No.

In the Supreme Court of the United States

U.S. FOOD AND DRUG ADMINISTRATION, ET AL.,
PETITIONERS

v.

ALLIANCE FOR HIPPOCRATIC MEDICINE, ET AL.

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FIFTH CIRCUIT

APPENDIX TO THE PETITION FOR A WRIT OF CERTIORARI

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APPENDIX A

UNITED STATES COURT OF APPEALS
FOR THE FIFTH CIRCUIT

No. 23-10362

ALLIANCE FOR HIPPOCRATIC MEDICINE; AMERICAN ASSOCIATION OF PRO-LIFE OBSTETRICIANS & GYNECOLOGISTS; AMERICAN COLLEGE OF PEDIATRICIANS; CHRISTIAN MEDICAL & DENTAL ASSOCIATIONS; SHAUN JESTER, D.O.; REGINA FROST-CLARK, M.D.; TYLER JOHNSON, D.O.; GEORGE DELGADO, M.D., PLAINTIFFS-APPELLEES

v.

U.S. FOOD & DRUG ADMINISTRATION; ROBERT M. CALIFF, COMMISSIONER OF FOOD AND DRUGS; JANET WOODCOCK, M.D., IN HER OFFICIAL CAPACITY AS PRINCIPAL DEPUTY COMMISSIONER, U.S. FOOD AND DRUG ADMINISTRATION; PATRIZIA CAVAZZONI, M.D., IN HER OFFICIAL CAPACITY AS DIRECTOR, CENTER FOR DRUG EVALUATION AND RESEARCH, U.S. FOOD AND DRUG ADMINISTRATION; UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES; XAVIER BECERRA, SECRETARY, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, DEFENDANTS-APPELLANTS

v.

DANCO LABORATORIES, L.L.C., INTERVENOR-APPELLANT

Filed: Aug. 16, 2023

Appeal from the United States District Court
for the Northern District of Texas
USDC No. 2:22-CV-223

Before ELROD, HO, and WILSON, *Circuit Judges*.

JENNIFER WALKER ELROD, *Circuit Judge*:

This complicated administrative law appeal concerns the regulation of mifepristone, a drug used to cause abortion. The United States Food and Drug Administration approved mifepristone for use in 2000 under the brand name Mifeprex. At the same time, FDA imposed a number of conditions designed to prevent the drug from causing serious medical side effects. FDA amended those conditions in 2016, generally lightening the prior protections. It then approved a generic version in 2019. And in 2021, FDA announced that it would not enforce an agency regulation requiring mifepristone to be prescribed and dispensed in person. The agency ultimately removed that requirement from mifepristone's conditions for use.

The subject of this appeal is those four actions: the 2000 Approval, 2016 Amendments, 2019 Generic Approval, and 2021 Non-Enforcement Decision. They are challenged by the Alliance for Hippocratic Medicine—an association of doctors who research, teach, and advocate for ethical medical practices—several similar organizations, and several individual doctors. At bottom, the Medical Organizations and Doctors contend that FDA overlooked important safety risks in approving mifepristone and amending its restrictions. They assert that FDA's actions were unlawful under the Administrative Procedure Act.

The Organizations seek relief on behalf of their members, many of whom are OB/Gyns or emergency-room doctors. Many women face severe complications as a result of taking mifepristone. The Doctors allege that they are harmed when they treat those kinds of patients.

According to the Doctors, when they treat women who are experiencing complications after taking mifepristone, they are required to perform or complete an abortion, or otherwise required to participate in a process that facilitates abortion. They maintain that personally conducting those procedures violates their sincerely held moral beliefs. The Doctors also contend that treatment of mifepristone patients diverts time and resources away from their ordinary patients, causes substantial mental and emotional distress, and exposes them to heightened malpractice risk and increased insurance costs.

Seeking to prevent those alleged injuries, the Medical Organizations and Doctors moved for preliminary injunctive relief. The district court granted the motion, but rather than entering a traditional injunction, the court stayed the effective date of each of the challenged actions under 5 U.S.C. § 705. FDA appealed, as did Intervenor Danco Laboratories, LLC, the pharmaceutical company that distributes Mifeprex.

After extensive briefing and oral argument, we hold that the district court's stay order should be VACATED in part and AFFIRMED in part. We conclude that the Medical Organizations and Doctors' claim as to the 2000 Approval is likely barred by the statute of limitations. Accordingly, that component of the district court's order must be VACATED. This means that, until final judg-

ment, Mifeprex will remain available to the public under the conditions for use that existed in 2016.

We also VACATE the portion of the order relating to the 2019 Generic Approval because the Medical Organizations and Doctors have not shown that they are injured by that particular action. The generic version of mifepristone will also be available under the same conditions as Mifeprex.

We AFFIRM the components of the stay order that concern the 2016 Amendments and the 2021 Non-Enforcement Decision. Those agency actions—which generally loosen the protections and regulations relating to the use of mifepristone—will be stayed during the pendency of this litigation.

Finally, we note that our holding is subject to the prior order of the Supreme Court, which stayed the district court's order pending resolution of this appeal and disposition of any petition for writ of certiorari. *Danco Lab'ys, LLC v. All. for Hippocratic Med.*, 143 S. Ct. 1075 (2023) (mem.).

I. Background

This case arises under the Federal Food, Drug, and Cosmetic Act and related amendments. 21 U.S.C. ch. 9. The Department of Health and Human Services is charged with responsibility for implementing that law, and has delegated that obligation to FDA, its subagency. *Id.* § 393. The relevant events center on the particular duty of approving new drugs.

The approval process begins with a new drug application. *Id.* § 355(a). At this stage, it is the applicant's burden to prove that the proposed drug is safe and effective. The Act directs FDA to deny a new drug ap-

plication if, among other reasons, the applicant fails to include tests and data that show that the drug "is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling"; if "any other information" before FDA tends to show that the drug is not safe; or if "there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions for use prescribed, recommended, or suggested in the proposed labeling thereof." *Id.* § 355(d); *see* 21 C.F.R. § 314.125 (regulations expanding on those requirements).

Certain new drug applications may be designated for "accelerated approval." 21 C.F.R. § 314 subpt. H. This category applies to drugs treating "serious or life-threatening illnesses" and that "provide meaningful therapeutic benefit to patients over existing treatments." *Id.* § 314.500. The regulations also require FDA to impose "postmarketing restrictions" where necessary to ensure the drug is used safely. *Id.* § 314.520(a). Relevant here, the agency may mandate that the drug be administered at "certain facilities or [by] physicians with special training or experience," or that "specified medical procedures" be used. *Id.* § 314.520(a)(1), (a)(2).

FDA has explained that it will consider accelerated approval in two situations: where the agency can reliably estimate effectiveness using a "surrogate endpoint"; and where FDA "determines that a drug, effective to the treatment of a disease, can be used safely only if distribution or use is modified or restricted." 57 Fed. Reg. 58942, 58942 (Dec. 11, 1992). The agency has understood approval under Subpart H as also satisfying the general approval conditions provided by the Food, Drug,

and Cosmetic Act. *See id.* ("Drugs or biological products approved under these procedures will have met the requisite standards for safety and effectiveness under the [Act] . . . and, thus, will have full approval for marketing.").

In March of 1996, an entity known as the Population Council applied for FDA to approve mifepristone as a new drug, as part of a two-drug regimen designed to cause abortion.[1] The regimen works like this: First, a pregnant woman takes mifepristone, which suppresses the production of the hormone progesterone. Progesterone is needed for the pregnancy to continue; it prepares and maintains the uterine lining and stimulates the production of nutrients. After taking mifepristone, a patient takes misoprostol, which causes the uterus to cramp and expel its contents.

As part of the new drug application, the Population Council relied on three clinical studies, one conducted in the United States and two conducted in France. The studies purported to show that mifepristone was effective in the majority of cases, under the conditions imposed in each study. Those conditions included: an ultrasound to verify gestational age and diagnose ectopic pregnancies; that prescribing physicians have experience performing surgical abortions and have admitting privileges at a nearby hospital; that the testing facilities

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[1] The Population Council is a non-profit organization. Roussel Uclaf—the French pharmaceutical company that originally developed mifepristone—donated the American patent rights to the Population Council in 1994. The Population Council then granted Danco an exclusive license to manufacture and distribute Mifeprex in the United States.

be located close to a local hospital; and a four-hour monitoring period after taking misoprostol.

Although mifepristone was effective for most patients, the studies showed a trend of adverse events for some women. According to FDA, "surgical intervention" was required in 7.9% of the subjects in the American trial and 4.5% of subjects in the French trials. The reasons for surgery included heavy bleeding, infection, incomplete abortion, and ongoing pregnancy—meaning that the embryo or fetus continued to grow and develop.

FDA approved the new drug application in September 2000. The letters that the agency sent to the Population Council explained that the approval was "under Subpart H." FDA Approval Memorandum to Population Council at 6 (Sept. 28, 2000). This was for two reasons. First, FDA understood Mifeprex to be a drug that treated a serious or life threatening illness. *Id.* ("FDA has determined that the termination of an unwanted pregnancy is a serious condition within the scope of Subpart H. The meaningful therapeutic benefit over existing surgical abortion is the avoidance of a surgical procedure."). And second, Subpart H was required because Mifeprex could not be administered safely without imposing certain use restrictions. *Id.* ("Subpart H applies when FDA concludes that a drug product shown to be effective can be safely used only if distribution or use is restricted. . . . ").

In order to address the safety risks discussed above, FDA imposed several safeguards. First, it required the following black-box warning:

> If Mifeprex results in incomplete abortion, surgical intervention may be necessary. Prescribers should

> determine in advance whether they will provide such care themselves or through other providers. Prescribers should also give patients clear instructions of whom to call and what to do in the event of an emergency following administration of Mifeprex.

Approval Memorandum at 2. FDA also set the following controls on the use and prescription of Mifeprex:

- Only women whose pregnancies have a gestational age of forty-nine days or less are eligible;
- Only physicians can prescribe Mifeprex;
- All prescribing physicians must be able to assess gestational age, diagnose ectopic pregnancies, and "provide surgical intervention in cases of incomplete abortion or severe bleeding" or have arranged for another physician to provide such care;
- Prescription must occur in person; and
- Prescribers must report any "hospitalization, transfusion, or other serious event[] to the sponsor."

Id. at 1, 6. Finally, FDA required three doctor's-office visits, which are summarized as follows. The patient first takes mifepristone at the doctor's office. Three days later, she returns to the office to take misoprostol. Finally, the patient visits the doctor for a follow-up appointment, to determine whether the drug has successfully terminated the pregnancy and to screen for any adverse effects.

In August of 2002, the American Association of Pro-Life Obstetricians and Gynecologists (a party to the instant case) and several other similar organizations filed

a citizen petition, asking FDA to revoke its approval of mifepristone. *See* 21 C.F.R. § 10.30. The petition argued that mifepristone was not safe to use under the approved conditions. FDA reviewed the petition over the next fourteen years, ultimately denying it in 2016.

Two significant developments occurred in the meantime. First, in 2007, Congress amended the Food, Drug, and Cosmetic Act. *See* Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, tit. IX, § 901, 121 Stat. 823, 922-43. The amendment authorizes FDA to require a "risk evaluation and mitigation strategy" (REMS) if it determines that such a strategy is "necessary to ensure that the benefits of the drug outweigh the risks of the drug." 21 U.S.C. § 355-1(a)(1). The Act further allowed FDA to impose use restrictions via the REMS, like physician qualifications or reporting requirements. *Id.* § 355-1(f). The law also regarded all drugs approved before the Act as having an approved REMS. *See* Amendments Act § 909(b), 121 Stat. at 950 ("A drug that was approved before the effective date of this Act is . . . deemed to have in effect an approved risk evaluation and mitigation strategy under section 505-1 of the [Act].").

Then in 2011, FDA approved a REMS for mifepristone, imposing essentially the same restrictions as those FDA required when it approved Mifeprex in 2000. The REMS included four essential parts: a general summary, medication guide, prescriber agreement, and patient agreement. The medication guide explains how to use mifepristone and the risks associated with doing so. Mifepristone REMS at 4-6 (June 8, 2011). The prescriber agreement requires prescribers to promise to follow FDA's restrictions. *Id.* at 7-8. And

the patient agreement is a form that women must sign prior to using mifepristone; it obliges a patient to confirm that she meets the conditions for using mifepristone and acknowledge the risk of adverse events. *Id.* at 9-10. The mifepristone REMS was later amended in several respects. But its general form—the summary, medical guide, prescriber's agreement, and patient agreement—remains the same.

In 2016, FDA addressed Mifeprex in two respects. First, it denied the 2002 citizen petition, defending Mifeprex's safety and effectiveness as approved in 2000. Second, FDA approved a supplemental new drug application by Danco. That application requested a number of amendments to Mifeprex's REMS that FDA described as "major" and "interrelated." FDA Summary Review of 2016 Amendments at 5 (Mar. 29, 2016). Those changes 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 2, 26. FDA also pointed to a number of studies as evidence that Mifeprex would be safe and effective despite the amendments. *Id.* at 5-17.

Several years later, in 2019, the American Association of Pro-Life Obstetricians and Gynecologists and American College of Pediatricians filed a citizen petition challenging the 2016 Amendments. The petition generally requested that FDA restore the restrictions it imposed in 2000. Separately, in April of 2019, FDA approved an "abbreviated new drug application" by GenBioPro, Inc. for a generic version of mifepristone. To assess whether the drug was safe, the agency relied on the same data that it had relied upon for the 2000 Approval and 2016 Amendments regarding Mifeprex.

FDA then took several notable steps in 2021. In April, it announced that, in connection with the COVID-19 pandemic, the agency would not enforce the in-person dispensing requirement. Effectively, this allowed mifepristone to be prescribed remotely and sent via mail.

> [FDA] intends to exercise enforcement discretion during the COVID-19 [pandemic] 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 . . . [FDA] intends to exercise enforcement discretion during the COVID-19 [pandemic] 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.

FDA Letter to American College of Obstetricians and Gynecologists at 2 (Apr. 12, 2021). Later that year, FDA stated that it would adopt the change on a permanent basis. It then amended mifepristone's REMS (which applies to Mifeprex and the generic version) in January of 2023 to formalize the removal of the in-person dispensing requirement. FDA Br. at 11.

Finally, in December of 2021, FDA denied the 2019 citizen petition. According to FDA, the agency "undertook a full review of the Mifepristone REMS Program" and ultimately concluded that the drug was safe to use as amended. FDA Denial Letter to American College of Obstetricians and Gynecologists at 6 (Dec. 16, 2021). FDA specifically addressed its reasons for removing the in-person dispensing requirement. *Id.* at 25-36.

* * *

Against this background, the Medical Organizations and Doctors filed the instant complaint in district court. As relevant here, they alleged that each FDA action—the 2000 Approval, 2016 Amendments, 2019 Generic Approval, and 2021 Non-Enforcement Decision—violates the Administrative Procedure Act. Danco intervened to represent its interest as the manufacturer and distributor of Mifeprex in the United States. GenBioPro filed an *amicus* brief before this court but did not intervene or otherwise participate in the litigation, either in the district court or on appeal.

The Medical Organizations and Doctors filed a motion for a preliminary injunction. The district court held a hearing on the matter and granted the motion in part. *All. for Hippocratic Med. v. FDA*, __ F. Supp. 3d __, 2023 WL 2825871 (N.D. Tex. Apr. 7, 2023). For relief,

the court "stayed" the "effective date" of FDA's actions under 5 U.S.C. § 705.

FDA and Danco appealed and moved to stay the district court's order pending appeal. A motions panel of this court stayed the district court's order in part. *All. for Hippocratic Med. v. FDA*, No. 23-10362, 2023 WL 2913725 (5th Cir. Apr. 12, 2023). The panel stayed the portion of the district court's order relating to the 2000 Approval but did not disturb the other components of the order—regarding the 2016 Amendments, 2019 Generic Approval, and 2021 Non-Enforcement Decision. FDA and Danco then applied to the Supreme Court for a full stay of the district court's order, which was granted. *Danco Lab'ys, LLC v. All. for Hippocratic Med.*, 143 S. Ct. 1075 (2023) (mem.). The Court further provided that its stay of the district court's order would extend through the request for a petition for certiorari, if any:

> The April 7, 2023 order of the United States District Court for the Northern District of Texas, case No. 2:22-cv-223, is stayed pending disposition of the appeal in the United States Court of Appeals for the Fifth Circuit and disposition of a petition for a writ of certiorari, if such a writ is timely sought. Should certiorari be denied, this stay shall terminate automatically. In the event certiorari is granted, the stay shall terminate upon the sending down of the judgment of this Court.

Id. at 1075. The parties then fully briefed the ultimate question of whether the district court erred in issuing the stay order. Over thirty *amici* filed separate briefs on various topics. Oral argument was held on May 17, 2023, in which each side was allowed forty minutes to

present its argument, double the ordinary allotted time. We now consider the merits of the appeal.

II. Standing

Before considering the Medical Organizations and Doctors' claims, we must determine whether they have standing to assert them; an injunction is always improper if the district court lacked jurisdiction. *Cruz v. Abbott*, 849 F.3d 594, 598-99 (5th Cir. 2017). At this stage, it is the plaintiffs' burden to "make a 'clear showing' that they have standing to maintain the preliminary injunction." *Barber v. Bryant*, 860 F.3d 345, 352 (5th Cir. 2017) (quoting *Winter v. Nat. Res. Def. Council, Inc.*, 555 U.S. 7, 22 (2008)). And so the Medical Organizations and Doctors must satisfy the three basic elements of standing: injury, traceability, and redressability. *Lujan v. Defs. of Wildlife*, 504 U.S. 555, 560 (1992).

Standing in this appeal turns principally on the "injury" prong. The Medical Organizations and Doctors seek prospective relief, so they must establish future injury. To do that, they must show that "the threatened injury is 'certainly impending,' or there is a 'substantial risk' that the harm will occur." *Susan B. Anthony List v. Driehaus*, 573 U.S. 149, 158 (2014) (quoting *Clapper v. Amnesty Int'l USA*, 568 U.S. 398, 414 n.5 (2013)). As those standards indicate, the plaintiffs must show that the threat of future injury is sufficiently likely. The Supreme Court has thus rejected standing theories that rely "on a highly attenuated chain of possibilities" or that "require guesswork as to how independent decisionmakers will exercise their judgment." *Clapper*, 568 U.S. at 410, 413.

Even so, a "substantial risk" does not require that the threatened injury be "literally certain." *Id.* at 414 n.5; *see Lujan*, 504 U.S. at 564 n.2 (acknowledging that imminence "is concededly a somewhat elastic concept"); *Babbitt v. United Farm Workers Nat'l Union*, 442 U.S. 289, 298 (1979) (requiring that the plaintiff "demonstrate a realistic danger of sustaining a direct injury"); *Kolender v. Lawson*, 461 U.S. 352, 355 n.3 (1983) ("a credible threat"); *Frame v. City of Arlington*, 657 F.3d 215, 235 (5th Cir. 2011) ("a sufficiently high degree of likelihood"). Instead, a plaintiff seeking prospective relief need only show that future injury is "fairly likely." *Crawford v. Hinds Cnty. Bd. of Supervisors*, 1 F.4th 371, 376 (5th Cir. 2021); *accord Arcia v. Fla. Sec'y of State*, 772 F.3d 1335, 1341 (11th Cir. 2014) ("a realistic probability").

In assessing whether the threatened injury is fairly likely to occur, evidence of prior injury is especially probative. *See Crawford*, 1 F.4th at 376 (citing *Los Angeles v. Lyons*, 461 U.S. 95, 102 (1983)). Said another way, it "is not unduly conjectural" to use the "predictable effect" of the defendant's prior actions as a method to predict what will happen in the future. *Apple Inc. v. Vidal*, 63 F.4th 1, 17 (Fed. Cir. 2023) (quoting *Dep't of Com. v. New York*, 139 S. Ct. 2551, 2566 (2019)). Injuries that are "one-off" instances or "episodic" in nature do not move the needle much. *Crawford*, 1 F.4th at 376. But where the causes that produced the first injury remain in place, past-injury evidence bears strongly "on whether there is a real and immediate threat of repeated injury." *O'Shea v. Littleton*, 414 U.S. 488, 496 (1974); *see Crawford*, 1 F.4th at 376; *accord In re Navy Chaplaincy*, 697 F.3d 1171, 1176-77 (D.C. Cir. 2012) ("The prospect of future injury becomes significantly

less speculative where, as here, plaintiffs have identified concrete and consistently-implemented policies claimed to produce such injury.").

Finally, a group of plaintiffs need not show that more than one of them is likely to be injured. "If at least one plaintiff has standing, the suit may proceed." *Biden v. Nebraska*, 143 S. Ct. 2355, 2365 (2023) (citing *Rumsfeld v. F. for Acad. and Institutional Rts., Inc.*, 547 U.S. 47, 52 n.2 (2006)).

A. Associational Standing

1. Factual Predicate

The Medical Organizations and Doctors chiefly rely on associational standing. That is, the organizations contend that they have standing because their members are likely to sustain injuries as a result of FDA's actions. *See Hunt v. Wash. State Apple Adv. Comm'n*, 432 U.S. 333, 343 (1977). We conclude that the Medical Organizations and Doctors have made a "clear showing" that their members face injury with sufficient likelihood to support entering a preliminary injunction. *Barber*, 860 F.3d at 352.

The standing theory forwarded here rests on several basic premises, which are recited as follows. Mifepristone causes adverse effects for a certain percentage of the women who take it. Those adverse events are traceable to FDA because it approved the drug. And hundreds of the Medical Organizations' members are OB/Gyns or emergency-room doctors who treat women who experience severe adverse effects.

The Doctors are allegedly injured when they treat mifepristone patients. They offer four reasons why that is so. First, when a doctor treats a woman suffer-

ing from a mifepristone complication, he or she will often be required to perform or complete an abortion. And even if not, the doctor must participate in the medical treatment that facilitates an abortion. The Doctors allege that being made to provide this treatment conflicts with their sincerely held moral beliefs and violates their rights of conscience.

Second, treating mifepristone patients imposes mental and emotional strain above what is ordinarily experienced in an emergency-room setting. Third, providing emergency treatment forces the Doctors to divert time and resources away from their ordinary patients, hampering their normal practice. And fourth, the Doctors allege that mifepristone patients involve more risk of complication than the average patient, and so expose the Doctors to heightened risk of liability and increased insurance costs.

The Organizations reason that, given the millions of women who take mifepristone, the number of women who experience complications from taking the drug, and the high number of the Organizations' members who treat such women, their members are likely to continue to treat women suffering complications as a result of mifepristone. For the reasons listed above, providing that treatment will injure the Doctors. Thus, the Medical Organizations (via their members) are likely to be injured by FDA's actions. We first examine the evidence supporting those contentions.

a. Adverse Effects

FDA and Danco do not dispute that a significant percentage of women who take mifepristone experience adverse effects. From Mifeprex's initial approval to

subsequent amendments to the REMS, FDA has acknowledged that a certain fraction of patients would require surgery due to miscellaneous complications. Approval Memorandum at 1; *see also* 2011 Mifepristone REMS at 5 ("[A]bout 5-8 out of 100 women taking Mifeprex will need a surgical procedure to end the pregnancy or to stop too much bleeding."). Similarly, as explained by the motions panel, the required patient agreement discloses that "the treatment will not work" in "about 2 to 7 out of 100 women" who use mifepristone. *All. for Hippocratic Med.*, 2023 WL 2913725, at * 5.

To be sure, not every woman who experiences complications will present to the emergency room or require surgery and/or some other form of urgent care. But many will. According to the most updated REMS medication guide, in studies conducted in the United States, between 2.9% and 4.6% of women visited the emergency room after taking mifepristone. Mifeprex Prescribing Information at 8 tbl.2 (Jan. 2023). Some women experience especially severe conditions, such as sepsis (.02%) or hospitalization relating to abortion (.04% to .06%), and some women require a blood transfusion because of heavy bleeding (.03% to .05%). *Id.*[2]

The data FDA cited in its 2000 approval memo is similar. For the American clinical trial, surgical intervention was required for 7.9% of women (4.5% for the French studies). Approval Memorandum at 1. Of that

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[2] To be clear, we do not understand the Medical Organizations and Doctors' standing theory as applying only to women who present to the emergency room with severe complications such as those listed above. Rather, they also contend that they are injured by treating women who experience less urgent medical side-effects because such treatment forces the doctor to participate in the abortion process.

percentage, 1.2% of women required surgery due to heavy bleeding (.3% for France) and .12% required a blood transfusion (.11% for France). *Id.* FDA and Danco agree that over five million women have taken Mifeprex since it was first approved. These figures show that thousands of women, and as many as hundreds of thousands, have experienced serious adverse effects as a result of taking the drug, and required surgery or emergency care to treat those effects.

The Medical Organizations contend that their members treat women who suffer serious complications after taking mifepristone. These doctors submitted declarations testifying to their experience giving this sort of emergency care. For example, Dr. Christina Francis recounted an instance where a patient took mifepristone at approximately ten weeks gestation. The woman experienced serious complications and the doctor was forced to perform a surgical abortion because the drug failed to terminate the pregnancy:

> [T]he 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. Due to the amount of bleeding that she was experiencing and evidence of hemodynamic instability, however, 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 my partner also needed to call in a back-up physician to care for another critically ill patient. And because the pre-

> born 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.

Dr. Francis Declaration ¶ 13. Dr. Francis also testified to another example where a woman had developed an infection as a result of using mifepristone:

> After taking the chemical abortion drugs, [the patient] began having very heavy bleeding followed by significant abdominal pain and a fever. When I saw her in the emergency room, she had evidence of retained pregnancy tissue along with endometritis, an infection of the uterine lining. She also had acute kidney injury, with elevated creatinine. She required a dilation and curettage (D&C) surgery to finish evacuating her uterus of the remaining pregnancy tissue and hospitalization for intravenous (IV) antibiotics, IV hydration, and a blood transfusion.

Id. ¶ 12.[3] Dr. Ingrid Skop also testified to caring for many women experiencing severe complications due to mifepristone:

> In my practice, I have cared for at least a dozen women who have required surgery to remove retained pregnancy tissue after a chemical abortion. Sometimes this includes the embryo or fetus, and

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[3] At oral argument, Defendants discounted the relevance of this instance because the patient obtained mifepristone from outside of the country. Mifeprex is only marketed and distributed in the United States, so the incident almost certainly did not involve FDA approved Mifeprex. We agree that the evidence is not as probative as other examples—discussed below—that involve brand name mifepristone. But the incident still supports the proposition that mifepristone sometimes causes severe adverse events.

> sometimes it is placental tissue that has not been completely expelled. I have cared for approximately five women who, after a chemical abortion, have required admission for a blood transfusion or intravenous antibiotics or both.
>
> For example, in one month while covering the emergency room, my group practice admitted three women to the hospital. Of the three women admitted in one month due to chemical abortion complications, one required admission to the intensive care unit for sepsis and intravenous antibiotics, one required a blood transfusion for hemorrhage, and one required surgical completion for the retained products of conception (*i.e.*, the doctors had to surgically finish the abortion with a suction aspiration procedure).

Dr. Skop Declaration ¶¶ 17-18, 22. She also described one occurrence where a woman's mifepristone prescriber did not offer surgical care in response to heavy bleeding. That, in turn, required Dr. Skop to perform the follow-up surgical procedure:

> In my office, I treated one young woman who had been bleeding for six weeks after she took the chemical abortion drugs given to her by a doctor at a Planned Parenthood clinic. After two follow-ups at Planned Parenthood, during which she was given additional misoprostol but not offered surgical completion, she presented to me for help. I performed a sonogram, identified a significant amount of pregnancy tissue remaining in her uterus, and performed a suction aspiration procedure to resolve her complication.

Id. ¶ 23. Dr. Nancy Wozniak also described a serious complication in detail, in which the patient was at risk of bleeding to death:

> One of my patients, who was about nine weeks pregnant, had previously been treated by hospital staff for a pulmonary embolism with anti-coagulants. She was advised that she could not seek a chemical abortion because it was contraindicated due to the medications; yet the woman left the hospital and sought an abortion at Planned Parenthood of Indiana.
>
> The woman was given mifepristone by the doctor at Planned Parenthood and took the drug. The woman called an Uber for a ride home from Planned Parenthood. The woman began to experience bleeding and other adverse side effects from the mifepristone. The woman's Uber driver did not take her home because she was so ill and instead brought her to the hospital's emergency department.
>
> At the hospital, the woman came under my care. The woman had not yet taken the second abortion drug, misoprostol. I treated the patient for the adverse effects she suffered and told her not to take the misoprostol given to her by Planned Parenthood because of the grave risk that she could bleed out and die. The woman had a subsequent ultrasound, which showed that her unborn child was still alive. I advised the internists treating this patient to avoid administering certain medications that could harm the patient and her unborn child.

Dr. Wozniak Declaration ¶ 24. The risk of complications, the Medical Organizations say, is only heightened in the case of ectopic pregnancy. Dr. Skop testified

about the dangers of taking mifepristone under that condition:

> [A]pproximately 2% of pregnancies are ectopic pregnancies, implanted outside of the uterine cavity. Chemical abortion drugs will not effectually end an ectopic pregnancy because they exert their effects on the uterus, which leaves women at risk of severe harm from hemorrhage due to tubal rupture, in need of emergent surgery or potentially at risk of death. Failure to perform an ultrasound prior to prescribing abortion drugs will cause some women to remain undiagnosed and at high risk for these adverse outcomes.

Dr. Skop Declaration ¶ 29; *see also* Dr. Barrows Declaration ¶ 18.

According to the Medical Organizations and Doctors, these are examples of medical cases that occur across the county. The occurrences extend not just to the declarants, they say, but to all of the Organizations' members who are doctors. The Organizations offered testimony from representatives of the American College of Pediatricians, American Association of Pro-Life Obstetricians and Gynecologists, Christian Medical and Dental Associations, and Catholic Medical Association —each of whom explained that their membership includes thousands of doctors and hundreds of OB/Gyns and emergency-room doctors. *See* Dickerson Declaration ¶¶ 3, 13; Dr. Harrison Declaration ¶ 8; Dr. Barrows Declaration ¶ 5; Dr. Van Meter Declaration ¶ 8. Given the large number of women who experience serious medical complications due to mifepristone, and the large number of association members who are emergency-room doctors, the Medical Organizations argue, it is highly likely that one or more of their members will be re-

quired to provide emergency care to a mifepristone patient in the near future.

b. Doctors' Injuries

The Medical Organizations and Doctors present evidence of four ways they are injured by providing emergency care to women who used mifepristone. First, that treatment violates their conscience rights, putting them in a position where they must perform or complete an abortion even though doing so is contrary to their moral beliefs. As described by one doctor:

> The FDA's expansion of chemical abortion . . . harms my conscience rights because it could force me to have to surgically finish an incomplete elective chemical abortion. I object to abortion because it ends a human life. My moral and ethical obligation to my patients is to promote human life and health. But the FDA's actions may force me to end the life of a human being in the womb for no medical reason.

Dr. Skop Declaration ¶ 34. And multiple doctors testified that others they knew have been required to complete a failed chemical abortion against their consciences, or to provide related care. Dr. Francis Declaration ¶ 13; *cf.* Dr. Barrows Declaration ¶ 26.

Second, treating mifepristone patients imposes considerable mental and emotional stress on emergency-room doctors. This is due to the unique nature of chemical abortions, which, according to the plaintiff-doctors, frequently cause "regret" or "trauma" for the patients and, by extension, the physicians. Alliance Br. at 18. Dr. George Delgado testified that his work with such patients is "some of the most emotionally taxing work I have done in my career." Dr. Delgado Declaration

¶ 14; *see also* Dickerson Declaration ¶ 14; Dr. Skop Declaration ¶ 33; Dr. Wozniak Declaration ¶ 17.

