FDA's being able to "complete a fulsome review" and "proper science-driven evaluation" of mifepristone protocols. Again, quite true. However, this challenge involves the existing 2023 REMS, not FDA's ongoing review. Granting a stay would do nothing to prevent FDA from completing its review of mifepristone's safety protocols.

And consider what spurred that review: the agency's concession that its prior evaluation of mifepristone—including the 2023 REMS—was marred by "procedural deficits" and a "lack of adequate consideration." As Louisiana points out, it "makes no sense to deny preliminary relief on the grounds that agency action is so unlawful that the agency openly concedes a review is necessary." That would mean an agency could forestall judicial review of admittedly unlawful regulations merely by promising to review them in the future. And here FDA cannot even say when its review will conclude—perhaps over a year from now because it has not finished collecting data.[9]

Finally, the district court was concerned that, because "this case arises amid multiple parallel lawsuits across the country," there is "a

[9] *See Questions and Answers on Mifepristone for Medical Termination of Pregnancy Through Ten Weeks Gestation*, FDA, https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/questions-and-answers-mifepristone-medical-termination-pregnancy-through-ten-weeks-gestation.

substantial risk of inconsistent judicial outcomes on a question of nationwide importance." That risk is inevitable in such litigation, however. *See, e.g.*, *BST Holdings, L.L.C. v. OSHA*, 17 F.4th 604, 610 (5th Cir. 2021) (observing OSHA's covid vaccine mandate was challenged "in federal courts of appeals across the nation"). It does not absolve courts from deciding the cases before them. If disagreement emerges, we have a Supreme Court. *See NFIB v. OSHA*, 595 U.S. 109, 117 (2022) (agreeing with us that "the Secretary lacked authority to impose the [covid vaccine] mandate").

It is true, as the district court noted, that a § 705 stay "would, as a practical matter, have a nationwide effect." *See Alliance II*, 78 F.4th at 254 (explaining "a stay [under § 705] temporarily voids the challenged authority").[10] We do not agree, however, that this result is somehow in tension with *Trump v. CASA*, 606 U.S. 831 (2025), as the district court suggested. In *CASA*, the Supreme Court plainly said it was addressing only equitable relief and not remedies under the APA. *See id.* at 846 n.10 ("Nothing we say today resolves the distinct question whether the [APA] authorizes federal courts to vacate federal agency action.").

In sum, we conclude that the balance of equities and public interest weigh in Louisiana's favor.

IV

Accordingly, IT IS ORDERED that the motion to stay the 2023 REMS under 5 U.S.C. § 705 pending appeal is GRANTED.

IT IS FURTHER ORDERED that the alternative motion for injunction pending appeal is DENIED AS MOOT.

[10] *See also Career Colleges*, 98 F.4th at 255 ("Nothing in the text of Section 705, nor of Section 706, suggests that either preliminary or ultimate relief under the APA needs to be limited to [parties].").

United States Court of Appeals

FIFTH CIRCUIT
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May 01, 2026

MEMORANDUM TO COUNSEL OR PARTIES LISTED BELOW:

No. 26-30203 State of Louisiana v. FDA
USDC No. 6:25-CV-1491

Enclosed is the opinion entered in the case captioned above.

Sincerely,

LYLE W. CAYCE, Clerk

Christy Combel

By: _____
Christy M. Combel, Deputy Clerk
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