Third, the Doctors are injured because they must divert time and resources away from their ordinary practice to treat mifepristone patients. In particular, the Doctors describe this treatment as often requiring extended physician attention, blood for transfusions, and other hospital resources. As one doctor testified:

> When I must perform surgery [for] complications from chemical abortions, this takes attention away from my other patients. As a hospitalist, I am often supervising multiple laboring patients on labor and delivery. When I am called to the operating room to address an emergency resulting from chemical abortion, this necessarily means I may not be immediately available if an emergency should occur with one of my laboring patients.

Dr. Skop Declaration ¶ 32; *see also* Dr. Francis Declaration ¶ 12 ("I spent several hours with [my patient] the day of her surgery/hospital admission, keeping me from my primary patient responsibilities in the labor and delivery unit and requiring me to call in an additional physician to help cover those responsibilities."); Dr. Harrison Declaration ¶ 30 ("Patients who suffer complications from chemical abortions require significantly more time and attention from providers than the typical OB/Gyn patient requires."). This diversion of resources, the Doctors say, directly harms their medical practices. *See* Dr. Harrison Declaration ¶¶ 27-30.

Fourth, such patients involve more risk than the average emergency room patient, which exposes the Doctors to greater malpractice liability and increased in-

surance costs. *See* Dr. Barrows Declaration ¶ 23 (testifying that providing emergency treatment to women suffering complications because of taking mifepristone puts doctors in "riskier, emergent medical situations"); Dr. Jester Declaration ¶ 20 ("These situations are naturally higher risk for both the patient and for the physician providing care."). The more mifepristone patients the Doctors treat, the higher their liability and greater their injury. *See* Dr. Barrows Declaration ¶¶ 21-24; Dr. Jester Declaration ¶¶ 20-21; Dr. Johnson Declaration ¶ 15. Having examined the factual basis for the Medical Organizations and Doctors' claims, we now answer the question of whether they have associational standing to assert those claims.

2. Analysis

a. Imminent Injury

We conclude that the Medical Organizations and Doctors have made a "clear showing" of associational standing. *Barber*, 860 F.3d at 352. To begin, it is "fairly likely" that the Doctors—both those who testified and those who are members of the Medical Organizations but did not testify—will continue treating women who experience severe complications after taking mifepristone. *Crawford*, 1 F.4th at 376. FDA's own data shows that a definite percentage of women who take mifepristone will require emergency-room care, be it a blood transfusion, a surgery to complete a failed abortion or ongoing pregnancy, or some other complication. The data further shows that millions of women take mifepristone. And the Medical Organizations testified that hundreds of their members are OB/Gyns and emergency-room doctors who care for women in these circumstances. The Medical Organizations and Doctors

therefore face a "substantial risk" of future injury. *Susan B. Anthony List*, 573 U.S. at 158.

That risk is supported by the fact that many Doctors have already been required to treat patients experiencing complications due to mifepristone. *Lyons*, 461 U.S. at 102. These are not merely "one-off" instances. *Crawford*, 1 F.4th at 376. On the contrary, FDA's data and the Doctors' testimony show that women will continue to present to the emergency room after taking mifepristone, requiring urgent treatment. That trend is not speculative—it is "predictable" and "consistent[]." *Vidal*, 63 F.4th at 17; *In re Navy Chaplaincy*, 697 F.3d at 1176. And it does not matter that the foundation of the Doctors' standing rests, in part, on "choices made by independent actors." *Lujan*, 504 U.S. at 562. That concern is alleviated where, as here, "third parties will likely act in predictable ways." *Dep't of Com.*, 139 S. Ct. at 2566.

It is worth repeating that the Medical Organizations and Doctors are not required to show that it is "literally certain" that they will be injured. *Clapper*, 568 U.S. at 414 n.5. They need only show a "substantial risk" that injury will occur. *Susan B. Anthony List*, 573 U.S. at 158; *see also United Farm Workers*, 442 U.S. at 298 ("a realistic danger"); *Kolender*, 461 U.S. at 356 n.3 ("a credible threat"); *Arcia*, 772 F.3d at 1341 ("a realistic probability"). At this preliminary-injunction stage, they have carried their burden. *All. for Hippocratic Med.*, 2023 WL 2913725, at *8.

FDA and Danco's primary objection to the Medical Organizations and Doctors' standing theory is that it is speculative and inconsistent with the Supreme Court's decision in *Summers v. Earth Island Institute*, 555 U.S.

488 (2009). We disagree. For one thing, testimony was offered from multiple doctors who have personally given emergency care to women suffering complications from mifepristone. Dr. Francis Declaration ¶¶ 12-13; Dr. Skop Declaration ¶¶ 17-18, 22; Dr. Jester ¶ 17. Given those prior instances, and given mifepristone's continued availability, the Medical Organizations reason that these members are reasonably likely to be injured again. The record amply supports that claim.

Moreover, it is not speculative to base standing on the likelihood that some members of a discrete group, but not all, will be injured. To be sure, the record must be specific enough to establish that a group of members who claim future injury are really at risk. But the evidence before us meets that standard. The Medical Organizations and Doctors have proven up each link in the chain of causation—that a percentage of women who take mifepristone will suffer serious medical complications; that hundreds of the Medical Organizations' members are physicians who treat patients in those circumstances; that many of the Doctors have in fact treated such patients; and that providing such treatment causes the Doctors to violate their rights of conscience, sustain mental and emotional distress, divert time and resources away from their ordinary practice, and incur additional liability and insurance costs. Contrary to what FDA and Danco argue, the conclusion the Doctors draw from that data is not speculative.

And the Medical Organizations' standing argument does not conflict with *Summers*. The problem in that case was *not* that plaintiffs' standing theory was invalid. It was that the organizational plaintiffs failed to prove that their members would be injured.

Summers concerned parks administered by the federal Forest Service. The Forest Service issued a regulation allowing it to sell burned timber and conduct fire-remediation activities on certain low-acreage lots without the ordinary notice and comment procedures. Various environmental organizations sued on behalf of their members, asserting recreational injury based on their members' professed intent to visit one of the hundreds of parks that might be affected by the new Service regulation. 555 U.S. at 490-92. Their primary evidence was an affidavit executed by one member who had visited a park already subject to fire-remediation activities, and who intended to visit the park again. The Service conceded that this plaintiff had standing, but the parties settled the dispute as to the particular park, and so it was "not at issue" once the case was before the Supreme Court. *Id.* at 491 (quoting *Earth Island Inst. v. Pengilly*, 376 F. Supp. 2d 994, 999 (E.D. Cal. 2005)).

The plaintiffs attempted to continue their challenge to the regulation, asserting that their other members were statistically likely to travel to one of the many parks that would likely be affected by the regulation. To be sure, the majority expressed skepticism with that theory. *See id.* at 497 (criticizing the dissent's "hitherto unheard-of test for organizational standing: whether . . . there is a statistical probability that some of [the plaintiffs'] members are threatened with concrete injury"). But its bigger concern was that plaintiffs failed to *prove* their claims: they lacked evidence of the number of association members who intended to visit the parks, and when:

> A major problem with the dissent's approach is that it accepts the organizations' self-descriptions of their membership, on the simple ground that "no one denies" them. But it is well established that the court has an independent obligation to assure that standing exists, regardless of whether it is challenged by any of the parties.

Id. at 499. A primary reason for the lack of evidence was the majority's decision to not consider several affidavits offered after the district court entered judgment —affidavits that would have made the required showing. *See id.* at 495 n.* (declining to consider the affidavits); *cf. id.* at 508-09 (Breyer, J., dissenting) (arguing that the Court should consider them). Without those affidavits, the majority understood itself as not having evidence of any other member's injury:

> In part because of the difficulty of verifying the facts upon which such probabilistic standing depends, the Court has required plaintiffs claiming an organizational standing to identify members who have suffered the requisite harm—surely not a difficult task here, when so many thousands are alleged to have been harmed.

Id. at 499. This understanding of *Summers* is reinforced by the Court's recent decision in *Department of Education v. Brown*, 143 S. Ct. 2343 (2023). There, the Court reiterated its view that no plaintiff had shown that he or she actively planned to visit the sites at issue. *See id.* at 2354 n.3 ("[N]o plaintiff in *Summers* had standing because none had alleged specific plans to observe nature in one of the areas at issue. . . . ").

Summers does not stand for the proposition that courts must categorically reject standing when a plain-

tiff alleges that a defendant's action puts hundreds of association members at risk of future injury. It stands for the proposition that courts must treat such assertions with caution. The standard for making this showing is high, but the Medical Organizations and Doctors have met it. They have provided multiple examples of organization members who sustained the exact harm they say will recur. They have explained that the conditions producing that harm remain in place. And they have testified to having hundreds of members who are reasonably likely to be harmed. At this stage, that is enough.

b. Cognizable Injury

In addition to being sufficiently imminent, threatened injuries must also be legally cognizable. *TransUnion LLC v. Ramirez*, 141 S. Ct. 2190, 2204-07 (2021); *Lujan*, 504 U.S. at 562. The injuries here are. To begin, economic harm—like damage to one's business interest—is a quintessential Article III injury. *TransUnion*, 142 S. Ct. at 2204; *see, e.g.*, *Greater Phila. Chamber of Com. v. City of Philadelphia*, 949 F.3d 116, 131 (3d Cir. 2020) (recognizing that businesses had standing to challenge local ordinance, which would hamper hiring and salary decisions). The Doctors therefore sustain a concrete injury when they are forced to divert time and resources away from their regular patients. Dr. Skop Declaration ¶ 32; Dr. Francis Declaration ¶ 12; Dr. Harrison Declaration ¶¶ 27-30; *see also All. for Hippocratic Med.*, 2023 WL 2913725, at *6-7. And by the same token, the Doctors sustain a concrete injury when mifepristone patients expose them to greater liability and increased insurance costs. Dr. Barrows Declaration

¶¶ 21-24; Dr. Jester Declaration ¶¶ 20-21; Dr. Johnson Declaration ¶ 15.

The Medical Organizations and Doctors also face a concrete injury when they are forced to choose between following their conscience and providing care to a woman experiencing complications as a result of taking mifepristone. As recounted above, evidence was offered of a doctor who personally gave care in these circumstances. Dr. Skop Declaration ¶ 17 ("In my practice, I have cared for at least a dozen women who have required surgery to remove retained pregnancy tissue after a chemical abortion. Sometimes this includes the embryo or fetus, and sometimes it is placental tissue that has not been completely expelled."). Another doctor testified about her partner, who experienced the same thing. Dr. Francis Declaration ¶ 13 ("Due to the amount of bleeding . . . my partner had no choice but to perform an emergency D&C. . . . 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."). And other doctors testified of fear that they or fellow physicians will be forced into similar situations. Dr. Barrows Declaration ¶ 26; Dr. Skop Declaration ¶ 34; *cf.* Dickerson Declaration ¶ 16.

FDA and Danco do not dispute that the Medical Organizations and Doctors' conscience injury is cognizable. But they defend FDA's actions on the ground that federal law would allow the Doctors to refuse care based on a conscientious objection. FDA Br. at 26; Danco Br. at 21 (citing 42 U.S.C. §§ 238n, 300a-7(c), (d)). The Medical Organizations and Doctors respond by

pointing out that the federal government has recently taken a contrary position. That is, in July 2022, the Department of Health and Human Services issued a guidance document that interprets the Emergency Medical Treatment and Active Labor Act to require hospitals to provide care to, among others, a woman with an "incomplete medical abortion," irrespective of objections of conscience. Reinforcement of EMTALA Obligations Specific to Patients Who Are Pregnant or Are Experiencing Pregnancy Loss, at 6, Centers for Medicare & Medicaid Services (July 11, 2022). A district court has enjoined that guidance, and an appeal is proceeding before this court. *Texas v. Becerra*, 623 F. Supp. 3d 696 (N.D. Tex. 2022) (entering preliminary injunction); *Texas v. Becerra*, No. 5:22-CV-185, 2023 WL 2467217 (N.D. Tex. Jan. 10, 2023) (final judgment and permanent injunction).

At oral argument, counsel for FDA disputed that EMTALA binds individual doctors, arguing instead that the obligation to provide abortion-related care runs to hospitals. That is, individual doctors may assert conscience objections so long as one doctor at the hospital can provide the required care. This raises the question of what would happen if no other doctor were available—a situation that seems particularly likely in smaller clinics. But setting that issue to the side, counsel's argument appears to conflict with the Government's position on appeal in the *Texas* case. *See* Br. for Appellants at 25, *Texas v. Becerra* (5th Cir. May 1, 2023) (No. 23-10246) ("EMTALA requires *doctors* to offer abortion care when that care is the necessary stabilizing treatment for an emergency medical condition.") (emphasis added); *id.* at 27 ("[W]hen pregnant women come to a Medicare-funded hospital with an emergency

medical condition, EMTALA obligates the treating physician to provide stabilizing treatment, including abortion care.") (quoting *United States v. Idaho*, 623 F. Supp. 3d 1096, 1109 (D. Idaho 2022)).

We conclude that the federal laws Defendants cite do not alleviate the Doctors' conscience injury, at least for purposes of this preliminary posture. The inconsistencies between the Government's position in *Texas v. Becerra* and FDA's position here tend to rebut the notion that Doctors are free to refuse treatment to mifepristone patients.

We next address the Doctors' argument that they will suffer an independent injury by way of the "enormous stress and pressure" that is involved with treating women suffering complications from taking mifepristone. Dr. Wozniak Declaration ¶ 17. They maintain that FDA's actions cause women to present at the emergency room with complications that involve a unique level of trauma and distress, due to the high amount of emotional and physical strain often associated with the experience. Dr. Delgado Declaration ¶ 14; Dickerson Declaration ¶ 14; Dr. Skop Declaration ¶ 33.

It is true that the Supreme Court has interpreted Article III to recognize injuries that "significantly affect[]" a plaintiff's "quality of life." *Sierra Club v. Morton*, 405 U.S. 727, 734-35 (1972). And several of our sister circuits acknowledge standing that is predicated on "emotional or psychological harm." *Maddox v. Bank of N.Y. Mellon Tr. Co.*, 19 F.4th 58, 65 (2d Cir. 2021) (quoting *TransUnion*, 141 S. Ct. at 2211 n.7); *see also Clemens v. ExecuPharm Inc.*, 48 F.4th 146, 155 (3d Cir. 2022) (same). However, the mental and emotional stress shown here is best understood as additional to

the Doctors' conscience injuries, not independent from them. The threat of being forced to violate a sincerely held moral belief is cognizable at least in part because the event would involve acute emotional and psychological harm. *Maddox*, 19 F.4th at 65; *Clemens*, 48 F.4th at 155. The emotional and mental strain of which the Doctors testify is of the same nature, albeit of an arguably lesser magnitude. In this way, the "enormous stress and pressure" that the Medical Organizations and Doctors cite augment the Doctors' conscience injuries, but does not provide a separate basis for Article III standing.[4]

Danco argues that the Medical Organizations and Doctors' standing argument is "limitless," and worries that its logic would allow doctors to challenge firearm laws based on the stress involved with treating gunshot victims. Danco Br. at 22-23 (citing *E.T. v. Paxton*, 41 F.4th 709, 721 (5th Cir. 2022)). But we see several limits. Foremost is the rigorous evidence needed to prove traceability and redressability. The plaintiffs in Danco's hypothetical would lack standing unless they could prove that a particular law caused there to be more gunshot victims, and that enjoining enforcement of the law would cause there to be fewer. That is a tall order, to say the least. Equally significant is the requirement that a plaintiff be threatened with injury akin to being forced to violate his or her sincerely held conscience beliefs. That sort of injury will be absent except in the most exceptional cases. We do not think

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[4] We understand the Doctors' conscience injuries as being supported by longstanding precedent of the Supreme Court and this court. We thus do not discuss our colleague's thoughtful comments on other types of injuries that may be cognizable. *Post* at 67-70.

that our holding will open the floodgates to the litigation Danco describes.

c. Traceability

Standing to challenge mifepristone's approval does not necessarily include standing to challenge FDA's subsequent actions. That is so because "standing is not dispensed in gross; rather, plaintiffs must demonstrate standing for each claim that they press and for each form of relief that they seek." *TransUnion*, 141 S. Ct. at 2208. As we have said many times, standing proceeds claim by claim. *E.g.*, *In re Gee*, 941 F.3d 153, 170-71 (5th Cir. 2019); *Friends of St. Frances Xavier v. FEMA*, 658 F.3d 460, 466 (5th Cir. 2011). The Medical Organizations and Doctors are correct, then, to acknowledge that they must show "harms to the plaintiff doctors and associations [that] flow from each of the relevant FDA actions." Alliance Br. at 22.

i. 2016 Amendments

The Medical Organizations and Doctors contend that the 2016 Amendments will increase the number of women who suffer complications as a result of taking mifepristone. That is so for three reasons, they say. First, the risk of complication increases with gestational age, and the Amendments increase the maximum permissible age from forty-nine days to seventy days. *See* Dr. Skop Declaration ¶ 28 (asserting that taking mifepristone at later stages of gestation increases the chance of "complications due to the increased amount of tissue, leading to hemorrhage, infection and/or the need for surgeries or other emergency care"); *see also* Dr. Barrows Declaration ¶ 22; Dr. Wozniak Declaration ¶ 10.

Second, the percentage of women who experience complications that present to the emergency room (as opposed to their mifepristone provider) will increase because the Amendments remove the requirement for a second and third in-person visit. One doctor explained this phenomenon:

> Under the current practice by those who prescribe and dispense chemical abortion drugs like mifepristone and misoprostol, there is no follow-up or additional care provided to patients. Instead, with no established relationship with a physician, patients are simply left to report to the emergency room when they experience adverse events.

Dr. Foley Declaration ¶ 11; *see also* Dr. Harrison Declaration ¶ 44 (testifying that eliminating in-person evaluations and follow-up care "places our member doctors at increased risk of being forced to violate their conscience rights"); Dr. Frost-Clark Declaration ¶ 21 (similar).

Third, and relatedly, the percentage of women who present to the emergency room will increase because the Amendments allow non-physicians to prescribe mifepristone. As the motions panel explained, women who receive the drug from someone other than a doctor "cannot possibly go back to their non-doctor-prescribers for surgical abortions." *All. for Hippocratic Med.*, 2023 WL 2913725, at *5. And multiple doctors testified that they have seen or expect to see more women with serious complications resulting from mifepristone. Dr. Harrison Declaration ¶ 26; Dr. Skop Declaration ¶¶ 20- 21; Dr. Wozniak Declaration ¶¶ 18, 29; Dr. Johnson Declaration ¶ 18; Dr. Frost-Clark Declaration ¶ 18; Dr. Jester Declaration ¶ 13. Given the already sub-

stantial risk of harm, the evidence of increased risk is sufficient to confer standing to challenge the 2016 Amendments. *See Nat. Res. Def. Council, Inc. v. EPA*, 464 F.3d 1, 6-7 (D.C. Cir. 2006) (holding that plaintiffs had standing based on "increased risk" of developing skin cancer); *Sutton v. St. Jude Med. S.C., Inc.*, 419 F.3d 568, 570-75 (6th Cir. 2005) (holding that plaintiffs had standing based on an "increased risk" of harm from a medical device).

ii. 2021 Non-Enforcement Decision

The Medical Organizations and Doctors have also shown that the 2021 Non-Enforcement Decision contributes to their injury. That decision effectively removes the in-person dispensing requirement, allowing women to request and take mifepristone without ever going to the doctor's office. Evidence was introduced that this change will cause additional severe complications. Among other things, several doctors testified that supervision is necessary to ensure patients' safety:

> The FDA's actions harm women, including my patients, because clinics and physicians prescribing or dispensing chemical abortion drugs, or websites that provide these drugs through mail order delivery without any physician involvement, often underprepare women for the severity and risks of chemical abortion, and they often provide insufficient or no follow-up care to those women.

Dr. Skop Declaration ¶ 27; *see also* Dr. Harrison Declaration ¶ 25 ("Mifepristone and misoprostol are serious drugs that should not be administered without medical supervision. The FDA's actions to eliminate the necessary supervision of these drugs harms women and ob-

stetrics professionals. . . . "); *cf.* Dickerson Declaration ¶ 12 ("[Mifepristone] can now be administered and dispensed with no in-person examination or oversight by a physician.").

Doctors also testified that, without in-person examination, the prescriber is less likely to accurately determine gestational age:

> Mifepristone and misoprostol are dangerous drugs that can potentially harm women. Relaxing the required medical supervision and oversight for patients taking these drugs puts women's health at risk.
>
> By eliminating the in-person dispensing requirement and the requirement for a post-abortion follow-up, the FDA has exposed women to a higher likelihood of undetected serious complications. Specifically, the expanded use of telemedicine for chemical abortions means that some women who are beyond 70 days' gestation because they are mistaken or wrong about the gestational age of their unborn child will take these drugs outside of the appropriate window.

Dr. Barrows Declaration ¶¶ 16-17; *see also* Dr. Skop Declaration ¶ 28 ("Unsupervised chemical abortion . . . harms women because they may have underestimated the gestational age of their unborn child."). And the Doctors say that the need for in-person supervision is even greater in cases of ectopic pregnancy. Dr. Skop Declaration ¶¶ 27, 29.

Finally, many doctors offered testimony that, as a result of the 2021 Non-Enforcement Decision, more women will suffer serious adverse events. Dr. Woz-

niak Declaration ¶ 14 ("The increasing number of chemical abortions through mail-order or telemedicine methods means that more women will suffer complications from unsupervised use of mifepristone and misoprostol."); Dr. Frost-Clark Declaration ¶ 12 ("The FDA's suspension of the in-person dispensing requirement of mifepristone and misoprostol harms women and doctors because it has resulted in an increase in complications."); *see also* Dr. Skop Declaration ¶¶ 20-21; Dr. Johnson Declaration ¶ 18; Dr. Jester Declaration ¶ 13. One doctor personally witnessed an increase in complications after a district court temporarily enjoined the in-person dispensing requirement in the midst of the COVID-19 pandemic. Dr. Francis Declaration ¶ 11 ("The frequency of these complications has increased since a federal district court first enjoined and set aside the FDA's in-person dispensing requirement of mifepristone in 2020."); *see generally Am. Coll. of Obstetricians & Gynecologists v. FDA*, 472 F. Supp. 3d 183 (D. Md. 2020) (district court opinion enjoining the in-person requirements).[5]

Based on that evidence, the Medical Organizations and Doctors have made a clear showing that the 2021 Non-Enforcement Decision causes an increased risk of injury. FDA and Danco resist this conclusion, arguing that any increase to the Medical Organizations and Doctors injury is speculative because the number of women who experience ectopic pregnancies is so small. FDA

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[5] FDA initially appealed that ruling, but the parties dismissed the appeal after FDA announced that it would decline to enforce the in-person dispensing and prescription requirements. *See Am. Coll. of Obstetricians & Gynecologists v. Indiana*, No. 20-1784, 2021 WL 3276054 (4th Cir. May 19, 2021).

Reply Br. at 24; Danco Reply Br. at 11-12. But that understates the bases of the alleged injury. The Medical Organizations and Doctors argue that ectopic pregnancy (and the possible failure to diagnose it) is *one of* the reasons why removing the in-person dispensing requirement will lead to more complications—not the only reason. As explained above, the declarants offer several other grounds for their contention, including the need for in-person supervision when a patient takes mifepristone, the need to accurately assess gestational age, and the need for in-person follow-up. We conclude that the Medical Organizations and Doctors have shown a substantial risk of injury due to the 2021 Non-Enforcement Decision. As such, they have associational standing to challenge this action.

* * *

Because we hold that the Medical Organizations and Doctors have associational standing, we need not consider whether they also have organizational or third-party standing. *See generally ACORN v. Fowler*, 178 F.3d 350, 356-57 (5th Cir. 1999); *see also All. for Hippocratic Med.*, 2023 WL 2913725, at *4 n.4. However, to the extent that it were necessary to consider third-party standing, it is likely that emergency-room doctors have a sufficiently "close relationship" with mifepristone patients. *Kowalski v. Tesmer*, 543 U.S. 125, 130 (2004); *cf. June Med. Servs. LLC v. Russo*, 140 S. Ct. 2103, 2118-19 (2020), *overruled on other grounds*, *Dobbs v. Jackson Women's Health Org.*, 142 S. Ct. 2228 (2022). Indeed, the Court has "long permitted abortion providers to invoke the rights of their actual or potential patients." *June Med. Servs.*, 140 S. Ct. at 2118. We fail to see how this case is materially different.

FDA and Danco deny that third-party standing applies, saying that the Doctors have a "diametrically opposed" or "antagonistic" relationship with women experiencing severe complications as a result of taking mifepristone. FDA Br. at 33; Danco Br. at 32. That is so, Defendants contend, because the relief the Doctors seek would reimpose certain conditions of using mifepristone. That dubious proposition misunderstands the nature of the would-be representation. The Doctors pursue third-party standing to represent their patients' interest in avoiding or limiting the dangerous side effects that sometimes occur when a woman takes mifepristone.

Although we do not fulsomely consider the issue here, we suspect that the Doctors—who have provided firsthand care to dozens of mifepristone patients experiencing acute physical and emotional distress in an emergency setting—have a relationship with their patients that is more than adequate to support third-party standing. In many respects, such a relationship may be closer than those previously recognized by the Supreme Court. *June Med. Servs.*, 140 S. Ct. at 2118-19; *Whole Women's Health v. Hellerstedt*, 136 S. Ct. 2292, 2314 (2016); *Gonzales v. Carhart*, 550 U.S. 124, 133 (2007).

B. 2019 Generic Approval

Unlike FDA's other actions, the Medical Organizations and Doctors did not introduce evidence showing that they are likely to be injured by the 2019 Generic Approval. They point to the 2000 Approval, arguing that the two actions impose the same injuries. Alliance Br. at 23 n.4 ("The generic drug comes with all the same harms as does the name brand—so the district

court's harm analysis applies fully to the 2019 ANDA approval."). That may be true, but the Medical Organizations and Doctors cannot carry their burden of proof with legal argument. There is nothing in the record tending to show that the 2019 Generic Approval contributes to the risk of harm—no evidence that the women the Doctors have treated took the generic version of mifepristone, and no evidence that the number of women experiencing medical complications after taking mifepristone has risen as a result of the generic.

Indeed, the preliminary-injunction exhibits do not mention generic mifepristone at all. Separate from associational standing, there is no evidence that the 2019 Generic Approval contributed to any organizational injury sustained by the Medical Organizations or any individual injury sustained by a third-party patient. In short, the Medical Organizations and Doctors did not prove that the 2019 Generic Approval affects their risk of future harm. Accordingly, we must vacate the component the district court's order staying the effective date of FDA's approval of the generic version of mifepristone.

This holding means that generic mifepristone, like the brand version, will remain available for use under the conditions provided by the relevant mifepristone REMS. FDA amended that REMS in 2016 and 2021, but for the reasons explained below, we affirm the portion of the district court's order that stays the effective dates of those amendments. And so pending trial on the merits, the current REMS will be the version that was in effect prior to the 2016 Amendments. Of course, the mifepristone REMS does not distinguish between branded and generic mifepristone. FDA Br. at 9

("The same REMS covers both versions of mifepristone."). As such, the generic version will be available under the same conditions as Mifeprex.

III. Merits

Having concluded that the Medical Organizations and Doctors have standing except as to the 2019 Generic Approval, we now turn to the merits of the district court's stay order. That inquiry involves the traditional four-factor test for a preliminary injunction. To merit relief, a movant must show: (1) a substantial likelihood of success on the merits, (2) a substantial threat of irreparable harm, (3) that the threat of injury outweighs any harm that an injunction would cause, and (4) that the public interest is not disserved by an injunction. *Garcia v. Jones*, 910 F.3d 188, 190 (5th Cir. 2018).

In reviewing those factors, we review legal conclusions *de novo* and findings of fact for clear error. *Jones v. Tex. Dep't of Crim. Just.*, 880 F.3d 756, 759 (5th Cir. 2018). The parties agree that these preliminary-injunction factors apply even though the district court entered a stay under 5 U.S.C. § 705. That is so because a stay has the practical effect of an injunction. 28 U.S.C. § 1292(a); *see All. for Hippocratic Med.*, 2023 WL 2913725, at *3 n.3; *accord Colorado v. EPA*, 989 F.3d 874, 883 (10th Cir. 2021) ("These four factors also determine when a court should grant a stay of agency action under section 705 of the APA.").

The first question is whether the Medical Organizations and Doctors have shown a substantial likelihood of success on the merits. At the outset, we note that "substantial" does not mean "certain." *Byrne v. Roemer*,

847 F.2d 1130, 1133 (5th Cir. 1988) (explaining that "the movant need not always show a probability of success on the merits") (quoting *Celestine v. Butler*, 823 F.2d 74, 77 (5th Cir. 1987)); *see Jefferson Cmty. Health Care Ctrs., Inc. v. Jefferson Parish*, 849 F.3d 615, 626 (5th Cir. 2017) ("Though there is no particular degree of likelihood of success that is required in every case, the party seeking a preliminary injunction must establish at least some likelihood of success on the merits before the court may proceed to assess the remaining requirements."). A plaintiff need not prove "its entitlement to summary judgment in order to establish a substantial likelihood of success on the merits." *Byrum v. Landreth*, 566 F.3d 442, 446 (5th Cir. 2009) (internal quotation marks omitted). But at a minimum, it must "present a substantial case on the merits." *Bryne*, 847 F.2d at 1133 (quoting *Celestine*, 823 F.2d at 77).

A. 2000 Approval

As explained above, the Medical Organizations and Doctors have standing to challenge the 2000 Approval, the 2016 Amendments, and the 2021 Non-Enforcement Decision. Before addressing the merits of the challenge as to the 2000 Approval, we must consider a threshold issue: whether that claim was timely asserted.

The Medical Organizations and Doctors admit that they did not raise a claim as to FDA's denial of their 2002 citizen petition within six years, as required for civil actions filed against the United States. 28 U.S.C. § 2401. They present two independent arguments for why their claim as to the 2000 Approval is nonetheless timely. The motions panel rejected both arguments. *All. for Hippocratic Med.*, 2023 WL 2913725, at *13-15. We do the same.

1. Reopening Doctrine

First, the Medical Organizations and Doctors point to a judge-made exception to the statute of limitations called the "reopening doctrine." Essentially, this doctrine allows a plaintiff to challenge an agency action past the ordinary timeline if the agency substantively reconsiders the original action in a subsequent decision. *See Nat'l Biodiesel Bd. v. EPA*, 843 F.3d 1010, 1017 (D.C. Cir. 2016); *Sierra Club v. EPA*, 551 F.3d 1019, 1024 (D.C. Cir. 2008). The Medical Organizations and Doctors maintain that the 2016 Amendments and 2021 Petition Denial each trigger reopening. We disagree.[6]

a. 2016 Amendments

The Medical Organizations and Doctors point both to FDA's denial of their 2002 citizen petition and to the agency's approval of the amendments to mifepristone's conditions for use. They argue that, when FDA denied the citizen petition, it denied their request to rescind approval of mifepristone. And when FDA approved the 2016 Amendments, it altered the regime by which mifepristone is prescribed and used. Taken together, they say, these actions show that FDA substantively reconsidered the 2000 Approval.

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[6] The Supreme Court has cast some doubt on whether the reopening doctrine is a legitimate exception to a statute of limitations. *See Biden v. Texas*, 142 S. Ct. 2528, 2545 n.8 (2022) ("[T]his Court has never adopted [the reopening doctrine], and [it] appears to be inapposite to the question of final agency action."). But the parties both assume that the doctrine is good law in this circuit. And in any event, we need not address that threshold question because we ultimately conclude that the doctrine does not apply here.

To begin, the 2016 petition denial does not inform the 2016 Amendments. They are plainly different in nature; the former reaffirms FDA's conclusion that the agency properly approved mifepristone for use in 2000 and the latter considers relaxed conditions for the drug's use. The Medical Organizations and Doctors likely could have challenged the 2000 Approval if they had timely filed suit in response to the petition denial. But they did not. The argument that the two decisions must be considered in tandem is really just an end-run around the fact that the Medical Organizations and Doctors were too late to challenge FDA's denial of their citizen petition.

Accordingly, we consider only whether the 2016 Amendments themselves give rise to the reopening doctrine. They do not. Nothing in FDA's approval of the amendments shows that it undertook a "serious, substantive reconsideration" of the 2000 Approval. *Texas v. Biden*, 20 F.4th 928, 951-52 (5th Cir. 2021), *rev'd on other grounds*, 142 S. Ct. 2528 (2022). Actually, the opposite is true. FDA took the restrictions imposed in 2000 as a given, and considered only whether the REMS amendments were safe and effective. As explained by the motions panel: "FDA's 2016 decision to relax many of the REMS was issued in response to Danco's supplemental application requesting as much." *All. for Hippocratic Med.*, 2023 WL 2913725, at *13.

The Medical Organizations and Doctors respond that the 2016 Amendments were so significant as to constitute a change to the "basic regulatory scheme," *Nat'l Biodiesel Bd.*, 843 F.3d at 1017, thereby constructively reopening the 2000 Approval. It is certainly true that the amendments meaningfully altered the conditions

under which mifepristone is prescribed and taken. But a regulatory amendment, even a major one, is insufficient to satisfy the reopening doctrine. *Nat. Res. Def. Council, Inc. v. EPA*, 571 F.3d 1245, 1265-66 (D.C. Cir. 2009); *see also Nat'l Ass'n of Reversionary Prop. Owners v. Surface Transp. Bd.*, 158 F.3d 135, 144-46 (D.C. Cir. 1998); *United Transp. Union-Ill. Legis. Bd. v. Surface Transp. Bd.*, 132 F.3d 71, 76 (D.C. Cir. 1998) (Ginsburg, J.). To meet this high bar and trigger the reopening doctrine, the amendment must fundamentally alter the nature of the regulation such that it "could not have been reasonably anticipated." *Env't Def. v. EPA*, 467 F.3d 1329, 1334 (D.C. Cir. 2006).

The 2016 Amendments do not clear that bar. They do not alter FDA's basic assumption that mifepristone is safe and effective, subject to certain conditions for use. To be sure, the amendments put the public on notice of a significant change in the degree of mifepristone's availability and restriction. Disagreement with that decision would support challenging the new amendments—and that is exactly what the Medical Organizations did. But as to mifepristone's approval *per se*, the 2016 Amendments tell the public nothing they did not already know. As before, FDA approved a drug that chemically induces abortion, with the knowledge that the drug causes medical complications in a definite percentage of women. We cannot say that the amendments "significantly alter[ed] the stakes of judicial review" so as to allow the Medical Organizations and Doctors to challenge the 2000 Approval sixteen years after the fact. *Sierra Club*, 551 F.3d at 1025.

b. 2019 Citizen Petition

The Medical Organizations and Doctors also contend that FDA reopened the 2000 Approval when it denied their 2019 citizen petition. They emphasize the agency's use of the phrase "full review," and argue that FDA actively questioned whether mifepristone was safe.

The record does not bear out that claim. To start, the citizen petition did not actually ask FDA to reconsider its approval of mifepristone; it requested that FDA "restore" previous restrictions and "retain" others currently in place. 2019 Citizen Petition at 1, 2. So FDA had no reason to reevaluate mifepristone from the ground up. Turning to the denial itself, FDA did not reexamine its prior approval. It certainly described its action as "a full review of the Mifepristone REMS Program," 2021 Denial Letter at 6, but the letter's context shows that the agency reviewed the conditions for use that the citizen petition had put at issue—not mifepristone's underlying approval.

Nor did FDA constructively reopen the 2000 Approval by adopting a significant amendment to the mifepristone REMS. As with the 2016 Amendments, removing the in-person dispensing requirement does not change the basic concept of allowing women to use mifepristone. *Nat'l Biodiesel Bd.*, 843 F.3d at 1017. Between an "incremental adjustment[]" to the 2000 Approval and a "substantive reconsideration" of it, the decision to allow remote prescription and dispensing of mifepristone looks more like the former. *Texas*, 20 F.4th at 953, 952 (citations omitted). And so if the reopening doctrine is a valid exception to the statute of limitations, and we are not sure that it is, that doctrine

does not apply here because neither the 2016 Amendments nor the 2021 Petition Denial reevaluated FDA's decision in 2000 to approve mifepristone. The reopening doctrine therefore does not permit the Medical Organizations and Doctors to challenge the 2000 Approval after the prescribed limitations period.

2. Equitable Tolling

The Medical Organizations and Doctors also point to equitable tolling as a justification for considering the 2000 Approval claim even though it is untimely. But that is a very narrow exception. *See Jones v. Lumpkin*, 22 F.4th 486, 490 (5th Cir. 2022) (reiterating that equitable tolling "is warranted in only 'rare and exceptional circumstances'") (quoting *Davis v. Johnson*, 158 F.3d 806, 811 (5th Cir. 1998)). It applies only if the plaintiff satisfies two conditions: "(1) that he has been pursuing his rights diligently, and (2) that some extraordinary circumstance stood in his way and prevented timely filing." *Menominee Indian Tribe of Wis. v. United States*, 577 U.S. 250, 255 (2016) (citation omitted).

Supposing that the Medical Organizations and Doctors could meet the first condition, they cannot meet the second. This court has stressed that equitable tolling does not apply if the party seeking its benefit could have complied with the relevant deadline. *Jones*, 22 F.4th at 490 ("[A] petitioner's failure to satisfy the statute of limitations must result from external factors beyond his control; delays of the petitioner's own making do not qualify.") (quoting *In re Wilson*, 442 F.3d 872, 875 (5th Cir. 2006)). Here, the Medical Organizations and Doctors offer no reason why they could not have filed their lawsuit within the six-year limitations period. *See All. for Hippocratic Med.*, 2023 WL 2913725, at *15 (ex-

plaining that FDA's delay in ruling on the 2002 Citizen Petition "had no impact on the length of the statute-of-limitations period or plaintiffs' capacity to challenge the 2016 Petition Denial"). Their failure to do so forecloses any possibility of relief.

* * *

For the reasons stated above, we conclude that the claim as to the 2000 Approval is untimely. Consequently, the Medical Organizations and Doctors are not likely to succeed on that claim. And that means that we must vacate the component of the district court's order that stays the 2000 Approval. *Willey v. Harris Cnty. Dist. Att'y*, 27 F.4th 1125, 1129 (5th Cir. 2022).

B. 2016 Amendments

In addition to the 2000 Approval claim, which is not likely to succeed, the Medical Organizations and Doctors challenge two other actions taken by FDA: the 2016 Amendments to the mifepristone REMS and the 2021 decision to not enforce regulations requiring in-person prescription. The parties agree that the claims as to the 2016 Amendments and the 2021 Non-Enforcement decision are timely, so we proceed to the merits.

The Medical Organizations and Doctors ground their claims in the Administrative Procedure Act. That law 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 Supreme Court has explained that the "arbitrary-and-capricious standard requires that agency action be reasonable and reasonably explained." *FCC v. Prometheus Radio Project*, 141 S. Ct. 1150, 1158

(2021). That standard of review is "deferential," *id.*, but "not toothless." *Sw. Elec. Power Co. v. EPA*, 920 F.3d 999, 1013 (5th Cir. 2019).

On the contrary, our review is "searching and careful." *Univ. of Texas M.D. Anderson Cancer Ctr. v. U.S. Dep't of Health and Hum. Servs.*, 985 F.3d 472, 475 (5th Cir. 2021) (quoting *Marsh v. Or. Nat. Res. Council*, 490 U.S. 360, 378 (1989)). Above all, an 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.'" *Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983) (quoting *Burlington Truck Lines v. United States*, 371 U.S. 156, 168 (1962)). 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." *Id.*; *see also Michigan v. EPA*, 576 U.S. 743, 752 (2015); *Mexican Gulf Fishing Co. v. U.S. Dep't of Com.*, 60 F.4th 956, 971 (5th Cir. 2023); *Sw. Elec. Power Co.*, 920 F.3d at 1018-19 (explaining that courts must set aside agency action where there are "shortcomings in the agency's explanations").

With those standards in mind, we first address the 2016 Amendments and hold that the Medical Organizations and Doctors are substantially likely to succeed on the merits of that claim. *Byrne*, 847 F.3d at 1133. That is so for two instances of the same defect: failing to consider an important aspect of the problem. *Michigan*, 576 U.S. at 752; *State Farm*, 463 U.S. at 43.

First, FDA did not consider the cumulative effect of the 2016 Amendments. Those changes include: 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). FDA Summary Review of 2016 Amendments at 2.

FDA admits that none of the studies it relied on examined the effect of implementing all of those changes together. It studied the amendments individually. FDA Medical Review of 2016 Amendments at 32-38 (Mar. 29, 2016) (gestational age); *id.* at 38-41 (in-person appointments); *id.* at 43-44 (prescription by non-physician). And some clinical trials considered "multiple changes." FDA Summary Review of 2016 Amendments at 5-9. But FDA neither considered the effects as a whole, nor explained why it declined to do so. The cumulative effect of the 2016 Amendments is unquestionably an important aspect of the problem; indeed, that was the whole point of FDA's action. Because FDA failed to seek data on the cumulative effect, and failed to explain why it did not, its decision to approve the amendments was likely arbitrary and capricious. *Michigan*, 576 U.S. at 752; *State Farm*, 463 U.S. at 43; *Sw. Elec. Power Co.*, 920 F.3d at 1019.

FDA and Danco defend the 2016 Amendments, asserting that FDA is not required to conduct a study that

perfectly mirrors the conditions under which the drug will be used. That is true, so far as it goes. Indeed, the APA gives agencies discretion "in determining whether a study is adequate and well controlled." FDA Br. at 43 (quoting *Weinberger v. Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609, 621 n.17 (1973)).

But Defendants attack a rule that is not at issue. The problem is not that FDA failed to conduct a clinical trial that included each of the proposed changes as a control. It is that FDA failed to address the cumulative effect at all. At a minimum, the agency needed to acknowledge the question, determine if the evidence before it adequately satisfied the concern, and explain its reasoning. *See All. for Hippocratic Med.*, 2023 WL 2913725, at *17 ("[FDA] relied on zero studies that evaluated the safety-and-effectiveness consequences of the 2016 Major REMS Changes *as a whole.* This deficiency shows that FDA failed to consider 'an important aspect of the problem' when it made the 2016 Major REMS Changes.") (quoting *Michigan*, 576 U.S. at 752). FDA did not do those things, and so likely violated the APA.

The second important aspect that FDA failed to consider is whether it needed to continue to collect data of non-fatal adverse events in light of the "major" changes to the mifepristone REMS. When considering the data-collection question, FDA reasoned that non-fatal adverse events did not have to be recorded because the risks associated with mifepristone were well known. FDA Summary Review of 2016 Amendments at 26 ("[A]fter 15 years of reporting serious adverse events, the safety profile for Mifeprex is essentially unchanged.").

But FDA failed to account for the fact that it was about to significantly loosen mifepristone's conditions for use. At no point during the decision did the agency acknowledge that the 2016 Amendments might alter the risk profile. And when FDA addressed this subject in its response to the 2019 citizen petition, it just referred back to its statement that the risks were minimal under the 2011 REMS. *See* 2021 Denial Letter at 20. We conclude that FDA ignored "an important aspect of the problem," *Michigan*, 576 U.S. at 752 (quoting *State Farm*, 463 U.S. at 43), and that its explanation of the basis for the change contains significant "shortcomings." *Sw. Elec. Power Co.*, 920 F.3d at 1018-19. This also likely violates the APA.

Defendants respond that the change is insignificant because Danco remains obligated to report serious adverse events to FDA. *See* FDA Br. at 53; Danco Br. 47 (citing 21 C.F.R. §§ 314.80, 314.98). True, Danco is still subject to some reporting requirements, but these are significantly different than the ones that were removed. Before, prescribers were required to report certain adverse events directly to FDA. Given that prescribers interact with the women taking mifepristone, they are well placed to know if a patient actually experiences an adverse event. By contrast, Danco has no direct relationship with Mifeprex patients and little ability to track events. Like any member of the public, Danco can access the FDA Adverse Event Reporting System (FAERS), a voluntary reporting website. But prescribers are not required to log non-fatal adverse events. Indeed, no one is required to report anything on FAERS. Nor are prescribers required to report to Danco. The end result is that the removal of the adverse-event reporting requirement significantly di-

minishes FDA's ability to collect this data. Danco's residual reporting requirements do not cure this APA violation.

C. 2021 Non-Enforcement Decision

We now assess whether the Medical Organizations and Doctors are likely to succeed on their claim regarding the 2021 Non-Enforcement Decision. That decision essentially involves three parts. First, in April 2021, FDA announced that it would temporarily suspend enforcement of the in-person dispensing requirement in light of the COVID-19 pandemic. Next, in December of that year, FDA stated its intent to eliminate the requirement permanently. *See* 2021 Denial Letter at 25 ("[W]e believe that the Mifepristone REMS Program must be modified to remove the requirement that mifepristone be dispensed only in certain healthcare settings . . . because this requirement is no longer necessary to ensure that the benefits of the drug outweigh the risks."). And then in January 2023, FDA amended mifepristone's REMS, for Mifeprex and the generic, formalizing the change.

FDA supported its decision by pointing to two sources of information. First, the agency examined adverse-events data collected during the period of time when the in-person dispensing requirement was enjoined. FDA obtained this data from FAERS—the voluntary reporting website. 2021 Denial Letter at 26. Danco also submitted its records of adverse events during the relevant interval, but its data set was the same as the one obtained via FAERS. *Id.* at 27 ("The information provided by the Applicants included the same cases identi-

fied in FAERS. . . . "). Five events[7] were reported during that time, but FDA concluded that there did not "appear to be a difference in adverse events when in-person dispensing was and was not enforced." *Id.*

Second, FDA considered published literature relating to remote prescription of mifepristone. It determined that those studies were "not inconsistent with our conclusion that . . . mifepristone will remain safe and efficacy will be maintained if the in-person dispensing requirement is removed from the Mifepristone REMS Program." *Id.* at 28. Based on these sources, FDA concluded that "mifepristone will remain safe and effective if the in-person dispensing requirement is removed." *Id.* at 35.

1. Mootness

Defendants first raise a threshold question: whether the Medical Organizations and Doctors' challenge to the 2021 non-enforcement policy is moot. They contend that the 2023 modification of mifepristone's REMS supersedes the 2021 policy, and also that the prior policy was tied to the Government's COVID-19 public health emergency, which has since expired. For these reasons, FDA and Danco say, there is no longer a live dispute as to the 2021 Non-Enforcement Decision.

Neither reason is availing. First, FDA is incorrect to say that it tied its December 2021 decision not to enforce the in-person dispensing requirement to the

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[7] According to FDA, the causes of those events are as follows: ongoing pregnancy, drug intoxication and death, death (unknown cause), sepsis and death, and pulmonary embolism. 2021 Denial Letter at 26.

COVID-19 pandemic. True, FDA cited the pandemic as a justification for taking the *initial* action. FDA Letter of April 2021 at 2 ("[FDA] intends to exercise enforcement discretion during the COVID-19 [pandemic] with respect to the in-person dispensing requirement of the Mifepristone REMS Program. . . . "). But when FDA "directed mifepristone's sponsors to submit a proposed REMS modification," several months later, it did so without regard to pandemic conditions. FDA Br. at 11; *see* 2021 Denial Letter at 6, 25-26. FDA simply did not tether its action in December of 2021 to the continued existence of the public health emergency.

Second, FDA's formalization of the policy it announced in 2021 does not render this claim moot. At bottom, the mootness doctrine asks whether the court faces a live dispute. *Freedom from Religion Found., Inc. v. Abbott*, 58 F.4th 824, 831 (5th Cir. 2023). That is, a case is moot if "the parties lack a legally cognizable interest in the outcome." *Id.* (quoting *Already, LLC v. Nike, Inc.*, 568 U.S. 85, 91, (2013)).

A live dispute exists as to the 2021 Non-Enforcement Decision. The decision that FDA made in 2021—to permanently not enforce in-person prescription and dispensing requirements—remains in force. FDA may have formalized that policy by modifying the mifepristone REMS. But the effect is the same, as is FDA's ultimate judgment that mifepristone can be safely used without in-person prescription and dispensing.

Moreover, the Supreme Court has recognized that the government does not moot a controversy when it introduces the final form of a previous, identical policy. *Biden v. Texas*, 142 S. Ct. 2528, 2544-45 (2022) (considering a prior agency action even after it was formalized

by a later, similar action); *see All. for Hippocratic Med.*, 2023 WL 2913725, at *2 n.2. That type of action is different in kind than the repeal or modification of a government policy. *Freedom from Religion Found.*, 58 F.4th at 832. Unlike a repealed policy, FDA's policy remains unchanged and on the books (albeit in a permanent form). We see no jurisdictional obstacle to reviewing the claim as to the 2021 Non-Enforcement Decision.

2. Merits

Because the 2021 Non-Enforcement claim is not moot, we must proceed to the question of whether that action was arbitrary and capricious. For two reasons, we hold that it likely was. First, FDA gave dispositive weight to adverse-event data in FAERS—despite the uncontested limitations of doing so. Recall that, because of the 2016 Amendments, FDA no longer had access to perhaps the best source of data: the prescribers. The agency is responsible for its own inability to obtain probative data; it cannot then cite its lack of information as an argument in favor of removing further safeguards. As the motions panel aptly put it: "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." *All. for Hippocratic Med.*, 2023 WL 2913725, at *17.

Moreover, considerable evidence shows that FAERS data is insufficient to draw general conclusions about adverse events. Indeed, in describing the database, FDA itself recognizes that "FAERS data cannot be used to calculate the incidence of an adverse event or medication error in the U.S. population." FDA admits that FAERS reporting is purely voluntary, FDA Br. at

53; consequently, many adverse events will go unreported.

For example, one doctor testified that she obtained adverse-event data from one provider (Planned Parenthood) and compared it to FAERS data for the same time period. For 2010, the provider reported 1,530 adverse events, whereas FAERS reported only 664 events for all providers nationwide. Dr. Harrison Declaration ¶ 17; *see also id.* ("These discrepancies render FAERS inadequate to evaluate the safety of mifepristone abortions.").

In addition, the Doctors introduced evidence that many physicians do not use FAERS, either because they are not aware of the system or because they believe that using the system is difficult, and takes time away from their ordinary medical practice:

> Many doctors likely do not know about the need to report adverse events related to chemical abortion to the FDA. Similarly, many doctors likely do not know how to report adverse events. . . . I personally know of practitioners . . . who have tried to report adverse events related to chemical abortion drugs to the FDA. The process is complicated, cumbersome, and time-consuming. The adverse event reporting requirements and the FAERS submission process harm medical practices by taking away significant time from a doctor to treat and meet with patients.

Dr. Harrison Declaration ¶¶ 33-34; *see also* Dr. Frost-Clark Declaration ¶ 23 ("I have not reported adverse events that I have witnessed as a result of chemical abortions because the process is so cumbersome.").

One doctor testified that it can take hours to report an adverse event to FAERS:

> [T]he process of reporting to [FAERS] is also cumbersome. The actual form to be filled out is not easy to find online—requiring several steps to get 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 the FAERS is thirty minutes—valuable time that should be spent in patient care.

Dr. Francis Declaration ¶ 18. FDA's decision to rely so heavily on data from FAERS "runs counter to" the critical limitations associated with that data. *State Farm*, 463 U.S. at 43; *Sw. Elec. Power Co.*, 920 F.3d at 1018-19.

FDA responds that it also considered adverse-event data submitted by Danco, but Danco's data was exactly the same as the data FDA obtained from FAERS. FDA acknowledged as much in its letter denying the 2019 citizen petition. 2021 Denial Letter at 27. ("The information provided by the Applicants included the same cases identified in FAERS. . . . "). If anything, the fact that Danco submitted identical data tends to confirm the assertion that FDA lacked sufficient information; it shows that neither FDA nor Danco had the means to collect data directly from prescribers.

The second defect in the Non-Enforcement Decision 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. Danco insists that the studies "all . . . sup-

ported the conclusion that mifepristone would still be safe and effective even with a relaxed in-person dispensing requirement," Danco Br. at 48, but that is not what FDA said in 2021. On the contrary, FDA candidly acknowledged that the literature was only "not inconsistent with [its] conclusion." 2021 Denial Letter at 28. In other words, the studies neither confirmed nor rejected the idea that mifepristone would be safe if the in-person dispensing requirement were removed. In discussing the various studies, FDA recognized many significant limitations:

> 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.

Id. Given those limitations, FDA concluded that the studies were "not adequate on their own to establish the safety of the model of dispensing mifepristone by mail." *Id.* at 35.

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. 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. *Sw. Elec. Power Co.*, 920 F.3d at 1018-19; *see also State Farm*, 463 U.S. at 56 ("While [an] agency is entitled to change its view . . . it is obligated to explain its reasons for doing so."). 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. We conclude that the Medical Organizations and Doctors are likely to succeed in showing that this action violated the APA.[8]

IV. Irreparable Harm and Balance of the Equities

We now proceed to the remaining steps of the preliminary-injunction analysis. First, we ask if the Medical Organizations and Doctors are likely to sustain irreparable harm absent an injunction. *Garcia*, 910

[8] Given this holding, we do not consider the Medical Organizations and Doctors' independent argument that the 2021 Non-Enforcement Decision violates the Comstock Act of 1873.

F.3d at 190. If so, we then balance the equities and consider whether an injunction serves the public interest. *Winter*, 555 U.S. at 20. And where the government appeals an injunction, its interests "merge" with the public interest. *Tex. Democratic Party v. Abbott*, 961 F.3d 389, 412 (5th Cir. 2020) (quoting *Veasey v. Abbott*, 870 F.3d 387, 391 (5th Cir. 2017)).

We have already concluded that the Medical Organizations and Doctors are likely to sustain injury; now we need only determine whether the threatened injuries are irreparable. They are. An irreparable harm is one "for which there is no adequate remedy at law." *Louisiana v. Biden*, 55 F.4th 1017, 1033-34 (5th Cir. 2022) (quoting *Daniels Health Scis., LLC v. Vascular Health Scis., LLC*, 710 F.3d 579, 585 (5th Cir. 2013)). No legal remedy can adequately redress the Doctors' conscience and mental-distress injuries. And the economic injuries —the potential damage to their medical practice, heightened exposure to malpractice liability, and increased insurance costs—are irreparable too. Monetary harm cannot be remedied where, as here, the defendant is entitled to sovereign immunity. *See Wages & White Lion Invs., LLC v. FDA*, 16 F.4th 1130, 1142 (5th Cir. 2021).

This risk of irreparable harm must be weighed against any injury FDA and Danco would sustain as a result of the stay order, as well as against the public interest. Starting with FDA, we recognize that anytime the Government is enjoined from enforcing its statutes or regulations, "it suffers a form of irreparable injury." *Maryland v. King*, 567 U.S. 1301, 1303 (2012) (Roberts, C.J., in chambers); *accord Valentine v. Collier*, 956 F.3d 797, 803 (5th Cir. 2020). But on the other hand, neither FDA nor the public has any interest in

enforcing a regulation that violates federal law. *Louisiana*, 55 F.4th at 1035 ("There is generally no public interest in the perpetuation of unlawful agency action.") (citations omitted).

In this regard, the government/public-interest analysis collapses with the merits. *See Sierra Club v. U.S. Army Corps of Eng'rs*, 990 F. Supp. 2d 9, 43 (D.D.C. 2013) (Jackson, J.) (explaining that "public interest arguments" are "derivative of . . . merits arguments and depend in large part on the vitality of the latter") (citing *Serono Lab'ys, Inc. v. Shalala*, 158 F.3d 1313, 1326 (D.C. Cir. 1998)); *see also Louisiana*, 55 F.4th at 1035; *League of Women Voters of U.S. v. Newby*, 838 F.3d 1, 12 (D.C. Cir. 2016). The Medical Organizations and Doctors are likely to succeed on their claims as to the 2016 Amendments and 2021 Non-Enforcement Decision. It follows that FDA and the public will not be injured by an order staying those likely unlawful actions.

FDA also points to the "disruptive practical effects" of a stay, FDA Br. at 66-67, arguing that it will incur substantial costs if it complies with the stay order, only for the order to be reversed later. As a preliminary matter, this argument is also highly duplicative of the merits. FDA's injury only comes into play if the stay order is vacated—that is, if the Medical Organizations and Doctors are not likely to succeed on the merits. After careful consideration, we have concluded that these claims are likely to succeed. Accordingly, we do not consider the costs that might be incurred if the stay order goes into effect and is later vacated. Moreover, we doubt whether an agency's interim compliance costs

could outweigh a threat of irreparable harm. *See Al Otro Lado v. Wolf*, 952 F.3d 999, 1008 (9th Cir. 2020).

Turning to Danco's interest, we acknowledge that the district court's stay order would impose significant injury. *See Texas v. EPA*, 829 F.3d 405, 434 (5th Cir. 2016) (explaining that financial harm may be irreparable "where the loss threatens the very existence of the [party's] business") (quoting *Wis. Gas Co. v. FERC*, 758 F.2d 669, 674 (D.C. Cir. 1985)). That threat, however, is substantially lessened because we vacate the component of the stay order that would pause FDA's initial approval of mifepristone in 2000.

What remains is any injury that Danco will face as a result of the stay order *as amended*. The Medical Organizations and Doctors point out that Danco already has drug labels and documentation that comply with the mifepristone REMS as of 2011. Danco does not deny this, but responds that "[r]equiring a return to a prior and outdated REMS and label would also create months-long loss of access, while FDA and Danco work through the sNDA process." Danco Br. at 61 (citing Declaration of Dr. Janet Woodcock ¶ 14). But this potential injury is greatly diminished by the fact that the Supreme Court's stay of the district court's order will remain in effect pending disposition of any petition for certiorari.

It is a well-established maxim that "equity regards substance rather than form." Dobbs, 1 Law of Remedies 83 (2d ed. 1993). This means, among other things, that courts exercising equitable power should account for the real, boots-on-the-ground circumstances, not those supposed or theorized by the parties. As Pomeroy has explained:

> Equity always attempts to get at the substance of things, and to ascertain, uphold, and enforce rights and duties which spring from the *real* relations of parties. It will never suffer the mere appearance and external form to conceal the true purposes, objects, and consequences of a transaction.

Pomeroy, II Equity Jurisprudence § 378 (5th ed. 1941); *see, e.g.*, *Freedom from Religion Found.*, 58 F.4th at 837. Applying this principle, we must take into consideration the fact that the district court's stay order will likely not go into effect for several months, if not more than a year.

The Supreme Court's stay alleviates (or at least greatly reduces) any possible harm to Danco because it establishes a substantial window to prepare to comply with the district court's stay order, as modified by this court. The soonest the district court's stay order could go into effect would be if neither party filed a petition for certiorari, and the deadline to do so is ninety days after the entry of this court's judgment. Sup. Ct. R. 13. Alternatively, if either of the Defendants seek certiorari, the stay will remain in effect at least until the denial of that petition, should it be denied. But even that would likely require a minimum of six months for briefing by the parties and disposition by the Supreme Court. And if the Court grants the writ, that would extend the stay for upwards of another year. Either way, Danco will have "months" of time needed to arrange for mifepristone to be distributed under the 2011 REMS and prevent any "loss of access."

Other public-interest considerations merit discussion. Various *amici* assert that eliminating access to mifepristone, even temporarily, may pose health risks

to certain women, including those who use the drug to manage miscarriage. Br. of American College of Obstetricians and Gynecologists et al. at 21-26; Br. of Physicians for Reproductive Health at 18-27; Br. of Over 200 Reproductive Health, Rights, and Justice Organizations at 14-25; Br. of Doctors for America et al. at 14-23; Br. of Advocates for Survivors of Intimate Partner Violence at 18-26. Other *amici* argue that "disrupting access to mifepristone" would burden state and local health-care systems. Br. of New York et al. at 4; *see also* Br. of Local Governments at 24-26; Br. of the City of New York et al. at 8-31; Br. of Medical Students for Choice at 3-22. And still other *amici* say that staying FDA's approval of mifepristone would destabilize the pharmaceutical industry, especially research-and-development sections. Br. of Pharmaceutical Companies, Executives, and Investors at 3-4; Br. of Pharmaceutical Research and Manufacturers of America et al. at 22-26; Br. of Patient and Provider Advocacy Organizations at 9-20.

These concerns are not insignificant. But they apply primarily (if not wholly) to the challenge to the 2000 Approval—a claim that we have concluded is not likely to succeed. *All. for Hippocratic Med.*, 2023 WL 2913725, at *20 ("[T]hese concerns center on the district court's removal of mifepristone from the market. [Defendants] make no arguments as to why the 2016 Major REMS Changes, the 2019 Generic Approval, or the 2021 and 2023 Mail Order Decisions are similarly critical to the public. . . . "). Insofar as these concerns translate to the 2016 Amendments and 2021 Non-Enforcement Decision, they are lessened by the fact that mifepristone would remain available under the 2011 REMS, as would options for surgical abortion.

And of course, the public interest is disserved by a drug that does not afford adequate protections to its users. *See Deerfield Med. Ctr. v. City of Deerfield Beach*, 661 F.2d 328, 338 (5th Cir. 1981); *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."). To be clear, the evidence does not show that mifepristone is unsafe in all applications. But on this record and at this preliminary stage, the Medical Organizations and Doctors have made a substantial showing that the 2016 Amendments and 2021 Non-Enforcement Decision were taken without sufficient consideration of the effects those changes would have on patients.

Weighing all of these considerations, we conclude that the balance of the equities favors the Medical Organizations and Doctors. They face a substantial risk of irreparable harm to their medical practice, mental and emotional health, and conscience. The limited relief affirmed by our judgment threatens neither FDA nor Danco with substantial harm. Nor does it offend the public interest. The Medical Organizations and Doctors therefore satisfy the remaining preliminary-injunction factors. *Winter*, 555 U.S. at 20.

V. Form of Relief

Finally, FDA and Danco challenge the form of the relief entered by the district court—a stay of the actions' effective dates. FDA argues that the Medical Organizations and Doctors were required to first seek an administrative stay, but failed to do so. *See* 21 C.F.R. § 10.45(c) ("A request that administrative action be stayed must first be the subject of an administrative decision based upon a petition for stay of action . . .

before a request is made that a court stay the action."). It also contends that § 705 authorizes only requests made at the same time the challenged action is enacted. Here, by contrast, the Medical Organizations and Doctors seek a stay years after the relevant policies took effect. And Danco maintains that injunctive relief is categorically unavailable, reasoning that if the Medical Organizations and Doctors prevailed, they would only be entitled to remand without vacatur.

We hold that the district court entered an appropriate form of relief. To begin, consider the nature of a "stay" under § 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. Between vacatur and an injunction, the former is the "less drastic remedy." *Monsanto Co. v. Geertson Seed Farms*, 561 U.S. 139, 165 (2010). That is so because vacatur does not order the defendant to do anything; it only removes the source of the defendant's authority. *See Nken v. Holder*, 556 U.S. 418, 428-29 (2009) ("[A] stay achieves this result by temporarily suspending the source of authority to act—the order or judgment in question—not by directing an actor's conduct."); *see also Texas v. United States*, 40 F.4th 205, 220 (5th Cir. 2022) ("Apart from the constitutional or statutory basis on which the court invalidated an agency action, vacatur neither compels nor restrains . . . agency decision-making.").

Upon a successful APA claim, vacatur effectively rescinds the unlawful agency action. *See Data Mktg. P'ship, LP v. U.S. Dep't of Lab.*, 45 F.4th 846, 859 (5th Cir. 2022) ("Vacatur . . . retroactively undoes or expunges a past state action. . . . Unlike an injunc-

tion, which merely blocks enforcement, vacatur unwinds the challenged agency action.") (quoting *Driftless Area Land Conservancy v. Valcq*, 16 F.4th 508, 522 (7th Cir. 2021)). Keeping with the preliminary-permanent injunction analogy, a stay temporarily voids the challenged authority.

Practically speaking, a stay means that—while the order is in effect—Danco will have legal authority to market and sell Mifeprex under the conditions that were in effect before 2016. Likewise, GenBioPro will have authority to market and sell the generic version of mifepristone under those same conditions—that is, those that appeared in the 2011 REMS. The in-person dispensing requirements, and FDA's obligation to enforce them, will continue to apply.

In terms of enforcement, unlike with a preliminary injunction, a stay does not actively prohibit conduct, and so does not carry the same threat of contempt. Plaintiffs could move to enforce the stay in the unlikely event that FDA or Danco took some action to violate it. But of course, we have absolutely no reason to believe that such a motion would be necessary. And we should reiterate that the Supreme Court's stay of the district court's order will remain in effect pending disposition of any petition for certiorari.

Turning to Danco's objection to a stay, we do not agree that the Medical Organizations and Doctors will be limited to remand without vacatur if they obtain a favorable judgment. "[V]acatur of an agency action is the default rule in this Circuit." *Cargill v. Garland*, 57 F.4th 447, 472 (5th Cir. 2023) (*en banc*) (plurality op.); *Data Mktg. P'ship*, 45 F.4th at 859; *accord United Steel v. Mine Safety & Health Admin.*, 925 F.3d 1279, 1287

(D.C. Cir. 2019) ("The ordinary practice is to vacate unlawful agency action."). Given that presumption, remand without vacatur is appropriate only if "there is at least a serious possibility that the agency will be able to substantiate its decision given an opportunity to do so." *Texas v. United States*, 50 F.4th 498, 529 (5th Cir. 2022) (quoting *Texas Assn. of Mfrs. v. U.S. Consumer Prod. Safety Comm'n*, 989 F.3d 368, 389-90 (5th Cir. 2021)); *accord Radio-Television News Dirs. Ass'n v. FCC*, 184 F.3d 872, 888 (D.C. Cir. 1999).

Remand without vacatur is likely not appropriate because "it is far from certain" that FDA could cure its mistakes with further consideration. *Env't Def. Fund v. FERC*, 2 F.4th 953, 976 (D.C. Cir. 2021). FDA erred by failing to consider the cumulative effects of the 2016 Amendments on mifepristone's safety and by disregarding the lack of recent data on adverse events when removing the in-person dispensing requirement. The record does not tend to show that FDA would have arrived at the same decision if it had considered those things. *See Oglala Sioux Tribe v. U.S. Nuclear Regul. Comm'n*, 896 F.3d 520, 536 (D.C. Cir. 2018) (declining to remand without vacatur because of the "seriousness" of the action's "deficiency"); *Pollinator Stewardship Council v. EPA*, 806 F.3d 520, 532 (9th Cir. 2015) (same); *cf. Sierra Club v. FERC*, 68 F.4th 630, 652 (D.C. Cir. 2023) (remanding without vacatur because it was possible that FERC could "adequately explain its decision" if given another opportunity). If the Medical Organizations and Doctors succeed on the merits, it is likely that the default remedy—vacatur—will be appropriate. And the temporary version of vacatur is a stay.

We are also unpersuaded by FDA's contentions. First, FDA argues Medical Organizations and Doctors cannot seek a stay before the district court because they failed to seek one from the agency. But the record shows that FDA would have denied any request for an administrative stay. *See Gulf Restoration Network v. Salazar*, 683 F.3d 158, 176 (5th Cir. 2012). FDA unequivocally denied the 2019 citizen petition, rejecting the premise that 2016 Amendments made mifepristone less safe. It discussed the 2021 Non-Enforcement Decision in the same document, and then formalized the policy in 2023. These pronouncements show that FDA was committed to implementing these changes, and foreclose any notion that the agency would have granted an administrative stay. *Tesoro Refin. & Mktg. Co. v. FERC*, 552 F.3d 868, 874 (D.C. Cir. 2009) (explaining that the exhaustion requirement does not apply "when resort to administrative remedies [would be] clearly useless") (citations omitted). That FDA denied a request to stay the 2000 Approval further aids this conclusion. *See* 2016 Denial Letter at 32 ("As described above, we are denying your Petition. Therefore, your request for a stay pending final action on your Petition is moot.").

Second, FDA provides no authority for its assertion that § 705 of the APA limits stays to contemporaneous agency actions. The text does not provide such a limitation. Instead, it empowers a reviewing 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. Circuit courts have interpreted this statute as providing something akin to the general stay power recognized by Rule 18 of the Fed-

eral Rules of Appellate Procedure, *see Ohio v. Nuclear Regul. Comm'n*, 812 F.2d 288, 290 (6th Cir. 1987); *In re GTE Serv. Corp.*, 762 F.2d 1024, 1026 (D.C. Cir. 1985), which weighs against construing § 705 as requiring that a stay be issued concurrently with an agency action. We are disinclined to reach a definitive answer on this question, given the cursory treatment by both parties. But we strongly doubt that § 705 should be read to impose the limit urged by FDA. Nothing about this argument persuades us that the district court abused its discretion by entering this particular form of relief.

VI. Conclusion

For the foregoing reasons, the stay order entered by the district court is VACATED in part and AFFIRMED in part. We vacate the component of the order that stayed the effective date of the 2000 Approval and the 2019 Generic Approval. Mifeprex will remain available under the safety restrictions that were in effect prior to 2016. Generic mifepristone will also remain available under those same restrictions.

We affirm the portions of the stay order regarding the 2016 Amendments and the 2021 Non-Enforcement Decision. In loosening mifepristone's safety restrictions, FDA failed to address several important concerns about whether the drug would be safe for the women who use it. It failed to consider the cumulative effect of removing several important safeguards at the same time. It failed to consider whether those "major" and "interrelated" changes might alter the risk profile, such that the agency should continue to mandate reporting of non-fatal adverse events. And it failed to gather evidence that affirmatively showed that mifepristone

could be used safely without being prescribed and dispensed in person.

At this preliminary stage, the Medical Organizations and Doctors have made a substantial showing that the 2016 Amendments and the 2021 Non-Enforcement Decision violate the APA. Accordingly, those actions will be stayed pending final judgment. But to repeat, all of this relief is subject to the Supreme Court's prior order, which stays the district court's order until the disposition of any petition for certiorari.

JAMES C. HO, *Circuit Judge*, concurring in part and dissenting in part:

The Constitution vests "the authority to regulate abortion" in "the people and their elected representatives." *Dobbs v. Jackson Women's Health Org.*, 142 S. Ct. 2228, 2279 (2022). Congress has enacted a number of laws that affect the regulation of abortion, including the Administrative Procedure Act and the Comstock Act. Those laws dictate the outcome in this case.

Congress has conferred significant regulatory power on administrative agencies such as the FDA. In exchange, Congress has enacted the APA to ensure that agency action is subject to meaningful judicial review. It requires courts to "hold unlawful and set aside agency action" that we determine to be "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A).

That's precisely what occurred here. Plaintiffs challenge the FDA's approval of mifepristone in 2000, as well as its 2016 and 2021 revisions to its mifepristone regulations. I agree with the panel majority that the FDA's 2016 and 2021 revisions to its mifepristone regulations must be set aside as arbitrary and capricious under the APA. I would add that the FDA's initial approval of mifepristone in 2000 also violates the agency's own rules and thus must be set aside under the APA as well.

The FDA approved mifepristone under its Subpart H regulations. But Subpart H only authorizes the FDA to approve drugs that "treat[] serious or life-threatening illnesses." 21 C.F.R. § 314.500. And pregnancy is plainly not an illness. So it was unlawful for the

FDA to approve mifepristone under Subpart H. To quote the Population Council, the entity that sought FDA approval of mifepristone in 2000: "Neither pregnancy nor unwanted pregnancy is an illness, and Subpart H is therefore inapplicable for that reason alone." Population Council Letter to FDA at 1-2 (Sep. 6, 2000).

Perhaps the FDA could have approved mifepristone through some other regulatory process. But established precedent requires us to review the FDA's action based on the path it took—not the path it might have taken. *See SEC v. Chenery Corp.*, 318 U.S. 80, 95 (1943); *DHS v. Regents of the Univ. of Cal.* 140 S. Ct. 1891, 1909 (2020) ("An agency must defend its actions based on the reasons it gave when it acted.").

The FDA's 2021 revisions also violate the Comstock Act. That Act makes it a federal crime to mail any "article or thing designed . . . or intended for producing abortion," as well as any "drug, medicine, or thing . . . advertised . . . in a manner calculated to lead another to use . . . it for producing abortion." 18 U.S.C. § 1461. It also makes it a crime to "use[] . . . [an] express company" to ship a "drug, medicine, article, or thing designed . . . or intended for producing abortion." 18 U.S.C. § 1462.

So I would affirm the district court. Accordingly, I concur in part and dissent in part.

I.

I agree with the thorough and well-reasoned panel majority opinion that Plaintiffs have demonstrated Article III standing to challenge both the FDA's 2000 approval of mifepristone and the 2016 and 2021 revisions. I write separately to elaborate on the historical pedi-

gree of Plaintiffs' conscience injury, and to explore how Plaintiffs suffer aesthetic injury as well.

A.

The Supreme Court has instructed that we look to "history and tradition" as "a meaningful guide to the types of cases that Article III empowers federal courts to consider." *United States v. Texas*, 143 S. Ct. 1964, 1970 (2023) (quoting *Sprint Communications Co. v. APCC Services, Inc.*, 554 U.S. 269, 274 (2008)). We ask whether the "injury to the plaintiff has a 'close relationship' to a harm 'traditionally' recognized as providing a basis for a lawsuit in American courts." *TransUnion LLC v. Ramirez*, 141 S. Ct. 2190, 2204 (2021) (quoting *Spokeo, Inc. v. Robins*, 578 U.S. 330, 341 (2016)).

By the standards of history and tradition, the harm to conscience that Plaintiffs suffer is a paradigmatically cognizable injury. American law has recognized conscience rights from the start. *See, e.g.*, N.H. CONST. of 1784, pt. I, art. IV ("Among the natural rights, some are in their very nature unalienable, because no equivalent can be given or received for them. Of this kind are the rights of conscience."); PA. CONST. of 1790, art. IX, § 3 ("[N]o human authority can, in any case whatever, control or interfere with the rights of conscience."); KY. CONST. of 1792, art. XII, § 3 (same); OHIO CONST. of 1803, art. VIII, § 3 (same); ALA. CONST. of 1819, art. I, § 4 ("No human authority ought, in any case whatever, to control or interfere with the rights of conscience."); TENN. CONST. of 1835, art. I, § 3 ("[N]o human authority can, in any case whatever, control or interfere with the rights of conscience."); MO. CONST. of 1820, art. XIII, § 4 ("[N]o human authority can control or interfere with the rights of conscience."); ARK. CONST. of 1836, art. II,

§ 3 ("[N]o human authority can, in any case whatever, interfere with the rights of conscience."); WIS. CONST. of 1848, art. I, § 18 ("Nor shall any control of, or interference with the rights of conscience be permitted."); MINN. CONST. of 1858, art. I, § 16 (same); KAN. CONST. of 1859, Bill of Rights, § 7 (same).

Throughout the nineteenth century, American courts granted relief to parties who challenged government action as injurious to conscience. *See*, *e.g.*, *White v. McBride*, 7 Ky. (4 Bibb) 61, 61 (1815) (suit brought against sheriff by plaintiffs who "entertained conscientious scruples against bearing arms"); *In re Dorsey*, 7 Port. 293, 345, 365-69 (Ala. 1838) (attorney seeking conscience-based exemption from anti-dueling oath required for bar admission); *State ex rel. Weiss v. Dist. Bd. of Sch. Dist. No. 8 of City of Edgerton*, 44 N.W. 967, 967-68, 976 (Wis. 1890) (writ of mandamus requested by public school students who raised conscience-based objection to curriculum).

And even where parties were not ultimately granted relief, courts entertained their suits alleging injuries to conscience and reached the merits of their claims. *See*, *e.g.*, *Donahoe v. Richards*, 38 Me. 379, 413 (1854) (public school student raised conscience-based objection to curriculum); *Innis v. Bolton*, 17 P. 264, 269 (Idaho 1888) (plaintiff brought conscience-based objection to anti-polygamy oath required for voting).

Here, Plaintiffs have alleged conscience injuries analogous to those historically recognized at law and in equity. The FDA's approval of mifepristone creates a substantial risk that Plaintiffs will be forced to participate in the abortion process. *See*, *e.g.*, Dr. Francis Declaration ¶ 14 ("[M]ore physicians with ethical and

medical objections to abortion will be forced to participate in completing unfinished elective chemical abortions, just as my partner was."); Dr. Skop Declaration ¶ 34 ("The FDA's expansion of chemical abortion . . . harms my conscience rights because it could force me to have to surgically finish an incomplete elective chemical abortion. I object to abortion because it ends a human life.").

The Supreme Court has recognized that intangible interests in free speech and free exercise are sufficiently concrete for Article III standing. *See Spokeo*, 578 U.S. at 340. So it's not surprising that both the FDA and intervenor Danco agree that conscience injuries can satisfy Article III. I agree with the panel majority that Plaintiffs have established Article III standing based on injury to conscience.

B.

In addition to the injuries analyzed by the majority, Plaintiffs have demonstrated another basis for Article III standing: the aesthetic injury they experience in the course of their work. *See*, *e.g.*, *Sierra Club v. Morton*, 405 U.S. 727, 734-35 (1972) (recognizing aesthetic harm as "injury to a cognizable interest"); *Lujan v. Defs. of Wildlife*, 504 U.S. 555, 562-63 (1992) ("[T]he desire to use or observe an animal species, even for purely esthetic purposes, is undeniably a cognizable interest for purpose of standing."); *id.* at 566 ("[T]he person who observes or works with a particular animal threatened by a federal decision is facing perceptible harm.").

It's well established that, if a plaintiff has "concrete plans" to visit an animal's habitat and view that animal, that plaintiff suffers aesthetic injury when an agency

has approved a project that threatens the animal. *See Lujan*, 504 U.S. at 564. *See also Humane Soc'y v. Hodel*, 840 F.2d 45, 52 (D.C. Cir. 1988) (standing where agency expanded approval for hunting, "depleting the supply of animals . . . that . . . [plaintiffs] seek to view" and causing plaintiffs to witness "animal corpses"); *Am. Bottom Conservancy v. Army Corps of Engineers*, 650 F.3d 652, 657 (7th Cir. 2011) (standing for bird-watchers to challenge agency permit that would allow development and thus "diminish the wildlife population visible to them"); *Ctr. for Biological Diversity v. EPA*, 861 F.3d 174, 183 (D.C. Cir. 2017) (standing where agency authorization to use pesticide created "demonstrable risk" to beetles and butterflies that plaintiffs intended to view).

Unborn babies are a source of profound joy for those who view them. Expectant parents eagerly share ultrasound photos with loved ones. Friends and family cheer at the sight of an unborn child. Doctors delight in working with their unborn patients—and experience an aesthetic injury when they are aborted.

Plaintiffs' declarations illustrate that they experience aesthetic injury from the destruction of unborn life. Dr. Francis testified to working with an unborn child who was subsequently killed by mifepristone:

> [A] partner of mine and I cared for another patient who also suffered complications from chemical abortion. I had taken care of her when she was hospitalized . . . at 9 weeks 5 days gestation. She was discharged home in good condition after 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. . . . Approximately one 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.

Dr. Francis Declaration ¶ 13.

Dr. Jester put Plaintiffs' interest in unborn life this way: "When my patients have chemical abortions, I lose the opportunity . . . to care for the woman and child through pregnancy and bring about a successful delivery of new life." Dr. Jester Declaration ¶ 19. *See Ctr. for Biological Diversity v. EPA*, 937 F.3d 533, 541 (5th Cir. 2019) (recognizing judicially cognizable injury where plaintiff experiences aesthetic harm at work).

The Supreme Court has recognized that "the person who observes or works with a particular animal threatened by a federal decision is facing perceptible harm, since the very subject of his interest will no longer exist." *Lujan*, 504 U.S. at 566. Every circuit, including our own, has concluded that, when a federal agency authorizes third parties to harm flora or fauna that a plaintiff intends to view or study, that satisfies all of the requirements for Article III standing. *See*, *e.g.*, *Housatonic River Initiative v. EPA*, _ F.4th_, 2023 WL 4730222, *9 (1st Cir. July 25, 2023); *NRDC v. FAA*, 564 F.3d 549, 555 (2nd Cir. 2009); *Sierra Club v. EPA*, 972 F.3d 290, 298-99 (3rd Cir. 2020); *Sierra Club v. Dep't of the Interior*, 899 F.3d 260, 282-85 (4th Cir. 2018); *Gulf Restoration Network v. Salazar*, 683 F.3d 158, 166-68 (5th Cir. 2012); *Meister v. Dep't of Agriculture*, 623 F.3d 363, 369-70 (6th Cir. 2010); *Am. Bottom Conservancy*, 650 F.3d at 656-60; *Sierra Club v. Army Corps of Engineers*, 645 F.3d 978, 985-86 (8th Cir. 2011); *Cottonwood*

Env't Law Ctr. v. Forest Service, 789 F.3d 1075, 1079-83 (9th Cir. 2015); *WildEarth Guardians v. EPA*, 759 F.3d 1196, 1206-07 (10th Cir. 2014); *Black Warrior Riverkeeper, Inc. v. Army Corps of Engineers*, 781 F.3d 1271, 1280-83 (11th Cir. 2015); *Ctr. for Biological Diversity v. EPA*, 56 F.4th 55, 66-69 (D.C. Cir. 2022).

In all of these cases, a federal agency approved some action—such as developing land or using pesticides—that threatens to destroy the animal or plant life that plaintiffs wish to enjoy. This injury is redressable by a court order holding unlawful and setting aside the agency approval.

And so too here. The FDA has approved the use of a drug that threatens to destroy the unborn children in whom Plaintiffs have an interest. And this injury is likewise redressable by a court order holding unlawful and setting aside approval of that abortifacient drug.

I see no basis for allowing Article III standing based on aesthetic injury when it comes to animals and plants —but not unborn human life.

II.

I now turn specifically to Plaintiffs' challenge to the FDA's 2000 approval of mifepristone. The FDA contends that the challenge is untimely. But it concedes that "the well-established reopening doctrine" is binding precedent in this circuit. *Texas v. Biden*, 20 F.4th 928, 951 (5th Cir. 2021), *rev'd on other grounds*, 142 S. Ct. 2528 (2022). And it accepts that, under that doctrine, the clock for an APA claim restarts when an agency revises its regulations in a manner that "significantly alters the stakes of judicial review." *Sierra Club v. EPA*, 551 F.3d 1019, 1025 (D.C. Cir. 2008). *See also*

NRDC v. EPA, 571 F.3d 1245, 1266 (D.C. Cir. 2009) (same).

That standard is easily met here. It seems obvious that the 2016 and 2021 revisions significantly altered the regulatory landscape. Indeed, the FDA recently told the Supreme Court that setting aside those revisions would "upend the regulatory regime for mifepristone" and "unleash[] regulatory chaos." Application to Stay the Order Entered by the United States District Court for the Northern District of Texas and for An Administrative Stay, 2023 WL 3127519, at *2-3, *FDA v. Alliance for Hippocratic Medicine*, 143 S. Ct. 1075 (2023). If switching from the 2016/2021 regime to the 2000-era regime significantly alters the "basic regulatory scheme," *NRDC*, 571 F.3d at 1266, then surely the reverse does, too.

So the district court was correct that "FDA's 2016 and 2021 Changes . . . significantly departed from the agency's original approval of the abortion regimen. FDA . . . altered its original decision by removing safeguards and changing the regulatory scheme for chemical abortion drugs." *Alliance for Hippocratic Medicine v. FDA*, _ F. Supp. 3d _, 2023 WL 2825871, at *11 (N.D. Tex. Apr. 7, 2023). As a result, the 2016 and 2021 revisions triggered the reopening doctrine. Plaintiffs' challenge to the 2000 approval is timely.

A.

Challenges to federal administrative action are subject to a six-year statute of limitations. *See* 28 U.S.C. § 2401(a). This six-year clock initially started ticking in March 2016, when the FDA denied Plaintiffs' 2002 petition objecting to the 2000 approval. *See* 21 C.F.R.

§ 10.45(d). Absent reopening, Plaintiffs' challenge to the 2000 approval would be barred by this six-year statute of limitations, because Plaintiffs filed this suit after March 2022.

But under the administrative reopening doctrine, the agency can restart the clock in two ways: (1) if "the agency opened the issue up anew, and then reexamined and reaffirmed its prior decision," *NRDC*, 571 F.3d at 1265 (cleaned up), or (2) "if the revision of accompanying regulations 'significantly alters the stakes of judicial review' as the result of a change that 'could have not been reasonably anticipated,'" *id.* at 1266 (quoting *Sierra Club v. EPA*, 551 F.3d 1019, 1025 (D.C. Cir. 2008)).

This second type of reopening is called "constructive reopening." *Id.* I would hold that constructive reopening applies here, rendering Plaintiffs' challenge to the 2000 approval timely.

"A constructive reopening occurs if the revision of . . . regulations 'significantly alters the stakes of judicial review.'" *Sierra Club*, 551 F.3d at 1025 (quoting *Kennecott Utah Copper Corp. v. Dep't of the Interior*, 88 F.3d 1191, 1227 (D.C. Cir. 1996)). The paradigmatic example of this is when the agency unexpectedly removes "necessary safeguards," thus giving "new significance" to the original action. *Id.* at 1025-26.

In *Sierra Club*, the EPA's initial 1994 rule exempted pollutant-emitting plants from emission limits when the plants were starting up, shutting down, or malfunctioning. *See id.* at 1022. To be eligible for the exemption, a plant had to show it was doing its "reasonable best" to stay under the emission limits. *Id.*

But in the early 2000s, new EPA rules removed this "reasonable best" requirement. To qualify for the exemption, plants no longer had to show they were doing their best to limit emissions. *See id.* at 1023. This elimination of safeguards "significantly altered the stakes of judicial review" for the environmental plaintiffs, thereby triggering reopening. *Id.* at 1025 (cleaned up).

The same is true here. Just as the EPA initially authorized emissions under certain safeguards to minimize harm, the FDA initially authorized mifepristone under certain safeguards to minimize harm. Remove these safeguards, and you've significantly altered the stakes of judicial review. The original scheme is now much more "worth challenging." *Id.* at 1026 (quotation omitted).

B.

Plaintiffs' challenge to the 2000 approval easily satisfies the reopening doctrine. Both the 2016 and 2021 revisions made significant and unexpected alterations to the basic regulatory scheme. They took away key safeguards, significantly raising the stakes of judicial review for the underlying approval.

When it approved mifepristone in 2000, the FDA included a number of "necessary safeguards" to minimize harm from this dangerous drug. *Sierra Club*, 551 F.3d at 1025. For example, the FDA required an in-person follow-up appointment to protect the woman from sepsis, which occurs if the child's remains are not removed from her body after the abortion. *See* FDA Approval Memorandum to Population Council at 3 (Sep. 28, 2000). It also limited the use of mifepristone to the first seven

weeks, ensuring that the abortion took place early in pregnancy. *See id.* at 1. And it required a physician to supervise the administration of mifepristone, in order to "date pregnancies and diagnose ectopic pregnancies." *Id.* at 5. *See also id.* at 6 (same).

The 2016 amendments removed these key safeguards. By approving the abortifacient for use up to ten weeks, by allowing non-physicians to prescribe and administer the drug, and by removing the in-person follow-up requirement, the 2016 revisions significantly altered the stakes of judicial review. "These are not mere 'minor changes.'" *Sierra Club*, 551 F.3d at 1025. By modifying its original restrictions, the FDA constructively reopened the drug's approval.

The 2016 amendments became final in 2021, when the FDA denied the 2019 Petition challenging them. *See* 21 C.F.R. § 10.45(d). Plaintiffs' challenge is therefore timely.

The 2021 Mail-Order Decision worked an even greater "sea change" to the "basic regulatory scheme." *NRDC*, 571 F.3d at 1266. From the getgo, the FDA's approval of mifepristone was explicitly premised on in-person dispensing. The initial 2000 approval required "[p]rovision of [the] drug through a direct, confidential physician distribution system that ensures only qualified physicians will receive the drug for patient dispensing." FDA Approval Memorandum to Population Council at 6. *See also id.* at 4 ("[T]he drug will be distributed directly to physicians. It will not be available from pharmacies."). The agency viewed this as necessary to "address[] the issue of physical security of the drug." *Id.*

So "[t]he in-person dispensing requirement . . . was critical to FDA's initial approval of mifepristone in 2000, which relied on the in-person dispensing requirement to dismiss concerns about provider qualifications, improper use, illicit distribution, and detection of adverse events." *Alliance for Hippocratic Medicine v. FDA*, 2023 WL 2913725, at *14 (5th Cir. Apr. 12, 2023). "[T]he in-person dispensing requirement was FDA's primary tool for ensuring the safe distribution and use of mifepristone." *Id.* at *15.

"[T]his change eliminates a major safeguard against complications and adverse effects arising from improper mifepristone use." *Id.* It "significantly alters the stakes of judicial review," triggering reopening. *NRDC*, 571 F.3d at 1266 (quoting *Sierra Club*, 551 F.3d at 1025).

C.

The FDA counters that the 2016 and 2021 revisions could not have significantly altered the stakes of judicial review or made the regulatory scheme worth challenging in a way it wasn't before. After all, the FDA says, Plaintiffs already challenged the original 2000 approval in their 2002 petition.

But not all of the Plaintiffs here participated in the 2002 petition. For those Plaintiffs, the FDA's current regime is clearly "worth challenging," even if the *ancien régime* of 2000 "may not have been" on its own. *Kennecott Utah Copper Corp.*, 88 F.3d at 1227.

Indeed, the FDA itself has characterized the switch from one regime to the other as a "sea change." *NRDC*, 571 F.3d at 1266. Under the limited stay issued by a previous panel of our court, the FDA was required to

return to the regulatory regime that existed between 2000 and 2016. *See Alliance*, 2023 WL 2913725, at *1. The FDA vigorously protested the substitution of the 2016 and 2021 regime with the original 2000 regulations. It urged the Supreme Court to restore the 2016 and 2021 regulations by granting a stay of the entire district court order. Switching back to the 2000 restrictions, it argued, would "upend the regulatory regime for mifepristone, with sweeping consequences for the pharmaceutical industry, women who need access to the drug, and FDA's ability to implement its statutory authority." FDA Stay Application, 2023 WL 3127519, at *3. It would "unleash[] regulatory chaos" for "patients, prescribers, and the health care delivery system." *Id.* at *2, *4.

In sum, the FDA insisted that switching from one regime to the other would "change the basic regulatory scheme." *NRDC*, 571 F.3d at 1266. It claimed that switching from the 2016/2021 scheme back to the 2000 scheme counts as a sweeping change with huge stakes. The same must be true of switching from 2000 to 2016/2021—that too "upend[ed] the regulatory regime for mifepristone, with sweeping consequences."

Plaintiffs' challenge to the 2000 approval of mifepristone is timely.

III.

Turning to the merits, I would hold the 2000 approval unlawful. It's a longstanding principle that agencies must follow their own regulations. *See Arizona Grocery Co. v. Atchison, Topeka & Santa Fe Ry. Co.*, 284 U.S. 370, 386 (1932) (agency's legislative rule "has the force of a statute"); *Fort Stewart Schools v.*

FLRA, 495 U.S. 641, 654 (1990) ("It is a familiar rule of administrative law that an agency must abide by its own regulations."). The FDA violated that principle when it approved mifepristone under Subpart H—as even the drug's sponsor, the Population Council, admitted in 2000.

A.

Subpart H authorizes the FDA to approve only those drugs that treat "serious or life-threatening illnesses." 21 C.F.R. § 314.500. *See also* 57 Fed. Reg. 58958 (Dec. 11, 1992) (Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses). It "applies to 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." 21 C.F.R. § 314.500 (emphasis added).

Pregnancy is not an illness. An "illness" is a "[b]ad or unhealthy condition of the body." Oxford English Dictionary (2nd ed. 1989), *s.v. illness*, sense 3. It's a "disease, ailment, sickness, malady." *Id.* Pregnancy, by contrast, is when a woman is "with child." Oxford English Dictionary, *s.v. pregnancy*, sense II.3.a.

Pregnancy is not a bad or unhealthy condition of the body—it's a natural consequence of a healthy and functioning reproductive system. *See*, *e.g.*, *Gudenkauf v. Stauffer Communications, Inc.*, 922 F. Supp. 465, 473 (D. Kan. 1996) ("Being the natural consequence of a properly functioning reproductive system, pregnancy cannot be called an impairment."); *Lacount v. South Lewis*, 2017 WL 319217, at *3 (N.D. Okla. Jan. 20, 2017) (same); *Whitaker v. Bosch Braking Sys. Div. of Robert*

Bosch Corp., 180 F. Supp. 2d 922, 928 (W.D. Mich. 2001) (pregnancy is "not a serious health condition"); *Brennan v. National Telephone Directory Corp.*, 850 F. Supp. 331, 343 (E.D. Pa. 1994) ("it cannot be said that [a woman's] reproductive system is negatively affected" by pregnancy).

To be sure, pregnancy can sometimes *result* in illness. *Cf. Spees v. James Marine, Inc.*, 617 F.3d 380, 397 (6th Cir. 2010) ("Pregnancy-related conditions have typically been found to be impairments where they are not part of a 'normal' pregnancy."). But that does not make the pregnancy itself an illness. *See Whitaker*, 180 F. Supp. 2d at 929 ("pregnancy per se does not constitute a serious health condition").

The same could be said about old age. Many people become ill as they grow older. But growing older itself is obviously not an illness. Like pregnancy, it's the "natural consequence" of a healthy and functioning body. It's entirely normal to celebrate pregnancies, just as it's normal to celebrate birthdays. We don't typically celebrate "bad or unhealthy conditions."

So pregnancy does not qualify as a "serious or life-threatening illness" within the meaning of 21 C.F.R. § 314.500. The FDA implausibly "determined" that it does. FDA Approval Memorandum to Population Council at 6. Courts do not defer to agency interpretations of unambiguous regulations. *See Kisor v. Wilkie*, 139 S. Ct. 2400, 2415 (2019). There's "only one reasonable construction" of the word "illness"—and it doesn't include pregnancy. *Id.*

There is accordingly no basis for deferring to the agency. The FDA simply got it wrong. As even the

sponsor of mifepristone, the Population Council, admitted, "[n]either pregnancy nor unwanted pregnancy is an illness, and Subpart H is therefore inapplicable for that reason alone." Population Council Letter to FDA at 1-2. "The plain meaning of these terms does not comprehend normal, everyday occurrences such as pregnancy and unwanted pregnancy." *Id.* at 2.

B.

The FDA does not even try to argue that pregnancy is an "illness." Instead, the FDA, along with intervenor Danco, points out that the preamble to Subpart H uses the terms "illness," "disease," and "condition" interchangeably. *See*, *e.g.*, 57 Fed. Reg. 58942, 58948 ("The drug in question must be for a serious or life-threatening condition."). So they argue that Subpart H allows the FDA to approve drugs that treat life-threating *conditions*, as well as life-threating *illnesses*. And although pregnancy is plainly not an "illness," the argument goes, pregnancy is at least a "condition."

There are two problems with this argument. First, we do not use preambles to expand the meaning of clear regulatory text. *See District of Columbia v. Heller*, 554 U.S. 570, 578 n.3 (2008) ("[I]n America 'the settled principle of law is that the preamble cannot control the enacting part of the statute in cases where the enacting part is expressed in clear, unambiguous terms.'"); ANTONIN SCALIA & BRYAN A. GARNER, READING LAW 218 (2012) ("[T]he prologue cannot give words and phrases of the dispositive text a meaning that they cannot bear.").

Second, this argument—that the preamble broadens "illness" to include "conditions"—equivocates between

two distinct meanings of the word "condition." As used in the preamble, "condition" means a "defective state of health." MERRIAM-WEBSTER'S COLLEGIATE DICTIONARY (11th ed. 2007), *s.v. condition*, sense 4c. In this sense, "condition" is a synonym of "illness." *See* MERRIAM-WEBSTER'S COLLEGIATE THESAURUS (1988), *s.v. condition*, sense 6 (listing "disease," "aliment," and "sickness" as synonyms of "condition").

Of course, "condition" can also mean "a state of being" more broadly. Merriam-Webster's Collegiate Dictionary, *s.v.*, *condition*, sense 4a. And pregnancy is certainly a "condition" in this broader sense.

But the fact that pregnancy is a "condition" in the broad sense of "state of being" does not make it a "condition" in the narrow sense of "illness." And Subpart H plainly contemplates the narrow sense, because it uses "condition" interchangeably with "illness." A regulation about "cars" doesn't cover bicycles just because its preamble sometimes mentions "vehicles." Likewise, a regulation about "illnesses" doesn't address pregnancy just because its preamble sometimes mentions "conditions."[9]

C.

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[9] Danco responds by citing a Government Accountability Office report, which observes that the FDA has used Subpart H to approve drugs for treating "breakthrough cancer pain, specific symptoms of narcolepsy, and severe acne." GAO, Approval and Oversight of the Drug Mifeprex at 10 (Aug. 2008). "Severe recalcitrant nodular acne" may well be a serious illness. *Id.* at 44. But that has nothing to do with whether pregnancy is a serious or life-threatening illness.

The agency's brief proclaims that "FDA Properly Approved Mifepristone Under Subpart H." Yet in the very next paragraph, the FDA turns around and *denies* that it used Subpart H to approve mifepristone—claiming that the approval was "based on FDA's statutory authority under 21 U.S.C. § 355, not Subpart H."

As the panel majority opinion details, Subpart H encompasses two different paths. The first is entitled "Approval based on a surrogate endpoint or on an effect on a clinical endpoint other than survival or irreversible morbidity." 21 C.F.R. § 314.510 (emphasis omitted). The second is entitled "Approval with restrictions to assure safe use." 21 C.F.R. § 314.520 (emphasis omitted).

Mifepristone was approved under § 314.520 of Subpart H—approval with restrictions. But the FDA now suggests that § 314.520 isn't really a method of approval at all—it's just a method of adding restrictions on use.

This argument is belied by the regulations. The header explicitly refers to this second path as a method of "[a]pproval." *Id.* § 314.520. More importantly, the regulatory text repeatedly refers to § 314.520 as a method of drug approval. *See id.* § 314.530(a) ("new drugs approved under . . . 314.520"); *id.* § 314.530(b) ("an application approved under . . . § 314.520"); *id.* § 314.560 ("drug products approved under § 314.520").

The FDA's argument contradicts not only the text, but also its own statements over the past 23 years. *See Chenery*, 318 U.S. at 95; *Motor Vehicle Mfrs. Ass'n v. State Farm*, 463 U.S. 29, 50 (1983) ("[C]ourts may not accept appellate counsel's *post hoc* rationalizations for agency action.").

In its original 2000 approval memo, the FDA expressly stated that "[t]his drug is being approved under Subpart H." FDA Approval Memorandum to Population Council at 8. And it has repeatedly reaffirmed this view in the years since. *See* FDA Supplemental Approval Letter to Danco Labs at 1 (June 6, 2011) (application "approved under the provisions of 21 CFR 314.520 (Subpart H)"); FDA Letter Denying 2002 Citizen Petition at 2 (Mar. 29, 2016) ("The application was approved under 21 CFR part 314, subpart H."); FDA Letter Denying 2019 Citizen Petition at 2 (Dec. 16, 2021) (same).

The GAO report cited by both the FDA and Danco likewise repeatedly describes mifepristone as having been "approved" under Subpart H. GAO, Approval and Oversight of the Drug Mifeprex at 1 (Aug. 2008) ("FDA approved the drug under a provision of the agency's Subpart H regulations."); *id.* at 5 ("FDA approved Mifeprex under the restricted distribution provision of its Subpart H regulations."); *id.* at 6 (FDA "approved the Mifeprex [application] under Subpart H."). *See also id.* at 10, 14-15, 21-24, 32, 44 (same). The report also notes that the FDA used Subpart H to "approve" other drugs. *See id.* at 5 n.13, 25 n.46, 27 n.50, 29 n.53, 36 n.63. And it explicitly refers to § 314.520 as an "approval provision." *Id.* at 1 n.2.

The FDA notes that its *statutory* authority to approve drugs comes from 21 U.S.C. § 355. But that doesn't change the fact that the *regulatory* path it chose was Subpart H. Section 355 gives the FDA the power to approve drugs. And the agency exercised that power when it promulgated Subpart H. The FDA did

not have to adopt Subpart H in the first place. But once it did, it was bound to follow it.

D.

As a final defense, the FDA contends that subsequent events cured any defects in its initial 2000 approval. Specifically, the FDA points to the 2007 Food and Drug Administration Amendments Act and to the agency's 2011 Risk Evaluation and Mitigation Strategy. It claims that both authorities render any faults with the 2000 approval irrelevant.

First, the FDA argues that the 2007 Act "deemed" mifepristone to be approved. But the statutory text contradicts this argument. The Act makes clear that "[a] drug that was *approved before the effective date of this Act* is . . . deemed to have in effect an approved risk evaluation and mitigation strategy . . . if there are in effect on the effective date of this Act elements to assure safe use . . . required under [21 C.F.R. §] 314.520." Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, tit. IX § 909(b)(1), 121 Stat. 823, 950 (emphasis added).

So the Act itself did not approve any drugs. It only approved any risk evaluation and mitigation strategies for those drugs that the FDA had *already* validly approved under § 314.520 of Subpart H. And as explained above, the FDA's attempted approval was invalid because it failed to comply with Subpart H. The FDA's reliance on the 2007 Act is entirely circular—it only works if you assume that the agency had already validly approved mifepristone in the first place.

The FDA also points to its 2011 Risk Evaluation and Mitigation Strategy, arguing that this too re-approved

mifepristone and cured any defects in its 2000 approval. It did not. To the contrary, the 2011 REMS letter made clear that the agency continued to rely on Subpart H for its approval of mifepristone—that it "is approved under the provisions of 21 CFR 314.520 (Subpart H)." FDA Supplemental Approval Letter to Danco Labs at 1. Moreover, the letter only approved the Risk Evaluation and Mitigation Strategy proposed in Danco's 2008 Supplemental Application—it did not re-approve the drug apart from Subpart H. In fact, the letter recognized the need for continued compliance with the conditions "required by" Subpart H. *Id.* at 2 (citing 21 C.F.R. § 314.550).

* * *

For these reasons, I would find that Plaintiffs are likely to succeed on the merits of their challenge to the 2000 approval. Plaintiffs also satisfy the remaining factors for equitable relief. The harm to Plaintiffs is irreparable. No relief at law can adequately address Plaintiffs' conscience injuries. *See BST Holdings, L.L.C. v. OSHA*, 17 F.4th 604, 618 (5th Cir. 2021). Nor can money damages remedy the destruction of life. *Cf. Amoco Production Co. v. Village of Gambell*, 480 U.S. 531, 545 (1987). The balance of equities and public interest also favor Plaintiffs. Plaintiffs seek to vindicate the "national policy of discountenancing abortion as inimical to the national life," as reflected in Congressional enactments including the Comstock Act. *Bours v. United States*, 229 F. 960, 964 (7th Cir. 1915). *See* 18 U.S.C. § 1461; *id.* § 1462. *Cf.* 19 U.S.C. § 1305(a).

IV.

With respect to the FDA's 2016 and 2021 revisions, I agree with the majority's thoughtful analysis explaining how the FDA "entirely failed to consider an important aspect of the problem" in 2016 and "offered an explanation for its decision that runs counter to the evidence before the agency" in 2021. *State Farm*, 463 U.S. at 43. The agency thus acted arbitrarily in violation of the APA.

I write separately to add that the 2021 revisions violate the Comstock Act, 18 U.S.C. §§ 1461-62, and are "not in accordance with law" for that reason as well. 5 U.S.C. § 706(2)(A).

A.

The text of the Comstock Act prohibits the mailing of abortifacient drugs:

> Every article or thing designed, adapted, or intended for producing abortion . . . and [e]very article, instrument, substance, drug, medicine, or thing which is advertised or described in a manner calculated to lead another to use 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.
>
> Whoever knowingly uses the mails for the mailing, carriage in the mails, or delivery of anything declared by this section . . . to be nonmailable . . . shall be fined under this title or imprisoned not more than five years, or both, for the first such offense, and shall be fined under this title or imprisoned not more than ten years, or both, for each such offense thereafter.

18 U.S.C. § 1461. This language derives from the original 1873 Comstock Act. *See* Act of Mar. 3, 1873, ch. 258, § 2, 17 Stat. 598, 599 ("No . . . article or thing designed or intended for the . . . procuring of abortion . . . shall be carried in the mail.").

Congress later extended the mailing prohibition to cover common carriers as well. *See* Act of Feb. 8, 1897, ch. 172, 29 Stat. 512, 512 ("[I]t shall be unlawful for any person to deposit with any express company or other common carrier . . . any article or thing designed or intended for the . . . procuring of abortion."). As currently in force, this provision states:

> Whoever brings into the United States . . . or knowingly uses any express company or other common carrier or interactive computer service . . . for carriage in interstate or foreign commerce . . . any drug, medicine, article, or thing designed, adapted, or intended for producing abortion . . . or [w]however knowingly takes or receives, from such express company or other common carrier or interactive computer service . . . any matter or thing the carriage or importation of which is herein made unlawful . . . [s]hall be fined under this title or imprisoned not more than five years, or both, for the first such offense and shall be fined under this title or imprisoned not more than ten years, or both, for each such offense thereafter.

18 U.S.C. § 1462.

In 1996, Congress added "interactive computer service" to the Comstock Act. *See* Telecommunications Act of 1996, Pub. L. No. 104-104, § 507(a), 110 Stat. 56, 137. So it's also illegal to use the internet to ship or

receive abortifacients. *See* 18 U.S.C. § 230(f)(2) (defining "interactive computer service"); *id.* § 230(f)(3) ("interactive computer service" includes "the Internet"); *Doe v. MySpace, Inc.*, 528 F.3d 413, 415 (5th Cir. 2008) ("interactive computer service" includes "a Web site").

The FDA's 2021 Mail-Order Decision violates the Comstock Act. That decision authorizes the dispensing of mifepristone "through the mail . . . or through a mail-order pharmacy." FDA Letter to American College of Obstetricians and Gynecologists at 2 (Apr. 12, 2021). But "us[ing] the mails for the mailing" of a "drug . . . for producing abortion" is precisely what the Comstock Act prohibits. 18 U.S.C. § 1461. *See Alliance*, 2023 WL 2913725, at *20 ("[A] user of those shipping channels violates the plain text merely by knowingly making use of the mail for a prohibited abortion item.").

The FDA's 2023 Risk Evaluation and Mitigation Strategy modification doubles down on this violation by permanently eliminating the in-person dispensing requirement. Under the 2023 REMS, pharmacies ship mifepristone to its users. To become certified to distribute mifepristone, a pharmacy must "[b]e able to ship mifepristone using a shipping service." FDA, REMS for Mifepristone at 3 (Jan. 2023). Pharmacies must also "[t]rack and verify receipt of each shipment" and "[m]aintain records of dispensing and shipping." *Id.* And distributors Danco and GenBioPro must "[s]hip mifepristone . . . to certified pharmacies." *Id.* at 4.

All of this violates the Comstock Act by "us[ing] [an] express company or other common carrier or interactive computer service" to ship a "drug . . . for pro-

ducing abortion." 18 U.S.C. § 1462(c). *See Alliance*, 2023 WL 2913725, at *20 ("Danco has no interest in continuing to violate the law, which . . . it does every time it ships mifepristone."); *Alliance*, 2023 WL 2825871, at *18 ("[T]he Comstock Act plainly forecloses mail-order abortion."); *Texas v. Becerra*, 623 F. Supp. 3d 696, 733 (N.D. Tex. 2022) ("[F]ederal law bar[s] the importation or delivery of . . . medicine designed to produce an abortion.") (citing 18 U.S.C. § 1461).

B.

The FDA asserts various atextual considerations in an effort to avoid the unambiguous meaning of the Act.

First, the FDA urges that the provisions only prohibit distribution by USPS and common carrier—and not by private carrier. But that reads the words "interactive computer service" out of the statute. The Comstock Act forbids using "any express company or other common carrier or interactive computer service" for carriage of abortifacients. 18 U.S.C. § 1462. As a practical matter, all carriers today, including private carriers, use online systems for shipping items.

Next, the FDA claims that the Comstock Act prohibits sending abortifacients only when they are used in violation of state law. To support this theory, it relies on a handful of early twentieth century cases outside our circuit. *See Application of the Comstock Act to the Mailing of Prescription Drugs That Can Be Used for Abortions*, 46 Op. O.L.C. _, _ (Dec. 23, 2022) (collecting cases).

But the earliest case it cites, *Bours v. United States*, 229 F. 960 (7th Cir. 1915), rejects the FDA's position. *Bours* says that "it is immaterial what the local statu-

tory definition of abortion is, what acts of abortion are included, or what excluded." *Id.* at 964. Rather, "the word 'abortion' in the national statute must be taken in its general medical sense." *Id.* And "[i]ts inclusion in the statute governing the use of the mails indicates a national policy of discountenancing abortion as inimical to the national life." *Id.* Under *Bours*, the Act's definition of "abortion" excludes "operation[s]" that are necessary to "save [the mother's] life." *Id.* But anyone who uses the mails to "destroy[] life" violates the statute. *Id.*

So the FDA can't invoke the prior-construction canon. Under that canon, legislative reenactment of a statute can, under certain conditions, effectively ratify preexisting, authoritative judicial interpretation of that statute. But the canon requires robust judicial consensus, such as "uniform holdings of lower courts." Scalia & Garner, *supra*, at 324. *See*, *e.g.*, *Armstrong v. Exceptional Child Ctr., Inc.*, 575 U.S. 320, 330 (2015) (quoting *Bragdon v. Abbott*, 524 U.S. 624, 645 (1998)) (canon applies when "judicial interpretations have *settled* the meaning of an existing statutory provision") (emphasis added); *Tex. Dep't of Housing & Community Affairs v. Inclusive Communities Project, Inc.*, 576 U.S. 519, 536 (2015) ("Congress accepted and ratified the *unanimous* holdings of the Courts of Appeals.") (emphasis added). The FDA can claim no such consensus here. To the contrary, the circuits were at best split. *Bours* rejects the FDA's reading of the statute. And the amicus brief from the Ethics and Public Policy Center puts forth a strong argument that no circuit court adopted the FDA's reading.

What's more, Congress certainly knew how to prohibit only those abortifacients used to violate state law. The Tariff Act of 1930, for example, prohibits all persons "from importing . . . any drug or medicine or any article whatever for causing *unlawful* abortion." 19 U.S.C. § 1305 (emphasis added). *See also* Act of June 17, 1930, ch. 497, tit. III, § 305, 46 Stat. 590, 688 (same). In response, the FDA suggests that it would be irrational for Congress to target all abortions in the Comstock Act, but only unlawful abortions in the Tariff Act. But different Congresses can reach different judgments about how to regulate abortion in different contexts. There's nothing irrational about the Congress that enacted the Comstock Act in 1873 making a different judgment from the Congress that enacted the Tariff Act decades later.

Moreover, Congress has actually considered amending the Comstock Act to apply only to "illegal abortions" —and chosen not to. In 1978, Congress rejected a proposed Comstock Act amendment to prohibit the shipment of "any drug, medicine, article, or thing, with the intent that such drug, medicine, article, or thing be used to produce an *illegal* abortion." H.R. 13959, 95th Cong. § 6702(1)(C)(i) (1978) (emphasis added). *See also id.* § 6701(a)(2) (same). A contemporaneous Congressional report explained:

> [R]evised title 18 *changes current law* by requiring proof that the relevant material or object to be used to produce an *illegal* abortion and that the offender specifically intended the material object to be so used. . . . [A]n abortion is "illegal" if it is contrary to the law of the state in which the abortion is performed.

Report of the Subcommittee on Criminal Justice on Recodification of Federal Criminal Law, H.R. Rep. No. 95-29, pt. 3, at 42 (1978) (emphasis added).

Congress also had the opportunity to remove "abortion" from the Comstock Act altogether. *See* Comstock Cleanup Act of 1996, H.R. 3057, 104th Cong. (1996). *See also* 142 Cong. Rec. 24313, 24313 (Sep. 24, 1996) (statement of Rep. Pat Schroeder, sponsor of H.R. 3057) ("[T]he Comstock Act has never been repealed; it is still on the books."); *id.* at 24313-14 ("[T]his body just allowed the Comstock Act to be enforced on the Internet vis-à-vis anything doing with abortion. . . . The Telecommunications Act passed this year extended the Comstock Act's prohibitions to anyone who uses an interactive computer service."). But again, Congress declined to remove "abortion" from the statute. To the contrary, it chose to repeal only the Act's prohibition on the shipment of contraceptives. *See* Pub. L. No. 91-662, §§ 3-4, 84 Stat. 1973, 1973 (1971).

So if the FDA wants us to look to the post-enactment history of the Comstock Act rather than its text, that history only reinforces the natural reading of the text. I would set aside the 2021 Mail-Order Decision because it violates the Comstock Act.

V.

In this appeal, neither the FDA nor Danco is content to simply argue that the district court erred. They disparage the ruling as "an unprecedented judicial assault on a careful regulatory process." The "non-expert" district court issued an "unprecedented order countermanding the scientific judgment of the Food and Drug Administration."

Their message is simple: The scientists at the FDA can do no wrong. So courts have no business reviewing their actions.

That's mistaken on multiple levels.

To begin with, Congress has directed the judiciary to review the legality of regulatory action by the FDA, no less than with other agencies.

Congress could have exempted the FDA generally—or its approval of drugs specifically—from APA review. *See* 5 U.S.C. § 701(a)(1) (no APA review where "statutes preclude judicial review"). But it didn't—and for understandable reasons.

Scientists have contributed an enormous amount to improving our lives. But scientists are human beings just like the rest of us. They're not perfect. *See*, *e.g.*, *Whole Woman's Health v. Paxton*, 10 F.4th 430, 464-70 (5th Cir. 2021) (en banc) (Ho, J., concurring). None of us are. We all make mistakes.

And the FDA has made plenty. Several of the FDA's past mistakes are detailed in the amicus briefs from the United States Medical Association and the Association of American Physicians and Surgeons Educational Foundation. I'll highlight just a few examples here.

Earlier this year, the FDA was forced to pull the drug Makena from the market. *See FDA News Release: FDA Commissioner and Chief Scientist Announce Decision to Withdraw Approval of Makena* (Apr. 6, 2023). The FDA had approved this drug in 2011 to treat premature birth, using Subpart H. *See* Frank J. Sasinowski & Alexander J. Varond, *FDA's Flexibility in Subpart H Approvals: Assessing Quantum of Effectiveness Evidence*, 71 Food & Drug L.J.

135, 167 (2016). Yet the drug turned out to have "no benefit for mothers or babies." Christina Jewett, *Preterm Birth Drug Withdrawn After 12 Years*, N.Y. Times (Mar. 7, 2023). As one headline put it, "F.D.A. Rushed a Drug for Preterm Births. Did it Put Speed Over Science?" Christina Jewett, N.Y. Times (Mar. 25, 2022). "Makena is another example . . . of a medication fast-tracked by the [FDA] onto the market even though considerable doubt remained about whether it worked." *Id.* (Makena involved the other Subpart H approval pathway—approval with a surrogate endpoint, not approval with restrictions. But an agency that relies on bad science for approval under one Subpart H pathway can surely do so under the other as well.)

The FDA hasn't just approved ineffective drugs—it's also approved harmful drugs. In 1941, for example, it approved DES for use by pregnant women to treat certain postpartum conditions. Several years later, the FDA approved it to prevent miscarriages as well. The FDA's approval has since been called a "tragedy." Jessica Dye, *FDA Outlines Initiatives Inspired by DES 'Tragedy'*, Law360 (Feb. 24, 2011). "Even before the [FDA] approved the drug in 1941, researchers knew that DES caused cancer and problems with sexual development in laboratory animals." Nancy Langston, *The Retreat from Precaution: Regulating Diethylstilbestrol (DES), Endocrine Disruptors, and Environmental Health*, 13 Environmental History 41, 42 (2008). "These concerns initially led [the] FDA Commissioner . . . to reject the drug." *Id.* But "by 1947, the FDA had abandoned its position of precaution." *Id.*

Only in 2000 did FDA finally and formally "withdraw[] approval" of DES—*nearly six decades* after it approved the drug. 65 Fed. Reg. 55264 ("Withdrawal of Approval of 28 New Drug Applications"). DES turned out to be a carcinogen. *See Diethylstilbestrol (DES) Exposure and Cancer*, Nat'l Cancer Inst. (Dec. 20, 2021). It also significantly increases the odds of infertility, miscarriage, stillbirth, and neonatal death. *See id.*

The FDA has been blamed for contributing to the opioid crisis. Opioid overdose was "once rare" in the United States. Andrew Kolodny, *How FDA Failures Contributed to the Opioid Crisis*, 22 AMA J. ETHICS 743, 743 (2020). But now "the vast oversupply of opioid drugs in the United States has caused a plague." *In re Nat'l Prescription Opiate Litigation*, 927 F.3d 919, 924 (6th Cir. 2019) (approvingly quoting the district court). As one noted scholar observed in the *AMA Journal of Ethics*, "[t]he FDA did not properly enforce the Food, Drug, and Cosmetic Act when it approved Purdue Pharma's new drug application for extended-release (ER) oxycodone in 1995." Kolodny, *supra*, at 744. And "despite mounting evidence that a surge in opioid consumption was resulting in adverse public health consequences, the FDA continued to approve new opioid formulations for chronic pain based on efficacy trials utilizing a controversial methodology." *Id.* at 745. It wasn't just that the studies were bad—the FDA suffered from regulatory capture by the pharmaceutical industry, which pursued its own interest rather than the interest of the American people. *See id.* at 745-46.

Finally, consider this statistic from the *Journal of the American Medical Association*: Of all the novel therapeutics approved by the FDA in the decade following its approval of mifepristone, nearly *one-third* experienced safety issues. *See* Nicholas S. Downing et al., *Postmarket Safety Events Among Novel Therapeutics Approved by the US Food and Drug Administration Between 2001 and 2010*, 317 J. Am. Med. Ass'n 1854, 1854 (2017).

Problems at the FDA have not escaped Congress's attention. Just last year, the chair of the Senate Committee on Health, Education, Labor, and Pensions criticized the FDA for its "unacceptable, longstanding" food safety failures. Letter of Senator Patty Murray, Chair, Senate Committee on Health, Education, Labor, and Pensions to FDA Commissioner (Apr. 11, 2022). As she put it, "[t]he FDA's failure over decades to regulate and enforce food safety standards . . . has put the health of Americans at risk." *Id.*

So it's not surprising that our court is far from the first to identify problems with FDA action sufficient to necessitate judicial intervention. Courts have held a number of FDA actions unlawful under the APA—including drug approval. *See*, *e.g.*, *Am. Bioscience, Inc. v. Thompson*, 269 F.3d 1077, 1078 (D.C. Cir. 2001) ("Appellant argues that the [FDA'] decision to approve . . . [an] Abbreviated New Drug Application (ANDA) for a generic version . . . was arbitrary and capricious. We agree and vacate that approval."). *See also*, *e.g.*, *R.J. Reynolds Vapor Co. v. FDA*, 65 F.4th 182, 191 (5th Cir. 2023) (FDA's "'unexplained' and 'inconsistent' positions are likely arbitrary and capricious."); *Genus Medical Technologies, LLC v. FDA*, 994 F.3d 631, 644

(D.C. Cir. 2021) ("FDA's decision must be set aside because it was based on an erroneous interpretation of law."); *Teva Pharmaceuticals, Inc. v. Sebelius*, 595 F.3d 1303, 1318 (D.C. Cir. 2010) (rejecting "the interpretation of the statute that the FDA has adopted in two recent adjudications"); *Teva Pharmaceuticals, Inc. v. FDA*, 441 F.3d 1, 5 (D.C. Cir. 2006) ("This error renders [the FDA's] decision arbitrary and capricious."); *Purepac Pharmaceutical Co. v. Thompson*, 354 F.3d 877, 883-84 (D.C. Cir. 2004) ("FDA's conclusion . . . was arbitrary and capricious."); *Teva Pharmaceuticals, Inc. v. FDA*, 182 F.3d 1003, 1007 (D.C. Cir. 1999) ("FDA's response was arbitrary and capricious."); *Zotos International, Inc. v. Young*, 830 F.2d 350, 354 (D.C. Cir. 1987) ("FDA's decision was arbitrary and capricious."); *Rhodia, Inc. v. FDA*, 608 F.2d 1376, 1376 (D.C. Cir. 1979) ("Finding the action arbitrary and capricious, we set aside the FDA order."); *Natural Nutritional Foods Ass'n v. Mathews*, 557 F.2d 325, 333 (2nd Cir. 1977) ("[T]he FDA's holding in this case was arbitrary and capricious and not in accordance with law.").

So it's simply wrong to claim—as the FDA and Danco and their supporting amici here have claimed—that the district court's decision in this case was unprecedented.

The scientists at the FDA deserve our respect and our gratitude, but not our blind deference. That would defy Congress's clear directive that courts conduct independent legal review of FDA action under the APA.

* * *

By the applicant's own admission, the FDA used an unlawful procedure when it approved mifepristone.

And the agency's later regulations are likewise invalid —both under the APA as the majority outlines, and under the Comstock Act as well. In sum, the regulations are "not in accordance with law" and therefore must be set aside. 5 U.S.C. § 706(2)(A).

Accordingly, we should affirm. I concur in part and dissent in part.

APPENDIX B

UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF TEXAS
AMARILLO DIVISION

No. 2:22-CV-223-Z

ALLIANCE FOR HIPPOCRATIC MEDICINE, ET AL.,
PLAINTIFFS

v.

U.S. FOOD AND DRUG ADMINISTRATION, ET AL.,
DEFENDANTS

Filed: Apr. 7, 2023

MEMORANDUM OPINION AND ORDER

Before the Court is Plaintiffs' Motion for Preliminary Injunction ("Motion") (ECF No. 6), filed on November 18, 2022. The Court **GRANTS** the Motion **IN PART**.

BACKGROUND

Over twenty years ago, the United States Food and Drug Administration ("FDA") approved chemical abortion ("2000 Approval"). The legality of the 2000 Approval is now before this Court. Why did it take *two decades* for judicial review in federal court? After all, Plaintiffs' petitions challenging the 2000 Approval date back to the year 2002, right?

Simply put, FDA stonewalled judicial review—until now. Before Plaintiffs filed this case, FDA ignored their petitions for over sixteen years, even though the law requires an agency response within "180 days of receipt of the petition." 21 C.F.R. § 10.30(e)(2)). But FDA waited 4,971 days to adjudicate Plaintiffs' first petition and 994 days to adjudicate the second. *See* ECF Nos. 1-14, 1-28, 1-36, 1-44 ("2002 Petition," "2019 Petition," respectively). Had FDA responded to Plaintiffs' petitions within the 360 total days allotted, this case would have been in federal court *decades* earlier. Instead, FDA postponed and procrastinated for nearly **6,000 days**.

Plaintiffs are doctors and national medical associations that provide healthcare for pregnant and post-abortive women and girls. Plaintiffs sued Defendants to challenge multiple administrative actions culminating in the 2000 Approval of the chemical abortion regimen for mifepristone. ECF No. 1 at 2. Mifepristone—also known as RU-486 or Mifeprex—is a synthetic steroid that blocks the hormone progesterone, halts nutrition, and ultimately starves the unborn human until death. ECF No. 7 at 7-8.[1] Because mifepristone alone

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[1] Jurists often use the word "fetus" to inaccurately identify unborn humans in *un*scientific ways. The word "fetus" refers to a specific gestational stage of development, as opposed to the zygote, blastocyst, or embryo stages. *See* ROBERT P. GEORGE & CHRISTOPHER TOLLEFSEN, EMBRYO 27-56 (2008) (explaining the gestational stages of an unborn human). Because other jurists use the terms "unborn human" or "unborn child" interchangeably, and because both terms are inclusive of the multiple gestational stages relevant to the FDA Approval, 2016 Changes, and 2021 Changes, this Court uses "unborn human" or "unborn child" terminology throughout this Order, as appropriate.

will not always complete the abortion, FDA mandates a two-step drug regimen: mifepristone to kill the unborn human, followed by misoprostol to induce cramping and contractions to expel the unborn human from the mother's womb. *Id.* at 8.

In 1996, the Population Council[2] filed a new drug application ("NDA") with FDA for mifepristone. ECF No. 1 at 35. Shortly thereafter, FDA reset the NDA from "standard" to "priority review." *Id.* In February 2000, FDA wrote a letter to the Population Council stating that "adequate information ha[d] *not* been presented to demonstrate that the drug, when marketed in accordance with the terms of distribution proposed, is safe and effective for use as recommended." ECF No. 1-24 at 6 (emphasis added). FDA also noted the "restrictions on distribution will need to be amended." *Id.*

Mere months later, FDA approved the chemical abortion regimen under Subpart H, commonly known as "accelerated approval" and originally designed to expedite investigational HIV medications during the

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[2] The Population Council was founded by John D. Rockefeller in 1952 after he convened a conference with "population activists" such as Planned Parenthood's director and several well-known eugenicists. MATTHEW CONNELLY, FATAL MISCONCEPTION: THE STRUGGLE TO CONTROL WORLD POPULATION 156 (2008). The conference attendees discussed "the problem of 'quality.'" John D. Rockefeller, *On the Origins of the Population Council*, 3 POPULATION AND DEV. REV. 493, 496 (1977). They concluded that "[m]odern civilization had reduced the operation of natural selection by saving more 'weak' lives and enabling them to reproduce," thereby resulting in "a downward trend in . . . genetic quality." *Id.*

AIDS epidemic.[3] Subpart H accelerates approval of drugs "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 (*e.g.*, ability to treat patients unresponsive to, or intolerant of, available therapy, or improved patient response over available therapy)." 21 C.F.R. § 314.500.

FDA then imposed post-approval restrictions "to assure safe use." *See* 21 C.F.R. § 314.520. These restrictions were later adopted when Subpart H was codified as a Risk Evaluation and Mitigation Strategy ("REMS") "to ensure that the benefits of the drug outweigh the risks." 21 U.S.C. § 355-1(a)(1)-(2). The drugs were limited to women and girls with unborn children aged seven-weeks gestation or younger. ECF No. 7 at 9. FDA also required three (3) in-person office visits: the first to administer mifepristone, the second to administer misoprostol, and the third to assess any complications and ensure there were no fetal remains in the womb. *Id.* Additionally, abortionists were required to be properly trained to administer the regimen and to report *all* adverse events from the drugs. *Id.*

Plaintiffs American Association of Pro-Life Obstetricians & Gynecologists ("AAPLOG") and Christian

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[3] *See, e.g.*, Jessica Holden Kloda & Shahza Somerville, *FDA's Expedited Review Process: The Need for Speed*, 35 APPLIED CLINICAL TRIALS 17, 17-18 (2015) ("In 1992, in response to a push by AIDS advocates to make the investigational anti-AIDS drug azidothymidine (AZT) accessible, the FDA enacted 'Subpart H' commonly referred to as accelerated approval; giving rise to expedited review of drugs by the FDA.").

Medical & Dental Associations filed the 2002 Petition with FDA challenging the 2000 Approval. *Id.* In 2006, the U.S. House Subcommittee on Criminal Justice, Drug Policy, and Human Resources expressed the same concerns and held a hearing to investigate FDA's handling of mifepristone and its subsequent monitoring of the drug.[4] Then-Chairman Souder remarked that mifepristone was "associated with the deaths of at least 8 women, 9 life-threatening incidents, 232 hospitalizations, 116 blood transfusions, and 88 cases of infection."[5] Additionally, Chairman Souder noted "more than 950 adverse event cases" associated with mifepristone "out of only 575,000 prescriptions, at most."[6] The subsequent Staff Report concluded that FDA's approval and monitoring of mifepristone was "substandard and necessitates the withdrawal of this dangerous and fatal product before more women suffer the known and anticipated consequences or fatalities."[7] The report stated the "unusual approval" demonstrated a lower standard of care for women, "and [mifepristone's] withdrawal from the market is justified and necessary to protect the public's health."[8]

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[4] *See The FDA and RU-486: Lowering the Standard for Women's Health: Hearing Before the Subcomm. on Crim. Just., Drug Pol'y, & Hum. Res. of the H. Comm. on Gov't Reform*, 109th Cong. 3 (2006) ("Subcommittee Report").

[5] The transcript of the hearing before the House Subcommittee is available at https://www.govinfo.gov/content/pkg/CHRG-109hhrg31397/html/CHRG-109hhrg31397.htm.

[6] *Id.*

[7] Subcommittee Report at 40.

[8] *Id.*

FDA rejected the 2002 Petition on March 29, 2016 — nearly *fourteen* years after it was filed. ECF No. 7 at 9. That same day, FDA approved several changes to the chemical abortion drug regimen, including the removal of post-approval safety restrictions for pregnant women and girls. *Id.* at 10. FDA increased the maximum gestational age from seven-weeks gestation to ten-weeks gestation. *Id.* And FDA also: (1) changed the dosage for chemical abortion; (2) reduced the number of required in-person office visits from three to one; (3) allowed non-doctors to prescribe and administer chemical abortions; and (4) eliminated the requirement for prescribers to report non-fatal adverse events from chemical abortion. *Id.*

In March 2019, Plaintiffs AAPLOG and American College of Pediatricians filed the 2019 Petition challenging FDA's 2016 removal of safety restrictions. *Id.* On April 11, 2019, FDA approved GenBioPro, Inc.'s abbreviated new drug application ("ANDA") for a generic version of mifepristone without requiring or reviewing *new* peer-reviewed science ("2019 Generic Approval"). *Id.* Two years later, on April 12, 2021, FDA announced it would "exercise enforcement discretion" to allow "dispensing of mifepristone through the mail . . . or through a mail-order pharmacy" during the COVID pandemic—notwithstanding the nearly 150-year-old Comstock Act banning the *mailing* of "[e]very article, instrument, substance, drug, medicine or thing" that produces "abortion." *Id.* Finally, on December 16, 2021, FDA denied most of Plaintiff's 2019 Petition. *Id.* at 11. Specifically, FDA expressly rejected the 2019 Petition's request to keep the in-person dispensing requirements and announced that the agency would *permanently* allow chemical abortion by mail. *Id.*

After Plaintiffs filed suit, Danco Laboratories, LLC ("Danco")—the holder of the NDA for mifepristone—moved to intervene as a defendant. ECF No. 19. On February 6, 2023, this Court granted Danco's motion. ECF No. 33. Plaintiffs now seek a preliminary injunction ordering Defendants to withdraw or suspend: (1) FDA's 2000 Approval and 2019 Approval of mifepristone tablets, 200 mg, thereby removing both from the list of Approved Drugs; (2) FDA's 2016 Changes and 2019 Generic Approval; and (3) FDA's April 12, 2021, Letter and December 16, 2021, Response to the 2019 Petition concerning the in-person dispensing requirement for mifepristone. ECF No. 7 at 12. Additionally, Plaintiffs seek to enjoin Defendants from taking actions inconsistent with these orders. *Id.*

LEGAL STANDARD

A court may issue a preliminary injunction when a movant satisfies the following four factors: (1) a substantial likelihood of success on the merits; (2) a substantial threat of irreparable harm if the injunction does not issue; (3) the threatened injury outweighs any harm that will result if the injunction is granted; and (4) the grant of an injunction is in the public interest. *See Louisiana v. Becerra*, 20 F.4th 260, 262 (5th Cir. 2021). "The purpose of a preliminary injunction is always to prevent irreparable injury so as to preserve the court's ability to render a meaningful decision on the merits." *Canal Auth. of State of Fla. v. Callaway*, 489 F.2d 567, 576 (5th Cir. 1974). The same standards apply "to prevent irreparable injury" under the Administrative Procedure Act ("APA"). *See* 5 U.S.C. § 705; *Wages & White Lion Invs., L.L.C. v. U.S. Food & Drug Admin.*, 16 F.4th 1130, 1143 (5th Cir. 2021).

ANALYSIS

A. Plaintiffs Have Standing

The judicial power of federal courts is limited to certain "Cases" and "Controversies." U.S. CONST. art. III, § 2. The case-or-controversy requirement requires a plaintiff to establish he has standing to sue. *See Cibolo Waste, Inc. v. City of San Antonio*, 718 F.3d 469, 473 (5th Cir. 2013). To have standing, the party invoking federal jurisdiction must show: "(i) that he suffered an injury in fact that is concrete, particularized, and actual or imminent; (ii) that the injury was likely caused by the defendant; and (iii) that the injury would likely be redressed by judicial relief." *TransUnion LLC v. Ramirez*, 141 S. Ct. 2190, 2203 (2021). Courts should assess whether the alleged injury to the plaintiff has a "close relationship" to harm "traditionally" recognized as providing a basis for a lawsuit in American courts. *Id.* at 2204. "[S]tanding is not dispensed in gross; rather, plaintiffs must demonstrate standing for each claim that they press and for each form of relief that they seek (for example, injunctive relief and damages)." *Id.* at 2208.

1. Plaintiff Medical Associations have Associational Standing

"An association or organization can establish an injury-in-fact through either of two theories, appropriately called 'associational standing' and 'organizational standing.'" *OCA-Greater Hous. v. Texas*, 867 F.3d 604, 610 (5th Cir. 2017). Under a theory of "associational standing," an association "has standing to bring a suit on behalf of its members when its members would otherwise have standing to sue in their own right, the

interests at stake are germane to the organization's purpose, and neither the claim asserted nor the relief requested requires the participation of individual members in the lawsuit." *Tex. Ass'n of Mfrs. v. U.S. Consumer Prod. Safety Comm'n*, 989 F.3d 368, 377 (5th Cir. 2021) (quoting *Friends of the Earth, Inc. v. Laidlaw Env't Servs. (TOC), Inc.*, 528 U.S. 167, 181 (2000)).

Here, the associations' members have standing because they allege adverse events from chemical abortion drugs can overwhelm the medical system and place "enormous pressure and stress" on doctors during emergencies and complications.[9] ECF No. 7 at 14. These emergencies "consume crucial limited resources, including blood for transfusions, physician time and attention, space in hospital and medical centers, and other equipment and medicines." ECF No. 1-5 at 9. This is especially true in maternity-care "deserts"—geographical areas with limited physician availability. *Id.* These emergencies force doctors into situations "in which they feel complicit in the elective chemical abortion by needing to remove a baby with a beating heart or pregnancy tissue as the only means to save the life of the woman or girl." ECF No. 1 at 85. Members of Plaintiff medical associations "oppose being forced to end the life of a human being in the womb for no medical reason, including by having to complete an

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[9] *See* James Studnicki et al., *A Longitudinal Cohort Study of Emergency Room Utilization Following Mifepristone Chemical and Surgical Abortions, 1999-2015*, 8 HEALTH SERV. RSCH.MGMT. EPIDEMIOLOGY 8 (2021) ("ER visits following mifepristone abortion grew from 3.6% of all postabortion visits in 2002 to 33.9% of all postabortion visits in 2015. The trend toward increasing use of mifepristone abortion requires all concerned with health care utilization to carefully follow the ramifications of ER utilization.").

incomplete elective chemical abortion." *Id.* at 86; *see also Texas v. Becerra*, No. 5:22-CV-185-H, 2022 WL 3639525, at *12 (N.D. Tex. Aug. 23, 2022) (unwanted participation in elective abortions is cognizable under Article III).

Plaintiffs also argue the challenged actions "prevent Plaintiff doctors from practicing evidence-based medicine" and have caused Plaintiffs to face increased exposure to allegations of malpractice and potential liability, along with higher insurance costs. ECF No. 7 at 15. The lack of information on adverse events "harms the doctor-patient relationship" because women and girls are prevented from giving informed consent to providers. *Id.*; *see also* American Medical Association Code of Medical Ethics, *Opinion 2.1.1: Informed Consent* (informed consent is "fundamental in both ethics and law"). To obtain informed consent, physicians must "[a]ssess the patient's ability to understand relevant medical information" and present to their patient "relevant information accurately and sensitively," including the burdens and risks of the procedure. *Id.*

Women also perceive the harm to the informed-consent aspect of the physician-patient relationship. In one study, fourteen percent of women and girls reported having received insufficient information about (1) side effects, (2) the intensity of the cramping and bleeding, (3) the next steps after expelling the aborted human, and (4) potential negative emotional reactions like fear, uncertainty, sadness, regret, and pain. *See* 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, 1485-94 (2021).

Plaintiff physicians' lack of pertinent information on chemical abortion harms their physician-patient relationships because they *cannot* receive informed consent from the women and girls they treat in their clinics. Plaintiffs allege these actions have "radically altered the standard of care." ECF No. 1-6 at 7.

Additionally, Plaintiff medical associations have associational standing via their members' third-party standing to sue on behalf of their patients. *See N.Y. State Club Ass'n, Inc. v. City of New York*, 487 U.S. 1, 9 (1988) ("It does not matter what specific analysis is necessary to determine that the members could bring the same suit."); *Pa. Psychiatric Soc. v. Green Spring Health Servs., Inc.*, 280 F.3d 278, 293 (3d Cir. 2002) ("So long as the association's members have or will suffer sufficient injury to merit standing and their members possess standing to represent the interests of third-parties, then associations can advance the third-party claims of their members without suffering injuries themselves."); *Ohio Ass'n of Indep. Schs. v. Goff*, 92 F.3d 419, 422 (6th Cir. 1996) (associational standing via member schools' third-party standing to assert constitutional rights of parents to direct their children's education); 13A Charles Alan Wright & Arthur R. Miller, *Federal Practice and Procedure* § 3531.9.3 (3d ed. 2022) ("Doctors regularly achieve standing to protect the rights of patients and their own related professional rights.").

The requirements for third-party standing are met here because: (1) the patients have "endure[d] many intense side effects and suffer[ed] significant complications requiring medical attention" and "suffer distress

and regret";[10] (2) the patients have a "close relation" to the physician members of the Plaintiff medical associations; and (3) "some hindrance" exists to the patients' ability to protect their interests. *See* ECF No. 7 at 13; *Powers v. Ohio*, 499 U.S. 400, 410-11 (1991); *Singleton v. Wulff*, 428 U.S. 106, 117 (1976) (women seeking abortions may be chilled "by a desire to protect the very privacy of [their] decision from the publicity of a court suit"); *Pa. Psychiatric*, 280 F.3d at 290 ("[A] party need not face insurmountable hurdles to warrant third-party standing."). The injuries suffered by patients of the Plaintiff medical associations' members are sufficient to confer associational standing.

Here, the physician-patient dynamic favors third-party standing. Unlike abortionists suing on behalf of women seeking abortions, here there are no potential conflicts of interest between the Plaintiff physicians and their patients. *See June Med. Servs. L.L.C. v. Russo*, 140 S. Ct. 2103, 2167 (2020) (Alito, J., dissenting), *abrogated by Dobbs v. Jackson Women's Health Org.*, 142 S. Ct. 2228 (2022) (abortionists have a "financial interest in avoiding burdensome regulations," while women seeking abortions "have an interest in the preservation of regulations that protect their health"). And the case for a close physician-patient relationship is even stronger here than in the abortion context. *See id.* at 2168 ("[A] woman who obtains an abortion typically does not develop a close relationship with the doctor who performs the procedure. On the contrary,

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[10] *Cf. TransUnion*, 141 S. Ct. at 2211 ("Nor did those plaintiffs present evidence that . . . they suffered some other injury (such as an emotional injury)"); *Denney v. Deutsche Bank AG*, 443 F.3d 253, 265 (2d Cir. 2006).

their relationship is generally brief and very limited."); *see also* ECF No. 1-9 at 7 ("[I]n many cases there is no doctor-patient relationship [between a woman and an abortionist], so [women] often present to overwhelmed emergency rooms in their distress, where they are usually cared for by physicians other than the abortion prescriber."); ECF No. 1-11 at 4 (because there "is no follow-up or additional care provided to patients" by abortionists, there is "no established relationship with a physician" and "patients are simply left to report to the emergency room"). Plaintiff physicians often spend several hours treating post-abortive women, even hospitalizing them overnight or providing treatment throughout several visits. *See* ECF No. 1-8 at 5-6. Given the Supreme Court's jurisprudence on the close relationship between abortionists and women, the facts of this case indicate that Plaintiffs' relationships with their patients are at least as close—if not closer—for purposes of third-party standing.

Finally, women who have *already* obtained an abortion may be *more* hindered than women who challenge restrictions on abortion. Women who have aborted a child—especially through chemical abortion drugs that necessitate the woman seeing her aborted child once it passes—often experience shame, regret, anxiety, depression, drug abuse, and suicidal thoughts because of the abortion. *See* ECF No. 96 at 25; David C. Reardon et al., *Deaths Associated with Pregnancy Outcome: A Record Linkage Study of Low Income Women*, 95 S. MED. J. 834, 834-41 (2002) (women who receive abortions have a 154% higher risk of death from suicide than if they gave birth, with persistent tendencies over time and across socioeconomic boundaries, indicating "self-destructive tendencies, depression, and other un-

healthy behavior aggravated by the abortion experience"); Priscilla K. Coleman, *Abortion and Mental Health: Quantitative Synthesis and Analysis of Research Published 1995-2009*, 199 BRITISH J. PSYCHIATRY 180, 180-86 (2011) (same). Subsequently, *in addition to* the typical privacy concerns present in third-party standing in abortion cases, adverse abortion experiences that are often deeply traumatizing pose a hindrance to a woman's ability to bring suit. In short, Plaintiffs—rather than their patients—are most likely the "least awkward challenger[s]" to Defendants' actions. *Craig v. Boren*, 429 U.S. 190, 197 (1976).

2. Plaintiff Medical Associations have Organizational Standing

"'[O]rganizational standing' does not depend on the standing of the organization's members." *OCA*, 867 F.3d at 610. The organization can establish standing in its own name if it "meets the same standing test that applies to individuals." *Id.* (internal marks omitted). An organization can have standing if it has "proven a drain on its resources resulting from counteracting the effects of the defendant's actions." *La. ACORN Fair Hous. v. LeBlanc*, 211 F.3d 298, 305 (5th Cir. 2000); *see also Zimmerman v. City of Austin, Tex.*, 881 F.3d 378, 390 (5th Cir. 2018) (changing one's "plans or strategies in response to an allegedly injurious law can itself be a sufficient injury to confer standing"). "Such concrete and demonstrable injury to the organization's activities —with the consequent drain on the organization's resources—constitutes far more than simply a setback to the organization's abstract social interests." *Havens Realty Corp. v. Coleman*, 455 U.S. 363, 379 (1982) (internal marks omitted).

One way an organization can establish standing is by "identifying specific projects that [it] had to put on hold or otherwise curtail in order to respond to the [challenged action]." *Tex. State LULAC v. Elfant*, 52 F.4th 248, 253 (5th Cir. 2022) (internal marks omitted). This is "not a heightening of the *Lujan* standard,[11] but an example of how to satisfy it by pointing to a nonlitigation- related expense." *OCA*, 867 F.3d at 612. Plaintiffs "need not identify specific projects that they have placed on hold or otherwise curtailed."[12] *La Unión del Pueblo Entero v. Abbott*, No. 5:21-CV-0844-XR, 2022 WL 3052489, at *31 (W.D. Tex. Aug. 2, 2022). Rather, this is simply the "most secure foundation" to establish organizational standing. 13A Charles Alan Wright & Arthur R. Miller, *Federal Practice and Procedure* § 3531.9.5 (3d ed. 2022). Furthermore, "'[a]t the pleading stage,' we 'liberally' construe allegations of injury." *Bezet v. United States*, 714 Fed. Appx. 336, 339 (5th Cir. 2017) (quoting *Little v. KPMG LLP*, 575 F.3d 533, 540 (5th Cir. 2009)).

Here, Plaintiff medical associations have standing via diversionary injury. Because of FDA's failure to require reporting of all adverse events, Plaintiffs allege FDA's actions have frustrated their ability to educate and inform their member physicians, their patients, and the public on the dangers of chemical abortion drugs.

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[11] *See Lujan v. Defs. of Wildlife*, 504 U.S. 555 (1992).

[12] At the hearing, Danco argued *Elfant* held there was no standing where organizations failed to identify specific projects put on hold. ECF No. 136 at 125. This is incorrect. The Fifth Circuit in *Elfant* assumed without deciding the plaintiffs pled an injury-in-fact but held they did not have standing because the causation and redressability elements were not met. *See* 52 F.4th at 255.

ECF No. 7 at 12. As a result, Plaintiffs attest they have diverted valuable resources away from advocacy and educational efforts to compensate for the lack of information. *See* ECF No. 1 at 91. Such diversions expend considerable time, energy, and resources, to the detriment of other priorities and functions and impair Plaintiffs' ability to carry out their educational purpose. *Id.* at 92; *N.A.A.C.P. v. City of Kyle, Tex.*, 626 F.3d 233, 238 (5th Cir. 2010).[13] Similarly, Plaintiffs allege their efforts to respond to FDA's actions have "tak[en] them away from other priorities such as fundraising and membership recruitment and retention." ECF Nos. 1-4 at 6, 1-5 at 11. Consequently, Plaintiffs have recalibrated their outreach efforts to spend extra time and money educating their members about the dangers of chemical abortion drugs. Combined, these facts are sufficient to confer organizational standing. *See OCA*, 867 F.3d at 612 (finding organizational standing even where the injury "was not large"); *Fowler*, 178 F.3d at 356 (injuries in fact "need not measure more than an 'identifiable trifle'") (internal marks omitted).

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[13] It is true that Plaintiffs must allege their activities in response to the challenged actions differ from their "routine" activities. *See, e.g.*, *City of Kyle*, 626 F.3d at 238. But Plaintiffs have done so. For example, Plaintiffs argue they conducted independent studies and analyses of available data to the detriment of their advocacy, educational, and recruitment efforts. ECF No. 1-8 at 8. The Fifth Circuit has found diversionary injuries to constitute injuries-in-fact even where it was less clear the plaintiffs diverted from routine activities. *See Ass'n of Cmty. Orgs. for Reform Now v. Fowler*, 178 F.3d 350, 360 (5th Cir. 1999) (injury-in-fact where organization regularly conducted voter registration drives and "expended resources registering voters in low registration areas who would have already been registered" if not for the challenged actions).

3. Plaintiffs' alleged Injuries are Concrete and Redressable

Defendants contend that Plaintiffs' theories of standing "depend upon layer after layer of speculation." ECF No. 28 at 20. But Plaintiffs allege FDA's chemical abortion regimen "caused" intense side effects and significant complications for their patients requiring medical intervention and attention. ECF No. 7 at 13; *see id.* ("The harms that the FDA has wreaked on women and girls have also injured, and will continue to injure, Plaintiff doctors and their medical practices."); *id.* at 14 ("The FDA's actions have placed enormous pressure and stress on Plaintiff doctors during these emergency situations."); *id.* at 15 ("The FDA has caused Plaintiff doctors to face increased exposure to allegations of malpractice and potential liability, along with higher insurance costs."). In fact, Plaintiffs' declarations list specific events where Plaintiff physicians provided emergency care to women suffering from chemical abortion. *See* ECF Nos. 1-8 at 5-6, 1-9 at 4-9, 1-10 at 6- 7, 1-11 at 5-6. And Defendants even concede the existence of adverse events related to chemical abortion drugs. *See* ECF No. 28 at 21. Consequently, Defendants misconstrue Plaintiffs' pleadings and mischaracterize Plaintiffs' evidence as "speculative." It is not.

Past injuries thus distinguish this case from *Clapper v. Amnesty Int'l USA*, where the Supreme Court held a "threatened injury must be certainly impending to constitute injury in fact." 568 U.S. 398, 410 (2013) (quoting *Whitmore v. Arkansas*, 495 U.S. 149, 157-58 (1990)). Were there no past injuries in this case, the alleged future harms are still less attenuated than those in *Clapper*. *See id.* (finding "a highly attenuated chain of"

five separate possibilities needed to align for the alleged harm to occur); *McCardell v. U.S. Dep't of Hous. & Urb. Dev.*, 794 F.3d 510, 520 (5th Cir. 2015) ("[U]nlike in *Clapper*, where the alleged injury depended on a long and tenuous chain of contingent events, the chain-of-events framework in this case involves fewer steps and no unfounded assumptions.") (internal marks omitted). *See also* ECF No. 1-31 at 10 (roughly eight percent of women who use abortion pills will require surgical abortion); ECF No. 1-14 at 23 (discussing a study in which 18.3 percent of women required surgical intervention after chemical abortion). And as post-*Whitmore* cases have demonstrated, the "certainly impending" standard for an "imminent" injury is not as demanding as it sounds. *See TransUnion*, 141 S. Ct. at 2197 (material risk of future harm can suffice "so long as the risk of harm is sufficiently imminent and substantial"); *Susan B. Anthony List v. Driehaus*, 573 U.S. 149, 158 (2014) ("An allegation of future injury may suffice if the threatened injury is 'certainly impending,' *or* there is a 'substantialrisk' that the harm will occur.") (emphasis added); *Clapper*, 568 U.S. at 414 n.5; *Massachusetts v. E.P.A.*, 549 U.S. 497, 526 n.23 (2007) ("Even a small probability of injury is sufficient . . . provided of course that the relief sought would, if granted, reduce the probability."); *Deanda v. Becerra*, No. 2:20-CV-092-Z, 2022 WL 17572093, at *2 (N.D. Tex. Dec. 8, 2022) (collecting cases).[14]

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[14] Defendants' reliance on *Spokeo, Inc. v. Robins* is also unavailing. 578 U.S. 330 (2016). Courts should indeed assess whether the alleged injury to the plaintiff has a "close relationship" to harm "traditionally" recognized as the basis for a lawsuit in American courts. *See TransUnion*, 141 S. Ct. at 2204. But "a plaintiff doesn't need

For similar reasons, Defendants' reliance on *City of Los Angeles v. Lyons* also fails. 461 U.S. 95 (1983). There, the Supreme Court held Lyons did not have standing to seek injunctive relief because "[t]here was no finding that Lyons faced a real and immediate threat of again being illegally choked" by Los Angeles police. *Id.* at 110. The *Lyons* holding "is based on the obvious proposition that a prospective remedy will provide no relief for an injury that is, and likely will remain, entirely in the past." *Am. Postal Workers Union v. Frank*, 968 F.2d 1373, 1376 (1st Cir. 1992). "No such reluctance, however, is warranted here." *Hernandez v. Cremer*, 913 F.2d 230, 234 (5th Cir. 1990). Considering FDA's 2021 decision to permit "mail-in" chemical abortion, many women and girls will consume mifepristone without physician supervision. And in maternity-care "deserts," women may not have ready access to emergency care. In sum, there are fewer safety restrictions for women and girls today than ever before. Plaintiffs have good reasons to believe their alleged injuries will continue in the future, and possibly with greater frequency than in the past.

Defendants next argue Plaintiffs' theories depend on "unfettered choices made by independent actors not

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to demonstrate that the level of harm he has suffered would be actionable under a similar, common-law cause of action." *Perez v. McCreary, Veselka, Bragg & Allen, P.C.*, 45 F.4th 816, 822 (5th Cir. 2022). Rather, Plaintiffs only need to show the *type* of harm allegedly suffered "is similar in kind to a type of harm that the common law has recognized as actionable." *Id.*; *see also Campaign Legal Ctr. v. Scott*, 49 F.4th 931, 940 (5th Cir. 2022) (Ho., J, concurring) (evidence of injury required by *TransUnion* is not burdensome). Harm resulting from unsafe drugs is similar to harm actionable under the common law.

before the courts and whose exercise of broad and legitimate discretion the courts cannot presume either to control or to predict." ECF No. 28 at 20 (quoting *Lujan*, 504 U.S. at 562). "[A] plaintiff must allege personal injury fairly traceable to the defendant's allegedly unlawful conduct and likely to be redressed by the requested relief." *Allen v. Wright*, 468 U.S. 737, 751 (1984), *abrogated on other grounds by Lexmark Int'l, Inc. v. Static Control Components, Inc.*, 572 U.S. 118, 134 (2014); *see also Simon v. E. Ky. Welfare Rts. Org.*, 426 U.S. 26, 41-42 (1976) ("In other words, the 'case or controversy' limitation of Art. III still requires that a federal court act only to redress injury that fairly can be traced to the challenged action of the defendant, and not injury that results from the independent action of some third party not before the court.").

In this case, a favorable decision would likely relieve Plaintiffs of at least some of the injuries allegedly caused by FDA. *See Larson v. Valente*, 456 U.S. 228, 243 n.15 (1982) ("[Plaintiffs] need not show that a favorable decision will relieve [their] *every* injury."); *Duke Power Co. v. Carolina Env't Study Grp., Inc.*, 438 U.S. 59, 74-75 (1978) (a "substantial likelihood" of the requested relief redressing the alleged injury is enough); *Sanchez v. R.G.L.*, 761 F.3d 495, 506 (5th Cir. 2014) (a plaintiff "need only show that a favorable ruling could potentially lessen its injury"); *Texas v. Becerra*, 577 F. Supp. 3d 527, 560 (N.D. Tex. 2021) ("That the plaintiffs have brought forth specific evidence and examples of how they *will* be harmed . . . distinguishes this case from others where a third party's actions *might* have hurt the plaintiff."). And redressability is satisfied even if relief must filter downstream through third parties uncertain to comply with the result, provided

the relief would either: (1) remove an obstacle for a nonparty to act in a way favorable to the plaintiff; or (2) influence a nonparty to act in such a way. *See, e.g.*, *Dep't of Com. v. New York*, 139 S. Ct. 2551, 2565-66 (2019) ("[T]hird parties will likely react in predictable ways."); *Bennett v. Spear*, 520 U.S. 154, 169 (1997) (defendants' actions need not be "the very last step in the chain of causation"); *Larson*, 456 U.S. at 242-44; *NiGen Biotech, L.L.C. v. Paxton*, 804 F.3d 389, 396-98 (5th Cir. 2015). Therefore, Plaintiffs' alleged injuries are fairly traceable to Defendants and redressable by a favorable decision.

4. Plaintiffs are within the "Zone of Interests"

Plaintiffs are also within the zone of interests of the Federal Food, Drug, and Cosmetic Act ("FFDCA") and the Comstock Act. Plaintiffs suing under the APA must assert an interest that is "arguably within the zone of interests to be protected or regulated by the statute that they say was violated." *Texas v. United States*, 809 F.3d 134, 162 (5th Cir. 2015) (internal marks omitted). The 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." *Id.* (internal marks omitted). The zone-of-interests 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. 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).

A federal court's obligation to hear and decide cases within its jurisdiction is "virtually unflagging." *Lexmark*, 572 U.S. at 126 (internal marks omitted). And "the trend is toward enlargement of the class of people who may protest administrative action." *Camp*, 397 U.S. at 154. No "explicit statutory provision" is necessary to confer standing. *Id.* at 155. "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." *Texas v. United States*, 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 omitted); *see also Barlow v. Collins*, 397 U.S. 159, 165 (1970) (courts "must decide if Congress has in express or implied terms precluded judicial review or committed the challenged action entirely to administrative discretion").

Defendants argue that Plaintiffs identify no particular provision of the FFDCA protecting their interests. ECF No. 28 at 26. But Plaintiffs' interests are *not* "marginally related" to the purposes implicit in the FFDCA. The statute's substantive provisions protect the safety of physicians' patients and the integrity of the physician-patient relationship. *See generally* 21 U.S.C. § 355. Furthermore, this Court finds Plaintiffs have third-party standing on behalf of their patients. Plaintiffs' patients are within the zone of interest of the FFDCA because patients seek safe and effective medical procedures.

Likewise, Plaintiffs are 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, 71 n.19 (1983) (the "thrust" of the Comstock Act was "to prevent the mails from being used to corrupt the public morals"). 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 under these statutes. *Camp*, 397 U.S. at 157. For all the aforementioned reasons, Plaintiffs have standing.

B. Plaintiffs' Claims Are Reviewable

Defendants aver that "[a]ll of Plaintiffs' claims are untimely or unexhausted except their challenge to FDA's December 16, 2021, response to the 2019 citizen petition." ECF No. 28 at 26. This includes Plaintiffs' challenges to: (1) the 2000 Approval and FDA's 2016 Response to the 2002 Petition challenging that approval; (2) the 2019 Generic Approval; and (3), the April 2021 letter. As for FDA's December 2021 Response to the 2019 Petition, Defendants maintain review is limited to the narrow issues presented in the 2019 Petition—which did not include arguments concerning the Comstock Act. *Id.* at 27-28.[15] The Court disagrees with each of these arguments.

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[15] The Court refers to the 2000 Approval, the 2016 Changes and denial of the 2002 Petition, and the 2019 Generic Approval collectively as FDA's "Pre-2021 Actions." Similarly, the Court refers to

1. FDA "Reopened" its Decisions in 2016 and 2021

FDA's final decision on a citizen petition constitutes "final agency action" under the APA. 21 C.F.R. § 10.45(c). Challenges to agency actions have a six-year statute of limitations period. *See* 28 U.S.C. § 2401(a). Therefore, the statute of limitations for challenging the 2000 Approval began running on March 29, 2016—the date of FDA's denial of the 2002 Petition. Because the 2016 Denial of the 2002 Petition occurred more than six years before Plaintiffs filed this suit, Defendants argue the challenge is untimely. ECF No. 28 at 26. But if "the agency opened the issue up anew, and then reexamined and reaffirmed its prior decision," the agency's second action—rather than the original decision—starts the limitations period. *See Texas v. Biden*, 20 F.4th 928, 951 (5th Cir. 2021), *rev'd in part on other grounds*, 142 S. Ct. 2528 (2022).

The reopening doctrine arises "where an agency conducts a rulemaking or adopts a policy on an issue at one time, and then in a later rulemaking restates the policy or otherwise addresses the issue again without altering the original decision."[16] *Wash. All. of Tech. Workers v. U.S. Dep't of Homeland Sec.*, 892 F.3d 332, 345 (D.C. Cir. 2018); *see also Nat'l Biodiesel Bd. v. EPA*, 843 F.3d 1010, 1017 (D.C. Cir. 2016) ("The reopener doctrine allows an otherwise untimely challenge to proceed where an agency has—either explicitly or

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FDA's April 2021 letter and December 2021 Response as FDA's "2021 Actions."

[16] Courts have even applied the doctrine where agencies decide *not* to engage in rulemaking and then revisit and reaffirm that decision. *See Pub. Citizen v. Nuclear Regul. Comm'n*, 901 F.2d 147, 152 (D.C. Cir. 1990).

implicitly—undertaken to reexamine its former choice.") (internal marks omitted); *CTIA-Wireless Ass'n v. F.C.C.*, 466 F.3d 105, 112 (D.C. Cir. 2006) (agency "reconsidered" policy by reaffirming policy and offering "two new justifications" not found in prior orders).

In the rulemaking context, courts have identified four non-exhaustive factors to apply the doctrine where the agency: (1) proposed to make some change in the rules or policies; (2) called for comment on new or changed provisions, but at the same time; (3) explained the unchanged, republished portions; and (4) responded to at least one comment aimed at the previously decided issue. *Tripoli Rocketry Ass'n, Inc. v. U.S. Bureau of Alcohol, Tobacco & Firearms*, No. 00CV0273(RBW), 2002 WL 33253171, at *6 (D.D.C. June 24, 2002) (internal marks omitted). But a court "cannot stop there"—it "must look to the entire context of the rulemaking including all relevant proposals and reactions of the agency to determine whether an issue was in fact reopened." *Pub. Citizen*, 901 F.2d at 150. For example, an agency can reopen a prior action if it removes restrictions or safeguards related to the first action or affects a "sea change" in the regulatory scheme. *See Sierra Club v. EPA*, 551 F.3d 1019, 1025 (D.C. Cir. 2008); *Nat'l Biodiesel*, 843 F.3d at 1017 (declining to apply doctrine when "the basic regulatory scheme remain[ed] unchanged"); *Pub. Citizen*, 901 F.2d at 152 (agency reopens decision when it reiterates a policy in such a way as to render the policy "subject to renewed challenge on any substantive grounds").

In the adjudication context, an agency need not solicit or respond to comments to reopen a decision because adjudication does not require notice and comment

procedures. *See* 5 U.S.C. §§ 553(c), 554. The reopening doctrine has been applied in the adjudication context where an agency undertakes a "serious, substantive reconsideration" of "a prior administrative decision." *Chenault v. McHugh*, 968 F. Supp. 2d 268, 275 (D.D.C. 2013); *see also Battle v. Sec'y U.S. Dep't of Navy*, 757 Fed. Appx. 172, 175 (3d Cir. 2018) (a petition for reconsideration can restart Section 2401(a)'s limitation period if the agency reopens the action based on a finding of "new evidence" or that the petition reflects some "changed circumstances"); *Peavey v. United States*, 128 F. Supp. 3d 85, 100 (D.D.C. 2015), *aff'd,* No. 15-5290, 2016 WL 4098768 (D.C. Cir. 2016) (reopening in 2011 occurred where agency "elected to conduct a substantive review" of servicemember's 1968 application to correct military records). For formal agency adjudications, even an order stating "only that it is denying reconsideration" is not conclusive if the agency has "altered its original decision." *Sendra Corp. v. Magaw*, 111 F.3d 162, 167 (D.C. Cir. 1997).

The standard for reopening is satisfied here. FDA's requirements for distribution in its 2000 Approval originally included:

- In-person dispensing from the doctor to the patient;
- Secure shipping procedures;
- Tracking system ability;
- Use of authorized distributors and agents; and
- Provision of the drug through direct, confidential physician distribution systems that ensures only qualified physicians will receive the drug for patient dispensing.

See ECF No. 1 at 40. FDA's 2016 Changes to this regulatory scheme included the following alterations:

- Extending the maximum gestational age at which a woman or girl can abort her unborn child from 49 days to 70 days;
- Altering the mifepristone dosage from 600 mg to 200 mg, the misoprostol dosage from 400 mcg to 800 mcg, and misoprostol administration from oral to buccal;
- Eliminating the requirement that administration of misoprostol occur in-clinic;
- Broadening the window for misoprostol administration to include a range of 24-48 hours after taking mifepristone, instead of 48 hours afterward;
- Adding a repeat 800 mcg buccal dose of misoprostol in the event of incomplete chemical abortion;
- Removing the requirement for an in-person follow-up examination after an abortion;
- Allowing "healthcare providers" other than physicians to dispense and administer the chemical abortion drugs; and
- Eliminating the requirement for prescribers to report all non-fatal serious adverse events from chemical abortion drugs.

Id. at 53-54. And in 2021, FDA removed the "in-person dispensing requirement" and signaled that it will soon allow pharmacies to dispense chemical abortion drugs. *Id.* at 68. Plaintiffs warn that without this re-

quirement, "there is a dramatically reduced chance that the prescriber can confirm pregnancy and gestational age, discover ectopic pregnancies, and identify a victim of abuse or human trafficking being coerced into having a chemical abortion." ECF No. 120 at 19.

FDA's 2016 and 2021 Changes thus significantly departed from the agency's original approval of the abortion regimen. FDA repeatedly altered its original decision by removing safeguards and changing the regulatory scheme for chemical abortion drugs. *Sierra Club*, 551 F.3d at 1025; *Nat'l Biodiesel*, 843 F.3d at 1017. Additionally, FDA's response to the 2019 Petition *explicitly* states FDA "undertook a *full review* of the Mifepristone REMS Program" in 2021. ECF No. 1-44 at 7 (emphasis added);[17] *see also Peavey*, 128 F. Supp. 3d at 100-02 (agency reopened decision by conducting "thorough review" of the merits, even where the order did not state it was a "reconsideration" and did not reference prior decision). And FDA even granted the 2019 Petition in part. ECF No. 1-44 at 3. A "full review" of a REMS for a drug with known serious risks necessarily considers the possibility that a drug is too dangerous to be on the market, any mitigation strategy notwithstanding. FDA has the authority to withdraw an approved drug application on this basis. *See* 21 U.S.C. § 355(e). Because the agency reaffirmed its prior actions after undertaking a substantive recon-

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[17] *See also Questions and Answers on Mifepristone for Medical Termination of Pregnancy Through Ten Weeks Gestation*, FDA (Jan. 4, 2023), https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-andproviders/questions-and-answers-mifepristone-medical-termination-pregnancy-through-ten-weeks-gestation (describing the 2021 review as "comprehensive").

sideration of those actions, the limitations period for those actions starts in 2021. *See Pub. Citizen*, 901 F.2d at 152 (an agency reconsidering and reaffirming original policy "necessarily raises the lawfulness of the original policy, for agencies have an everpresent duty to insure that their actions are lawful").[18]

Alternatively, the Court finds Plaintiffs' claims are not time-barred under the equitable tolling doctrine. *See United States v. Patterson*, 211 F.3d 927, 931 (5th Cir. 2000) (courts "must be cautious not to apply the statute of limitations too harshly"); *P & V Enters. v. U.S. Army Corps of Engr's*, 466 F. Supp. 2d 134, 149 (D.D.C. 2006), *aff'd,* 516 F.3d 1021 (D.C. Cir. 2008) (a "rebuttable presumption of equitable tolling" applies to lawsuits governed by the six-year limitations period of Section 2401(a)); *Bornholdt v. Brady*, 869 F.2d 57, 64 (2d Cir. 1989) ("The existence of § 2401 as a catchall provision . . . does not necessarily mean that Congress intended the six-year period to be applied whenever a substantive statute does not specify a limitations period."). "[A] litigant is entitled to equitable tolling of a statute of limitations only if the litigant establishes two elements: (1) that he has been pursuing his rights diligently, and (2) that some extraordinary circumstance stood in his way and prevented timely filing."

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[18] To date, it is unclear whether the reopening doctrine has been applied in the precise context of FDA's approval of an NDA. However, much of the rationale courts have applied in both the rulemaking and adjudication context applies here. And the Court is unaware of any legal principle that would preclude the doctrine from being applied to these facts. Assuming *arguendo* Plaintiffs' allegations are true, a contrary holding would mean there is *no* judicial remedy to FDA's insistence on keeping an unsafe drug on the market, so long as enough time has passed.

Menominee Indian Tribe of Wis. v. United States, 577 U.S. 250, 255 (2016) (internal marks omitted); *see also Holland v. Florida*, 560 U.S. 631, 650 (2010) ("The flexibility inherent in equitable procedure enables courts to meet new situations that demand equitable intervention, and to accord all the relief necessary to correct particular injustices.") (cleaned up).

Equitable tolling is appropriate here in large part because of FDA's unreasonable delay in responding to Plaintiff's 2002 and 2019 Petitions. *See WildEarth Guardians v. U.S. Dep't of Just.*, 181 F. Supp. 3d 651, 670 (D. Ariz. 2015) (it is "grossly inappropriate" to apply a statute of limitations where the agency unreasonably delayed a claim because the agency "could immunize its allegedly unreasonable delay from judicial review simply by extending that delay for six years") (internal marks omitted). It took FDA 13 years, 7 months, and 9 days to respond to the 2002 Petition. FDA then moved the goalposts by substantially changing the regulatory scheme on the *same day* it issued its Response. And it took FDA 2 years, 8 months, and 17 days to respond to the 2019 Petition which challenged those changes. Thus, in the 20 years between the 2002 Petition and the filing of this suit, Plaintiffs were waiting on FDA for over 16 of those years. *See Hill Dermaceuticals, Inc. v. U.S. Food & Drug Admin.*, 524 F. Supp. 2d 5, 9 (D.D.C. 2007) ("Once citizen petitions are submitted, the FDA Commissioner is required to respond in one of three manners 'within 180 days of receipt of the petition.'") (quoting 21 C.F.R. § 10.30(e)(2)).[19]

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[19] Incidentally, the delayed FDA Response is extreme but not unprecedented. *See, e.g.*, *Bayer HealthCare, LLC v. U.S. Food & Drug*

Additionally, statutes of limitations "are primarily designed to assure fairness to defendants," and "to promote justice by preventing surprises through the revival of claims that have been allowed to slumber until evidence is lost, memories have faded, and witnesses have disappeared." *Clymore v. United States*, 217 F.3d 370, 376 (5th Cir. 2000), *as corrected on reh'g* (Aug. 24, 2000) (internal marks omitted). But it "has not been argued, and cannot seriously be, that the government was unfairly surprised" when Plaintiffs filed this suit. *Id.* Plaintiffs have been reasonably diligent in pursuing their claims. *See, e.g.*, ECF No. 1-4 at 6 (after years of waiting for FDA to respond to the Petition, Plaintiff "called upon" FDA to issue a response in 2005 and again in 2015). And the public interest in this case militates toward resolving Plaintiffs' claims on the merits. Accordingly, Plaintiffs' challenges to FDA's Pre-2021 Actions concerning chemical abortion drugs are not time-barred.

2. FDA's April 2021 Decision on In-Person Dispending Requirements is not "Committed to Agency Discretion by Law"

Defendants also argue any challenge to FDA's decision regarding the in-person dispensing requirement is foreclosed under *Heckler v. Chaney*, 470 U.S. 821, 832 (1985). ECF No. 28 at 30. In *Heckler*, the Supreme Court held that FDA's decision not to recommend civil or criminal enforcement action to prevent violations of the FFDCA was "committed to agency discretion by law." 470 U.S. at 837-38; *see also Texas v. Biden*, 20 F.4th at 982 ("In other words, a litigant may not waltz

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Admin., 942 F. Supp. 2d 17, 22 (D.D.C. 2013) (FDA had yet to respond to a 2006 petition when it approved a related ANDA in 2013).

into court, point his finger, and demand an agency investigate (or sue, or otherwise enforce against) 'that person over there.'"). "[T]he Supreme Court and the Fifth Circuit have consistently read *Heckler* as sheltering one-off nonenforcement decisions rather than decisions to suspend entire statutes." *Texas v. Biden*, 20 F.4th at 983. The "committed to agency discretion by law" exception to judicial review is a "very narrow exception" that applies *only* where "statutes are drawn in such broad terms that in a given case there is no law to apply." *Citizens to Pres. Overton Park, Inc. v. Volpe*, 401 U.S. 402, 410 (1971), *overruled on other grounds by Califano v. Sanders*, 430 U.S. 99 (1977).

That is not the case here. The Secretary has the authority to determine that drugs with "known serious risks" may be dispensed "only in certain health care settings, such as hospitals." *See* 21 U.S.C. § 355-1(f)(3)(C); *Gomperts v. Azar*, No. 1:19-CV-00345-DCN, 2020 WL 3963864, at *1 (D. Idaho July 13, 2020) ("[T]hese restrictions mandate that Mifeprex be dispensed only in certain healthcare settings").[20] The statute also provides other "elements to assure safe use" of dangerous drugs. 21 U.S.C. § 355-1(f)(1), (3). The Secretary must publicly explain "how such elements will mitigate the observed safety risk." 21 U.S.C. § 355-1(f)(2). The Secretary must also consider whether the elements would "be unduly burdensome on patient access to the

[20] *See also Frequently Asked Questions (FAQS) about REMS*, FDA (Jan. 26, 2018), https://www.fda.gov/drugs/riskevaluation- and-mitigation-strategies-rems/frequently-asked-questions-faqs-about-rems ("A REMS is required to ensure the drug is administered only in a health care facility with personnel trained to manage severe allergic reactions and immediate access to necessary treatments and equipment to managing such events.").

drug" and must "minimize the burden on the health care delivery system." *Id.* Additionally, the elements "shall include [one] or more goals to mitigate a specific serious risk listed in the labeling of the drug." 21 U.S.C. § 355-1(f)(3). And as the Court will later explain, federal law prohibits the mailing of chemical abortion drugs. Thus, unlike in *Heckler*, there *is* "law to apply" to FDA's decision. *See Texas v. Biden*, 20 F.4th at 982 ("[T]he executive *cannot* look at a statute, recognize that the statute is telling it to enforce the law in a particular way or against a particular entity, and tell Congress to pound sand."). And even if Defendants have significant discretion in how they administer Section 355-1, that does not mean *all* related actions are immune to judicial review under Section 701(a)(2) of the APA.

In sum, Defendants cannot shield their decisions from judicial review merely by characterizing the challenged action as exercising "enforcement discretion." ECF No. 28 at 15; *see also Texas v. Biden*, 20 F.4th at 987 ("The Government is still engaged in enforcement —even if it chooses to do so in a way that ignores the statute. That's obviously not nonenforcement."); *id.* at 985 ("*Heckler* cannot apply to agency actions that qualify as rules under 5 U.S.C. § 551(4)."); *Heckler*, 470 U.S. at 833 n.4 (a decision to consciously and expressly adopt a general policy that is "so extreme as to amount to *abdication* of its statutory responsibilities" is not "committed to agency discretion") (emphasis added). Furthermore, the suggestion that FDA has full discretion under Section 355-1 to not require *any* REMS for dangerous drugs would likely present nondelegation problems even under a modest view of that doctrine. *See, e.g.*, *Gundy v. United States*, 139 S. Ct. 2116, 2123

(2019). So too the notion that FDA could exercise its nonenforcement discretion in violation of other federal laws. Therefore, FDA's decision to not enforce the in-person dispensing requirement is reviewable because the decision is not committed to agency discretion by law.

3. Plaintiffs' Failure to Exhaust Certain Claims is Excusable

Plaintiffs allege FDA's 2021 Decision to dispense mifepristone through the mail did not acknowledge or address federal criminal laws that "expressly prohibit[] such downstream distribution." ECF No. 7 at 26. Defendants maintain Plaintiffs' argument is unexhausted because they failed to present it at any stage of any administrative proceeding. ECF No. 28 at 38. Similarly, Plaintiffs have not exhausted their challenge to FDA's approval of the supplemental NDA for generic mifepristone. *Id*. at 26. These failures to exhaust claims do not preclude judicial review.

"The general rule of nonreviewability is not absolute." *Myron v. Martin*, 670 F.2d 49, 52 (5th Cir. 1982). To begin, exhaustion is not required where the agency action is "in excess of" the agency's authority. *Id.* And a court will review for the first time "a particular challenge to an agency's decision which was not raised during the agency proceedings" where the agency action is "likely to result in individual injustice" or is "contrary to an important public policy extending beyond the rights of the individual litigants." *Id.*; *see also Mathews v. Eldridge*, 424 U.S. 319, 330 (1976) ("[C]ases may arise where a claimant's interest in having a particular issue resolved promptly is so great that deference to the agency's judgment is inappropriate.");

Abbott Laboratories v. Gardner, 387 U.S. 136, 149 (1967) (injunctive remedies applied to administrative determinations should evaluate "both the fitness of the issues for judicial decision and the hardship to the parties of withholding court consideration"); *Dawson Farms, LLC v. Farm Serv. Agency*, 504 F.3d 592, 606 (5th Cir. 2007) (exhaustion may be excused when "irreparable injury will result absent immediate judicial review"); *Bd. of Pub. Instruction of Taylor Cnty., Fla. v. Finch*, 414 F.2d 1068, 1072 (5th Cir. 1969) (exceptional circumstances include "where injustice might otherwise result").

Courts have also excused a claimant's failure to exhaust administrative remedies where exhaustion "would be futile because the administrative agency will clearly reject the claim." *Gulf Restoration Network v. Salazar*, 683 F.3d 158, 176 (5th Cir. 2012) (internal marks omitted); *see also Oregon Nat. Desert Ass'n v. McDaniel*, 751 F. Supp. 2d 1151, 1159 (D. Or. 2011) (exceptional circumstances include evidence of administrative bias). Additionally, courts will consider any issue that was "raised with sufficient clarity to allow the decision maker to understand and rule on the issue raised, whether the issue was considered sua sponte by the agency or was raised by someone other than the petitioning party." *Pac. Choice Seafood Co. v. Ross*, 976 F.3d 932, 942 (9th Cir. 2020). In short, "there is no bright-line standard as to when this requirement has been met." *Nat'l Parks & Conservation Ass'n v. Bureau of Land Mgmt.*, 606 F.3d 1058, 1065 (9th Cir. 2010). Finally, "[a]dministrative remedies that are inadequate need not be exhausted." *Coit Indep. Joint Venture v. Fed. Sav. & Loan Ins. Corp.*, 489 U.S. 561,

587 (1989) (a lack of reasonable time limits in the claims procedure renders the procedure inadequate).

a. Contrary to Public Policy

Judicial review of Plaintiffs' unexhausted claims is appropriate for several reasons. First, Defendants' alleged violation of the Comstock Act would be "contrary to an important public policy." *Myron*, 670 F.2d at 52. As a case Defendants rely upon explains, the word "abortion" in the statute "indicates a national policy of discountenancing abortion as inimical to the national life." *See Bours*, 229 F. at 964; ECF No. 28-1 at 206. And twenty-two states filed an amicus brief arguing FDA's decision to permit mail-in chemical abortion harms the public interest by undermining states' ability to enforce laws regulating abortion.[21] ECF No. 100 at 17.

b. Individual Injustice and Irreparable Injury

Second, the agency's actions are "likely to result in individual injustice" or cause "irreparable injury." *Myron*, 670 F.2d at 52; *Dawson*, 504 F.3d at 606. Plaintiffs allege "many intense side effects" and "significant complications requiring medical attention" resulting

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[21] *See* David S. Cohen et al., *Abortion Pills*, 76 STAN. L. REV. 1, 9 (forthcoming 2024) ("Despite state laws, mailed medication abortion can cross borders in ways that undermine state laws . . . A new organization, Mayday Health, for example, focuses on those who live in states with abortion bans, giving users step-by-step instructions on how to set up temporary addresses in an abortion permissive state and forward the mail into the banned state.") (internal marks omitted).

from Defendants' actions.[22] ECF No. 7 at 13. Many women also experience intense psychological trauma and post-traumatic stress from excessive bleeding and from seeing the remains of their aborted children. *See* ECF No. 96 at 25-29; Pauline Slade et al., *Termination of pregnancy: Patient's perception of care*, J. OF FAMILY PLANNING & REPRODUCTIVE HEALTH CARE Vol. 27, No. 2, 72-77 (2001) ("Seeing the foetus, in general, appears to be a difficult aspect of the medical termination process which can be distressing, bring home the reality of the event and may influence later emotional adaptation."). Parenthetically, said "individual justice" and "irreparable injury" analysis also arguably applies to the unborn humans extinguished by mifepristone — especially in the post-*Dobbs* era. *See Dobbs*, 142 S. Ct. at 2261 ("Nothing in the Constitution or in our Nation's legal traditions authorizes the Court to adopt [the] the-

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[22] At least 4,213 adverse events from chemical abortion drugs have been reported. *See* ECF No. 96 at 12 n.16. But the actual number is likely far higher because non-fatal adverse events are no longer required to be reported, and because more than 60 percent of women and girls' emergency room visits after chemical abortions are miscoded as miscarriages. *See* James Studnicki et al., *A Post Hoc Exploratory Analysis: Induced Complications Mistaken for Miscarriage in the Emergency Room are a Risk Factor for Hospitalization*, 9 HEALTH SERV. RSCH. MGMT. EPIDEMIOLOGY 1, 1 (2022); *see also* ECF No. 1-8 at 7 (describing Plaintiffs' difficulty in submitting adverse event reports to mifepristone manufacturer Danco). Other data sources such as the Center for Disease Control and Prevention Abortion Surveillance Reports are "profoundly flawed" because state reporting "is voluntary, with many states reporting intermittently and some not at all." Studnicki et al., *supra* note 9, at 2. One Plaintiff physician alleges that when she reported an adverse event to her state's health department, the "report was rejected because the State said it was not a 'true' adverse event because the patient ultimately recovered." ECF No. 1-10 at 7.

ory of life" that States are *required* "to regard a fetus as lacking even the most basic human right—to live—at least until an arbitrary point in a pregnancy has passed.") (internal marks omitted); Brief of *Amici Curiae* Scholars of Jurisprudence John M. Finnis and Robert P. George in Support of Petitioners, *Dobbs*, 142 S. Ct. 2228 (2022) (arguing unborn humans are constitutional "persons" entitled to equal protection).

c. Administrative Procedures are Inadequate

Third, FDA's combined response time of over sixteen years to Plaintiffs' two petitions shows their procedures have been inadequate. *See Coit*, 489 U.S. at 587; *Bowen v. City of New York*, 476 U.S. 467, 476 (1986) ("[T]he harm imposed by exhaustion would be irreparable."). FDA slow-walked—or rather, *snail*-walked—its response to the 2002 Petition by waiting nearly *fourteen years* to deny the petition. ECF No. 7 at 9. Requiring Plaintiffs to exhaust their administrative remedies may equate to another decade-plus of waiting for the agency to give them the time of day.

d. Exhaustion would be Futile

Alternatively, any attempt by Plaintiffs to challenge Defendants' actions would likely be futile. Even if Plaintiffs did not endure sixteen years of delay, dawdle, and dithering, their efforts would surely "be futile because the administrative agency will clearly reject the claim." *Gulf Restoration Network*, 683 F.3d at 176. "President Biden has emphasized the need to protect access to mifepristone" since the day of the Supreme

Court's decision in *Dobbs*.[23] President Biden stated that "protecting reproductive rights is essential to our Nation's health, safety, and progress.[24] He also criticized States' efforts to impose restrictions on mifepristone because such efforts "have stoked confusion, sowed fear, and may prevent patients from accessing safe and effective FDA-approved medication."[25] Thus, it is unlikely FDA would reverse course on its "mail-order" abortion regimen. ECF No. 7 at 7. Defendants' position on the Comstock Act in this litigation only confirms that fact. *See* ECF No. 28 at 38 ("Plaintiffs misconstrue the Comstock Act.").[26]

e. The Comstock Act was raised with Sufficient Clarity

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[23] *See FACT SHEET: President Biden to Sign Memorandum on Ensuring Safe Access to Medication Abortion*, THE WHITE HOUSE (Jan. 22, 2023), https://www.whitehouse.gov/briefing-room/statements-releases/2023/01/22/factsheet-president-biden-to-sign-presidential-memorandum-on-ensuring-safe-access-to-medication-abortion/.

[24] *Memorandum on Further Efforts to Protect Access to Reproductive Healthcare Services*, THE WHITE HOUSE (Jan. 22, 2023), https://www.whitehouse.gov/briefing-room/presidential-actions/2023/01/22/memorandum-on-further-efforts-to-protect-access-to-reproductive-healthcare-services/.

[25] *Id.*

[26] The D.C. Circuit has hinted that the futility doctrine is ordinarily predicated on the "worthlessness of an argument before an agency that *has rejected it* in the *past*" rather than the likelihood that "the agency *would reject it* in the *future*." *Tesoro Refin. & Mktg. Co. v. FERC*, 552 F.3d 868, 874 (D.C. Cir. 2009). But in this case, there is no principled distinction between the two scenarios. Defendants do not even pretend the agency might have accepted Plaintiffs' arguments. Other cases may involve uncertainty about *future* agency rejection, but it is not this case.

Finally, the Comstock Act issue was "raised with sufficient clarity." *Ross*, 976 F.3d at 942. This is because: (1) the 2019 Petition requested FDA to retain the in-person requirement for dispensing of chemical abortion drugs; and (2) the Comstock Act issue was also raised by the United States Postal Service and the Department of Health & Human Services on July 1, 2022, "[i]n the wake of" *Dobbs*.[27] The Office of Legal Counsel specifically mentioned FDA's regimen for chemical abortion drugs when concluding "the mere mailing of such drugs to a particular jurisdiction is an insufficient basis for concluding that the sender intends them to be used unlawfully." OLC Memo at *1. This shows not only that the issue was raised with sufficient clarity, but also the *futility* of raising the issue before the agency. Therefore, Plaintiffs' failure to exhaust their claims does not preclude judicial review.

C. Plaintiffs' Challenges to FDA's 2021 Actions Have a Substantial Likelihood of Success on the Merits

"To satisfy the first element of likelihood of success on the merits," Plaintiffs "must present a prima facie case but need not show that [they are] certain to win." *Janvey v. Alguire*, 647 F.3d 585, 595-96 (5th Cir. 2011) (internal marks omitted). Under the APA, courts must "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 law," or "in excess of statutory jurisdic-

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[27] *See Application of the Comstock Act to the Mailing of Prescription Drugs That Can Be Used for Abortions*, 2022 WL 18273906 (O.L.C. Dec. 23, 2022) ("OLC Memo").

tion, authority, or limitations, or short of statutory right." 5 U.S.C. § 706(2)(A) & (C).

The Court will first address FDA's 2021 Actions that eliminated the in-person dispensing requirement and announced that FDA would allow abortionists to dispense chemical abortion drugs by mail or mail-order pharmacy. Plaintiffs have a substantial likelihood of success on their claims that these actions violate federal law.

1. The Comstock Act prohibits the Mailing of Chemical Abortion Drugs

The Comstock Act declares "[e]very obscene, lewd, lascivious, indecent, filthy or vile article, matter, thing, device, or substance" to be "nonmailable matter" that "shall not be conveyed in the mails or delivered from any post office or by any letter carrier." 18 U.S.C. § 1461. The next clauses declare nonmailable "[e]very article or thing designed, adapted, or intended for producing abortion, or for any indecent or immoral use; and [e]very article, instrument, substance, drug, medicine, or thing which is advertised or described in a manner calculated to lead another to use or apply it for producing abortion, or for any indecent or immoral purpose." *Id.* Similarly, Section 1462 forbids the use of "any express company or other common carrier" to transport chemical abortion drugs "in interstate or foreign commerce."

Defendants' argument that the Comstock Act does not prohibit the mailing of chemical abortion drugs relies on the "reenactment canon." That is, courts may distill a statute's meaning when "federal courts of appeals settled upon a consensus view" and "Congress

never modified the relevant statutory text to reject or displace this settled construction." ECF No. 28 at 39. This purported "consensus view" is that the Comstock Act does not prohibit the mailing of items designed to produce abortions "where the sender does not intend them to be used unlawfully." *Id.* This argument is unpersuasive for several reasons.

"Congress is presumed to be aware of an administrative or judicial interpretation of a statute and to adopt that interpretation when it re-enacts a statute without change." *Lorillard v. Pons*, 434 U.S. 575, 580 (1978). But "[t]here is an obvious trump to the reenactment argument": "'[w]here the law is plain, subsequent reenactment does not constitute an adoption of a previous administrative construction.'" *Brown v. Gardner*, 513 U.S. 115, 121 (1994) (quoting *Demarest v. Manspeaker*, 498 U.S. 184, 190 (1991)); *see also Milner v. Dep't of Navy*, 562 U.S. 562, 576 (2011) ("[W]e have no warrant to ignore clear statutory language on the ground that other courts have done so."). Additionally, the presumption only applies when the judicial or administrative gloss "represented settled law when Congress reenacted the [language in question]." *Keene Corp. v. United States*, 508 U.S. 200, 212 (1993); *see also Jama v. Immigr. & Customs Enf't*, 543 U.S. 335, 349 (2005) (presumption applies only when the supposed judicial consensus at the time of reenactment was "so broad and unquestioned that we must presume Congress knew of and endorsed it"); *Davis v. United States*, 495 U.S. 472, 482 (1990); *Fed. Deposit Ins. Corp. v.*

Phila. Gear Corp., 476 U.S. 426, 437 (1986); *United States v. Powell*, 379 U.S. 48, 55 n.13 (1964).[28]

The canon is easily overcome for one simple reason: it is a dubious means of ascertaining congressional intent. "There are plenty of reasons to reenact a statute that have nothing to do with codifying the glosses that courts have already put on the statute." CALEB NELSON, STATUTORY INTERPRETATION 481 (2011). For example, perhaps the original statute contained a "sunset" provision. Maybe Congress wanted to change the statute in some other respects but found it easier to communicate those changes by reenacting a modified version of the complete statute "than by casting each discrete change as an amendment to the existing language." *Id.* at n.14. Or Congress was perhaps conducting "a more general codification or reorganization of the statutes in a particular field, for the sake of making the structure of its statutes easier to follow." *Id.* "Or maybe Congress simply wanted to enact the relevant title of the United States Code into positive law." *Id.* "To the extent that Congress reenacts statutory language for one of those other reasons, members of Congress may well not mean to be expressing any view at all about the glosses that have piled up in the meantime." *Id.*; *see also* HENRY M. HART, JR., & ALBERT M. SACKS, THE LEGAL PROCESS: BASIC PROBLEMS IN

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[28] *See also* ANTONIN SCALIA & BRYAN A. GARNER, READING LAW: THE INTERPRETATION OF LEGAL TEXTS 325 (2012) ("But how numerous must the lower-court opinions be, or how prominent and long-standing the administrative interpretation, to justify the level of lawyerly reliance that justifies the canon? What about two intermediate-court decisions? (We doubt it—though some cases have relied on just a single intermediate-court decision.) Or seven courts of first instance? (Perhaps.)").

THE MAKING AND APPLICATION OF LAW 1367 (William N. Eskridge, Jr., & Philip P. Frickey eds., 1994) (tent. ed. 1958) (criticizing the canon for adding to the costs of the legislative process in counterproductive ways).

Here, the plain text of the Comstock Act controls. *See Bostock v. Clayton Cnty., Ga.*, 140 S. Ct. 1731, 1749 (2020) ("[W]hen the meaning of the statute's terms is plain, our job is at an end."); *Lawson v. FMR LLC*, 571 U.S. 429, 441 (2014) ("Absent any textual qualification, we presume the operative language means what it appears to mean."). The Comstock Act declares "nonmailable" every "article, instrument, substance, drug, medicine, or thing which is advertised or described in a manner calculated to lead another to use it or apply it for producing *abortion*." 18 U.S.C. § 1461 (emphasis added). It is indisputable that chemical abortion drugs are both "drug[s]" and are "for producing abortion." Therefore, federal criminal law declares they are "nonmailable." *See Texas v. Becerra*, No. 5:22-CV-185-H, 2022 WL 3639525, at *26 n.21 (N.D. Tex. Aug. 23, 2022) ("[F]ederal law bar[s] the importation or delivery of any device or medicine designed to produce an abortion.").

The statute plainly does *not* require intent on the part of the seller that the drugs be used "unlawfully." To be sure, the statute does contain a catch-all provision that prohibits the mailing of such things "for producing abortion, *or for any indecent or immoral purpose*." 18 U.S.C. § 1461 (emphasis added). But "or" is "almost always disjunctive." *Encino Motorcars, LLC v. Navarro*, 138 S. Ct. 1134, 1141 (2018) (internal marks omitted). Additionally, the "or" in Section 1461 is preceded by a comma, further disjoining the list of nonmailable mat-

ter. Thus, the Court does not read the "or" as an "and." Similarly, the Act requires that the defendant "knowingly uses the mails for the mailing" of anything declared by the Act "to be nonmailable." 18 U.S.C. § 1461. A defendant could satisfy this *mens rea* requirement by mailing mifepristone and knowing it is for producing abortion. The statute does not require anything more. *See, e.g.*, *United States v. Lamott*, 831 F.3d 1153, 1157 (9th Cir. 2016) (where Congress "intends to legislate a specific intent crime," the statute typically uses the phrase "with the intent to") (internal marks omitted).

Even if the statute were ambiguous, the legislative history also supports this interpretation.[29] *See* H.R. Rep. No. 91-1105, at 2 (1970) ("Existing statutes completely prohibit the importation, interstate transportation, and mailing of contraceptive materials, or the mailing of advertisement or information concerning how or where such contraceptives may be obtained or how conception may be prevented."). Congress unsuccessfully tried to modify Section 1461 to prohibit mailing drugs "intended by the offender . . . to be used to produce an *illegal* abortion." *See* REP. OF THE SUBCOMM. ON CRIM. JUST., 95TH CONG., REP. ON RECODIFICATION OF FED. CRIM. LAW 40 (Comm. Print 1978) (emphasis added); *Bostock*, 140 S. Ct. at 1824 (Kavanaugh, J., dissenting) ("In the face of the unsuccessful legislative ef-

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[29] This Court reviews the legislative history as mere evidence of the ordinary public meaning of the current statutory language. *See* ANTONIN SCALIA, A MATTER OF INTERPRETATION 17 (1997) ("It is the *law* that governs, not the intent of the lawgiver . . . Men may intend what they will; but it is only the laws that they enact which bind us.").

forts . . . judges may not rewrite the law simply because of their own policy views.").[30] In fact, the House Subcommittee Report on the proposed amendment acknowledged the plain meaning of the statute: "[U]nder current law, the offender commits an offense whenever he 'knowingly' mails any of the designated abortion materials," and the proposed amendment would "require proof that the offender *specifically intended* that the mailed materials be used to produce an illegal abortion."[31] If Congress believed the statute *already* contained the "intentionality" requirement gloss in prior reenactments, there is little reason why Congress would amend the provision to *include* that requirement.

Defendants aver Plaintiffs' interpretation of the Comstock Act is foreclosed by the Food and Drug Administration Amendments Act of 2007 ("FDAAA") for one reason: "Congress was well aware that it was directing mifepristone's preexisting distribution scheme to continue" in enacting the FDAAA. ECF No. 28 at 40. But neither "critics [of FDA's 2000 Approval of mifepristone] nor anyone else in the congressional debate

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[30] *Bostock*'s majority opinion warns that "speculation about why a later Congress declined to adopt new legislation offers a 'particularly dangerous' basis on which to rest an interpretation of an existing law a different and earlier Congress did adopt." 140 S. Ct. at 1747. But the opinion does not suggest judges can "rewrite the law." Instead, *Bostock*'s stated rationale was that the disputed term was implicit in the statutory text all along. No such "textualist" analysis could plausibly justify Defendants' interpretation of the Comstock Act, and Defendants offer none.

[31] REP. OF THE SUBCOMM. ON CRIM. JUST., 95TH CONG., REP. ON RECODIFICATION OF FED. CRIM. LAW 40 (Comm. Print 1978) (emphasis added).

mentioned the Comstock Act." OLC Memo at *7 n.18; *see also In re Lively*, 717 F.3d 406, 410 (5th Cir. 2013) ("Repeals by implication are disfavored and will not be presumed unless the legislature's intent is 'clear and manifest.'") (internal marks omitted). Because the Comstock Act is not even implicitly mentioned in the FDAAA's enactment, there is no repeal by implication. And in any case, Defendants' arguments based on legislative history cannot overcome clear statutory text.

Consequently, reenactment of the Comstock Act does not constitute an adoption of prior constructions because "the law is plain." *Brown*, 513 U.S. at 121 (1994). Even if that were not the case, the reenactment canon does not apply here because the relevant judicial glosses do not represent a "broad and unquestioned" consensus. *Jama*, 543 U.S. at 349. Defendants rely heavily on the OLC Memo that purports to establish this "consensus." But none of the cases cited in the OLC Memo support the view that the Comstock Act bars the mailing of abortion drugs only when the sender has the specific intent that the drugs be used unlawfully.

On the contrary, the Seventh Circuit reasoned that the word "abortion" in the context of the Act indicates "a national policy of discountenancing abortion as inimical to the national life." *Bours*, 229 F. at 964. *Bours* further declared "it is immaterial what the local statutory definition of abortion is, what acts of abortion are included, or what excluded." *Id.* Similarly, the Sixth Circuit's decision in *Davis v. United States* only suggests that legitimate uses of drugs should not fall within the scope of the statute "merely because they are capable of illegal uses." 62 F.2d 473, 474 (6th Cir. 1933).

In other words, the *Davis* holding reflects the position that *legitimate* uses—uses beyond the purposes the statute condemns—should be excluded from the scope of the statute, *not* that whatever uses are *lawful under state law* should be. ECF No. 114 at 10. Likewise, the Second Circuit interpreted the statute to embrace articles the 1873 Congress "would have denounced as immoral if it had understood all the conditions under which they were to be used." *United States v. One Package*, 86 F.2d 737, 739 (2d Cir. 1936). The court further observed that "[t]he word 'unlawful' would make this clear as to articles for producing abortion." *Id.*; *see also* James S. Witherspoon, *Reexamining Roe: Nineteenth-Century Abortion Statutes and the Fourteenth Amendment*, 17 ST. MARY'S L.J. 29, 33 (1985) (explaining that thirty of thirty-seven states had statutory abortion prohibitions in 1868—just five years before Congress enacted the Comstock Act).

Defendants maintain "the legality of the agency actions needs to be judged at the time of the decision, all of which occurred when *Roe* and *Casey* were still good law." ECF No. 136 at 109. Even assuming that is true in all cases, *Roe* did not prohibit *all* restrictions on abortions. And it is not obvious that enforcement of the Comstock Act post-*Casey* would have necessarily run afoul of *Casey*'s "arbitrary 'undue burden' test." *Dobbs*, 142 S. Ct. at 2266. Therefore, there is no reason why the Act should not have at least been considered. In any case, the Comstock Act plainly forecloses mail-order abortion in the present, and Defendants have stated no present or future intention of complying with the law. Defendants cannot immunize the illegality of their actions by pointing to a small window in the past where those actions might have been legal.

In sum, the reenactment canon is inapplicable here because the law is plain. Even if that were not true, the cases relied on in the OLC Memo do not support Defendants' interpretation. And even if they did, a small handful of cases cannot constitute the "broad and unquestioned" consensus required under the reenactment canon. Therefore, Plaintiffs have a substantial likelihood of prevailing on their claim that Defendants' decision to allow the dispensing of chemical abortion drugs through mail violates unambiguous federal criminal law.

2. FDA's 2021 Actions violate the Administrative Procedure Act

Because FDA's 2021 Actions violate the Comstock Act, they are "otherwise not in accordance with law." 5 U.S.C. § 706(2)(A). Additionally, the actions were likely "arbitrary and capricious." *Id.* FDA relied on FDA Adverse Event Reporting System data despite the agency's 2016 decision to eliminate the requirement for abortionists to report non-fatal "adverse events." ECF No. 7 at 25. Defendants maintain that "Plaintiffs offer no explanation for why it was impermissible to rely on the reported data." ECF No. 28 at 33. The explanation should be obvious—it is circular and self-serving to practically eliminate an "adverse event" reporting requirement and then point to a low number of "adverse events" as a justification for removing even *more* restrictions than were already omitted in 2000 and 2016. In other words, it is a predetermined conclusion in search of non-data—a database designed to produce a null set. But even if FDA's explanation were well-reasoned, the actions would still run afoul of the Comstock Act and therefore violate the APA.

D. Plaintiffs' Challenges to FDA's Pre-2021 Actions Have a Substantial Likelihood of Success on the Merits

1. FDA's 2000 Approval violated Subpart H

In 1992, FDA issued regulations "needed to assure safe use" of *new* drugs designed to treat life-threatening diseases like HIV and cancer. *See* 57 Fed. Reg. 58,942, 58,958 (Dec. 11, 1992) (codified at 21 C.F.R. § 314.520). Subpart H—titled "Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses"—applies to drugs that satisfy two requirements. First, the drug must have been "studied for [its] safety and effectiveness in treating serious or life-threatening illnesses." 21 C.F.R. § 314.500. And second, the drug must "provide [a] meaningful therapeutic benefit to patients over existing treatments." *Id.* "These rules were promulgated by FDA . . . as part of an attempt to correct perceived deficiencies in FDA's approval process made apparent by the need to quickly develop drugs for HIV/AIDS patients." ECF No. 1-13 at 20.

"When FDA originally approved Mifeprex, the agency relied upon Subpart H to place certain restrictions on the manufacturer's distribution of the drug product to assure its safe use." ECF No. 28 at 14; *see also* ECF No. 1-13 at 9 (the American Medical Association explained that "[Mifepristone] poses a severe risk to patients unless the drug is administered as part of a complete treatment plan under the supervision of a physician"). Thus, to satisfy Subpart H, FDA deemed pregnancy a "serious or life-threatening illness[]" and concluded that mifepristone "provide[d] [a] meaningful therapeutic benefit to patients over existing treatments."

See 21 C.F.R. §§ 314.500; 314.560. FDA was wrong on both counts.

a. Pregnancy is not an "Illness"

Pregnancy is a normal physiological state most women experience one or more times during their childbearing years—a natural process essential to perpetuating human life. Defendants even admit pregnancy is not an "illness." FDA claims the Final Rule explained Subpart H was available for serious or life-threatening "conditions," whether or not they were understood colloquially to be "illnesses." ECF No. 28 at 36. But the Final Rule says no such thing. "One comment asserted that neither depression nor psychosis is a disease, nor is either one serious or life-threatening." 57 Fed. Reg. 58,946. FDA responded to the comment that "signs of these diseases are readily studied" and that its reference to depression and psychosis "was intended to give examples of conditions or diseases that can be serious for certain populations or in some or all of their phases." *Id.* In other words, FDA's response to this comment was *not* that depression and psychosis qualify because they are "conditions" even though they are not colloquially understood as "illnesses." Rather, FDA simply disagreed with the comment's characterization of these conditions and explained that they *were* examples of "diseases" that can be "serious." Nothing in the Final Rule supports the interpretation that pregnancy is a serious or life-threatening illness.

FDA's 2016 Denial of the 2002 Petition is similarly unpersuasive. For example, FDA noted that approximately fifty percent of pregnancies in the United States are unintended and that unintended pregnancies may

cause depression and anxiety. ECF No. 1-28 at 5. But categorizing complications or negative psychological experiences arising *from* pregnancy as "illnesses" is materially different than classifying pregnancy *itself* as a serious or life-threatening illness *per se*. Tellingly, FDA never explains how or why a "condition" would *not* qualify as a "serious or life-threatening illness." Suppose that a woman experiences depression because of lower back pain that inhibits her mobility. Under FDA's reading, a new drug used to treat lower back pain—which can cause depression, just like unplanned pregnancy—could obtain accelerated approval under Subpart H.

Defendants cite zero cases reading Subpart H like FDA reads Subpart H. On the contrary, courts have read "serious or life-threatening illnesses" to mean what it says. *See, e.g.*, *Tummino v. Hamburg*, 936 F. Supp. 2d 162, 182 (E.D.N.Y. 2013) ("Whether an illness is 'serious or life threatening' 'is based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one.'") (quoting 57 Fed. Reg. at 13235). The preamble to the final rule also clarified the terms "would be used as FDA has defined them in the past." 57 Fed. Reg. at 13235.

Likewise, the Final Rule expressly stated this nomenclature "is the same as FDA defined and used the terms" in two rulemakings: the first in 1987; the second in 1988. 57 Fed. Reg. at 58,945. In the 1988 rulemaking, FDA defined "life-threatening" to include *diseases or conditions* "where the likelihood of death is high unless the course of the disease is interrupted (*e.g.*,

AIDS and cancer), as well as diseases or conditions with potentially fatal outcomes where the end point of clinical trial analysis is survival (*e.g.*, increased survival in persons who have had a stroke or heart attack)." *See* 53 Fed. Reg. at 41517; *id.* at 41516 (referencing "AIDS, cancer, Parkinson's disease, and other serious conditions"); *CSX Transp., Inc. v. Ala. Dep't of Revenue*, 562 U.S. 277, 294 (2011) (the canon of *ejusdem generis* "limits general terms that follow specific ones to matters similar to those specified") (internal marks omitted). Therefore, "diseases" and "conditions" are used interchangeably, and even "conditions" must be "serious" or "life-threatening" as defined.

Food and Drug scholars have understood Subpart H's scope the same way. *See, e.g.*, Charles Steenburg, *The Food and Drug Administration's Use of Postmarketing (Phase IV) Study Requirements: Exception to the Rule?*, 61 FOOD & DRUG L.J. 295, 323 (2006) (Subpart H "extend[s] only to drugs and biological products that target[] 'serious or life-threatening illnesses' and offer[] a 'meaningful' benefit over existing treatments"). Even the Population Council argued to FDA that "the imposition of Subpart H is unlawful" because "[t]he plain meaning of these terms does not comprehend normal, everyday occurrences such as pregnancy and unwanted pregnancy." ECF No. 1-14 at 21. This reading is also consistent with the fact that aside from mifepristone, FDA had approved fewer than forty NDAs under Subpart H by early 2002. *See id.* at 20. And of those *other* approvals, twenty were for the treatment of HIV and HIV-related diseases, nine were for the treatment of various cancers and their symptoms, four were for severe bacterial infections, one was for chronic hypertension, and one was for leprosy. *Id.*

"One of these things is not like the others, one of these things just doesn't belong." *See Sesame Street*.

b. Defendants are not entitled to Auer *Deference*

Courts sometimes extend *Auer* deference "to agencies' reasonable readings of genuinely ambiguous regulations." *Kisor v. Wilkie*, 139 S. Ct. 2400, 2408 (2019). *Auer* deference is rooted in an "always rebuttable" presumption "that Congress would generally want the agency to play the primary role in resolving regulatory ambiguities." *Id.* at 2412. "*Auer* deference is sometimes appropriate and sometimes not." *Id.* at 2408. "First and foremost, a court should not afford *Auer* deference unless the regulation is genuinely ambiguous." *Id.* at 2415. "And before concluding that a rule is genuinely ambiguous, a court must exhaust all the traditional tools of construction." *Id.* (internal marks omitted). "That means a court cannot wave the ambiguity flag just because it found the regulation impenetrable on first read." *Id.* If genuine ambiguity remains, the agency's reading must still be "reasonable." *Id.* And even if the regulation is genuinely ambiguous, the agency's interpretation "must in some way implicate its substantive expertise." *Id.* at 2417. Finally, an agency's reading of a rule must reflect "fair and considered judgment" to receive *Auer* deference. *Id.* (internal marks omitted).

Here, *Auer* deference is not appropriate because "the language of [the] regulation is plain and unambiguous." *McCann v. Unum Provident*, 907 F.3d 130, 144 (3d Cir. 2018). As explained, FDA's definitions in prior rulemakings foreclose its interpretation of Subpart H. If there is any ambiguity in "serious or life-threatening illnesses," the ordinary meaning principle resolves that

ambiguity. *See Bostock*, 140 S. Ct. at 1825 (Kavanaugh, J, dissenting) ("The ordinary meaning principle is longstanding and well settled."). "[C]ommon parlance matters in assessing the ordinary meaning" of a statute or regulation "because courts heed how most people would have understood the text." *Id.* at 1828 (internal marks omitted). The word "illness" refers to "poor health; sickness," or "a specific sickness or disease, or an instance of such."[32] Merriam- Webster invokes the definition for "sickness"—"an unhealthy condition of body or mind."[33] Likewise, a Wikipedia search for "illness" re-directs to the entry for "Disease," which is defined as "a particular *abnormal* condition that negatively affects the structure or function of all or part of an organism, and that is not immediately due to any external injury."[34] Pregnancy, on the other hand, is defined as "the time during which one or more offspring develops (gestates) inside a woman's uterus (womb)."[35]

Most readers would not define pregnancy to be a serious or life-threatening illness. Even FDA does not earnestly defend that position. True, complications can arise during pregnancy, and said complications *can* be serious or life-threatening. But that does not make

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[32] *Illness*, Dictionary.com, https://www.dictionary.com/browse/illness (last visited Mar. 22, 2023); *see also Bostock*, 140 S. Ct. at 1766 (Alito, J, dissenting) ("Dictionary definitions are valuable because they are evidence of what people at the time of a statute's enactment would have understood its words to mean.").

[33] *Illness*, Merriam-Webster.com, https://www.merriam-webster.com/dictionary/illness (last visited Mar. 22, 2023).

[34] *Disease*, Wikipedia, https://en.wikipedia.org/wiki/Disease (emphasis added) (last visited Mar. 22, 2023).

[35] *Pregnancy*, Wikipedia, https://en.wikipedia.org/wiki/Pregnancy (last visited Mar. 22, 2023).

pregnancy *itself* an illness. *See* ECF No 1-13 at 21. And even if the regulation were genuinely ambiguous after exhausting all traditional tools of statutory construction, Defendants' interpretation: (1) is *not* reasonable; (2) does not implicate their substantive expertise; and (3) does not reflect fair and considered judgment. Accordingly, Defendants are not entitled to *Auer* deference on their interpretations of "serious or life-threatening illnesses." By interpreting Subpart H's scope as reaching any state or side effect that can be considered an undefined "condition," Defendants broaden the regulation on accelerated approval of new drugs farther than the text of the regulation would ever suggest. Therefore, FDA's approval of chemical abortion drugs under Subpart H exceeded its authority under the regulation's first requirement.

c. Chemical Abortion Drugs do not provide a "Meaningful Therapeutic Benefit"

FDA also exceeded its authority under the second requirement of Subpart H. In addition to treating a serious or life-threatening illness, chemical abortion drugs must also provide a "meaningful therapeutic benefit" to patients over surgical abortion. 21 C.F.R. § 314.500. As explained, this cannot be the case because chemical abortion drugs do not treat "serious or life-threatening illnesses"—a prerequisite to reaching the second requirement. *Id.* Similarly, chemical abortion drugs cannot be "therapeutic" because the word relates to the treatment or curing of disease.[36] But even putting that aside, chemical abortion drugs do

[36] *Therapeutic*, Dictionary.com, https://www.dictionary.com/browse/illness (last visited Mar. 28, 2023).

not provide a meaningful therapeutic benefit over surgical abortion. *See* 21 C.F.R. § 314.500 (examples include where the benefit is the "ability to treat patients unresponsive to, or intolerant of, available therapy, or improved patient response over available therapy"). To the extent surgical abortion can be considered a "therapy," the clinical trials did not compare chemical abortion with surgical abortion to find such a benefit. ECF No. 1 at 44.

Defendants argue just one "meaningful therapeutic benefit": chemical abortion drugs avoided "an invasive surgical procedure and anesthesia in 92 percent of" patients in the trial. ECF No. 28 at 37. But "[b]y defining the 'therapeutic benefit' solely as the avoidance of the current standard of care's delivery mechanism, FDA effectively guarantees that a drug will satisfy this second prong of Subpart H as long as it represents a different method of therapy." ECF No. 1-14 at 22. And even if that *were* a benefit, chemical abortions are over fifty percent more likely than surgical abortion to result in an emergency room visit within thirty days. ECF No. 7 at 21.[37] Consequently, the number of chemical abortion-related emergency room visits increased by over *five hundred percent* between 2002 and 2015. ECF No. 1 at 19. One study revealed the overall incidence of adverse events is "fourfold higher" in chemical abortions when compared to surgical abortions.[38] Women

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[37] Some studies report that the exact number is *fifty-three* percent. *See* Studnicki et al., *supra* note 22.

[38] *See* Maarit Niinimäki et al., *Immediate Complications After Medical Compared with Surgical Termination of Pregnancy*, 114 OBSTETRICS & GYNECOLOGY 795 (2009). FDA agrees with this study but finds it "not surprising" given that chemical abortion "is

who underwent chemical abortions also experienced far higher rates of hemorrhaging, incomplete abortion, and unplanned surgical evacuation.[39] Chemical abortion patients "reported significantly higher levels of pain, nausea, vomiting and diarrhea during the actual abortion than did surgical patients . . . Post-abortion pain occurred in 77.1% of mifepristone patients compared with only 10.5% of surgical patients." ECF No 1-13 at 24. And before the approval, an FDA medical officer recognized the "medical regimen had *more* adverse events, particularly bleeding, than did surgical abortion. Failure rates exceeded those for surgical abortion . . . This is a serious potential disadvantage of the medical method." *Id.* at 23 (emphasis added).

Other studies show eighty-three percent of women report that chemical abortion "changed" them—and seventy-seven percent of those women reported a *negative* change.[40] Thirty-eight percent of women reported issues with anxiety, depression, drug abuse, and suicidal thoughts because of the chemical abortion.[41] Bleeding from a chemical abortion, unlike surgical abor-

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associated with longer uterine bleeding." ECF No. 1-44 at 38. *See also* ECF No 1-13 at 15, n.68-72 (collecting studies demonstrating the far higher rates of adverse events in chemical abortion over surgical abortion).

[39] *Id.*

[40] *See* Katherine A. Rafferty & Tessa Longbons, *#Abortion-Changes You: A Case Study to Understand the Communicative Tensions in Women's Medication Abortion Narratives*, 36 HEALTH COMM. 1485, 1485-94 (2021), https://www.tandfonline.com/doi/full/10.1080/10410236.2020.1770507.

[41] *Id.*

tion, can last up to several weeks.[42] And the mother seeing the aborted human "appears to be a difficult aspect of the medical termination process which can be distressing, bring home the reality of the event and may influence later emotional adaptation."[43] "For example, one woman was surprised and saddened to see that her aborted baby 'had a head, hands, and legs' with '[d]efined fingers and toes.'" ECF No. 1 at 21. The entire abortion process takes place within the mother's home, without physician oversight, potentially leading to undetected ectopic pregnancies, failure of rH factor incompatibility detection, and misdiagnosis of gestational age—all leading to severe or even fatal consequences. *See* ECF No. 96 at 15-17. Contrary to popular belief and talking points, the evidence shows chemical abortion is *not* "as easy as taking Advil." *Id.* at 20.

Compelling evidence suggests the statistics provided by FDA on the adverse effects of chemical abortion *understate* the negative impact the chemical abortion regimen has on women and girls. When women seek emergency care after receiving the chemical abortion pills, the abortionist that prescribed the drugs is usually *not* the provider to manage the mother's com-

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[42] *After Mifepristone: When bleeding will start and how long will it last?*, WOMEN ON WEB, https://www.womenonweb.org/en/page/484/when-will-you-start-bleeding-and-how-long-will-it-last. *See also* ECF No. 1-28 at 25 ("Up to 8% of all subjects may experience some type of bleeding for 30 days or more.").

[43] Pauline Slade et al., *Termination of Pregnancy: Patient's Perception of Care*, 27 J. OF FAMILY PLANNING & REPRODUCTIVE HEALTH CARE 72, 76 (2001).

plications.[44] Consequently, the treating physician may not know the adverse event is due to mifepristone. *Id.* at 13. Studies support this conclusion by finding *over sixty percent* of women and girls' emergency room visits after chemical abortions are miscoded as "miscarriages" rather than adverse effects to mifepristone.[45] Simply put, FDA's data are incomplete and potentially misleading, as are the statistics touted by mifepristone advocates.

Lastly, chemical abortion does not "treat patients unresponsive to, or intolerant of, available therapy." *See* 21 C.F.R. § 314.500. "To the contrary, because 'medical abortion failures should be managed with surgical termination' the option for surgical abortion must be available for any Mifeprex patient." ECF No. 1-14 at 23 (quoting the Mifeprex "Warnings" label). One study showed that 18.3 percent of women required surgical intervention after the chemical abortion regimen failed. *Id.* Hence, "any patient who would be intolerant of surgical abortion, if such a class of patients exists, cannot use the Mifeprex Regimen." *Id.* at 24. On balance, the data reflect little to no benefit over surgical abortion—much less a "meaningful therapeutic" benefit.

d. Defendants' Misapplication of Subpart H has not been Cured by Congress

Defendants contend "Plaintiffs' arguments about Subpart H have been overtaken by congressional ac-

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[44] Kathi Aultman et al., *Deaths and Severe Adverse Events after the use of Mifepristone as an Abortifacient from September 2000 to February 2019*, 36 ISSUES IN LAW & MED., 3-26 (2021).

[45] Studnicki et al., *supra* note 9.

tion." ECF No. 28 at 35. In the FDAAA, "Congress specifically directed" that drugs with elements to assure safe use "in effect on the effective date on this Act" would be "deemed to have in effect an approved" REMS. *Id.* (citing Pub. L. No. 110-85, § 909(b)(1)). But the sponsors of such drugs were also required to submit a proposed REMS within 180 days. *See* Pub. L. No. 110-85, § 909(b)(3). Hence, Congress "deemed" preexisting safety requirements to be a sufficient REMS until a *new* REMS was approved. The FDAAA did not affect, however, whether an NDA was properly approved or authorized under Subpart H in the first place. Rather, the FDAAA required that such drugs needed continued restrictions in place to mitigate risks. Implementation of a REMS under the FDAAA does not somehow repeal or supplant the approval process under Subpart H or 21 U.S.C. § 355(d). The FDAAA only eased the regulatory transition from Subpart H to the REMS provision. Simply stated, Congress's *general* reiteration that dangerous drugs should carry a REMS did not codify FDA's *specific* approval of the mifepristone NDA. It did not consider the chemical abortion approval at all.

In sum, Subpart H doubly forecloses FDA's approval of mifepristone. *At most*, FDA might have lawfully approved mifepristone under Subpart H for cases where a pregnant woman's life or health is in danger. But even a limited approval of this sort would still not render pregnancy an "illness." And surgical abortion—a statistically far safer procedure— would still be available to her. But in any case, that is not what FDA did. Instead, FDA manipulated and misconstrued the text of Subpart H to greenlight elective chemical abortions on a wide scale. Therefore, Plaintiffs have a substantial

likelihood of prevailing on their claim that Defendants violated Subpart H.

2. FDA's Pre-2021 Actions were Arbitrary and Capricious

Under the FFDCA, a pharmaceutical company seeking to market a new drug must first obtain FDA approval via an NDA. *See* 21 U.S.C. § 355(a), (b). The NDA must include "adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof." 21 U.S.C. § 355(d). The trials must "provide an adequate basis for physician labeling." 21 C.F.R. § 312.21(c). In those trials, "the drug is used *the way it would be administered when marketed*."[46] The Secretary must deny the NDA if "he has insufficient information to determine whether such drug is safe for use under such conditions." 21 U.S.C. § 355(d)(4).

Here, the U.S. trials FDA relied upon when approving mifepristone required that: (1) each woman receive an ultrasound to confirm gestational age and exclude an ectopic pregnancy;[47] (2) physicians have expe-

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[46] *Glossary*, WEILL CORNELL MEDICINE, https://research.weill.cornell.edu/compliance/human-subjects-research/institutional-review-board/glossary-faqs-medical-terms-lay-3 (last visited Mar. 22, 2023) (emphasis added).

[47] The 2016 Denial of the 2002 Petition briefly notes the two French clinical trials did not *require* an ultrasound but instead left the decision to the investigator's discretion. ECF No. 1-28 at 19 n.47. Defendants do not explain how many investigators chose to perform an ultrasound. The higher that number is, the more it supports Plaintiffs' argument. But in any case, the U.S. trial was

rience in performing surgical abortions and admitting privileges at medical facilities that provide emergency care; (3) all patients be within one hour of emergency facilities or the facilities of the principal investigator; and (4) women be monitored for four hours to check for adverse events after taking misoprostol. ECF No. 7 at 23. However, FDA included *none* of these requirements—which were explicitly stated in the clinical trial FDA relied on most—in the 2000 Approval. *Id.* Likewise, FDA's 2016 Changes omitted the requirements of the underlying tests: (1) gestational age confirmed by ultrasounds; (2) participants required to return for clinical assessment; and (3) surgical intervention if necessary. *Id.* at 24.

Defendants maintain "there is no legal basis for Plaintiffs' contention that the approved conditions of use of a drug must duplicate the protocol requirements for the clinical trials supporting its approval." ECF No. 28 at 35. But FDA's actions must not be arbitrary and capricious.[48] *See* 5 U.S.C. § 706(2)(A); *United States*

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larger than the two French trials combined and is therefore the more reliable study. *Id.* at 9.

[48] Plaintiffs also frame what the Court characterized as the "study-match problem" as a statutory violation of the FFDCA. *See* ECF No. 7 at 22. The Court does not read 21 U.S.C. § 355(d) as necessarily *requiring* an exact "match" between trial conditions and the conditions on the approved labeling of a new drug. But Section 355(d) does mandate the Secretary "issue an order refusing to approve the application" if he finds the investigations do not show the drug is safe for use under the suggested conditions in the proposed labeling. FDA made such a finding yet did not deny the Application. *See* ECF No. 1-24 at 6 ("We have concluded that adequate information has not been presented to demonstrate that the drug, when marketed in accordance with the terms of distribution proposed, is safe and effective for use as recommended."). Thus, even

v. An Article of Device . . . Diapulse, 768 F.2d 826, 832-33 (7th Cir. 1985) (concluding FDA's denial was not arbitrary and capricious because the proposed labeling did not "specify conditions of use that are similar to those followed in the studies"). "The scope of review under the arbitrary and capricious standard is narrow and a court is not to substitute its judgment for that of the agency." *Motor Vehicle Mfrs. Ass'n of U.S., Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983) (internal marks omitted). "Nevertheless, the 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." *Id.* (internal marks omitted); *see also Sw. Elec. Power Co. v. EPA*, 920 F.3d 999, 1013 (5th Cir. 2019) (judicial review of agency action "is not toothless"). Courts must "consider whether the decision was based on a consideration of the relevant factors and whether there has been a clear error of judgment." *Id.* (internal marks omitted). An agency's action is "arbitrary and capricious" if it "entirely failed to consider an important aspect of the problem, offered 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." *Id.* Defendants fail this test.

a. The 2000 Approval

To begin, FDA "entirely failed to consider an important aspect of the problem" by omitting any evaluation of the psychological effects of the drug or an eval-

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if Defendants could survive "arbitrary and capricious" analysis of the "study-match problem," Defendants still violated Section 355(d) on their own terms.

uation of the long-term medical consequences of the drug. *State Farm*, 463 U.S. at 43; ECF No. 84 at 12. Considering the intense psychological trauma and post-traumatic stress women often experience from chemical abortion, this failure should not be overlooked or understated. Nor was the drug tested for under-18 girls undergoing reproductive development.[49] But that is not all. Clinical trial protocols in the United States for the 2000 Approval required a transvaginal ultrasound for each patient to accurately date pregnancies and identify ectopic pregnancies. ECF No. 1-28 at 19. But FDA ultimately concluded that "a provider can accurately make such a determination by performing a pelvic examination and obtaining a careful history." *Id.* Thus, FDA determined it was inappropriate "to mandate how providers clinically assess women for duration of pregnancy and for ectopic pregnancy." ECF No. 1-28 at 19. FDA believed "it is reasonable to expect that the women's providers would not have prescribed Mifeprex if a pelvic ultrasound examination had clearly identified an ectopic pregnancy." *Id.* at 20.

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[49] In 1998, FDA issued the "Pediatric Rule," which "mandated that drug manufacturers evaluate the safety and effectiveness of their products on pediatric patients, absent an applicable exception." *Ass'n of Am. Physicians & Surgeons, Inc. v. U.S. Food & Drug Admin.*, 391 F. Supp. 2d 171, 173-74 (D.D.C. 2005). Two years after approving mifepristone, FDA was enjoined from enforcing the Pediatric Rule because it lacked statutory authority in issuing the rule. *See Ass'n of Am. Physicians & Surgeons v. FDA*, 226 F. Supp. 2d 204, 222 (D.D.C. 2002). In response, Congress enacted the Pediatric Research Equity Act of 2003 to codify the Pediatric Rule. *See* 21 U.S.C. § 355c. In the 2000 Approval, FDA clarified that the Mifeprex NDA was covered by the Pediatric Rule. *See* ECF No. 1-26 at 4. However, FDA fully waived the rule's requirements without explanation. ECF No. 1-28 at 30.

FDA thus assumes physicians will ascertain gestational age. But put another way, there is simply *no requirement* that *any* procedure is done to rule out an ectopic pregnancy—which *is* a serious and life-threatening situation. This is arbitrary and capricious. The mere fact that other clinical methods can be used to date pregnancies does not support the view that it should be the provider's decision to decide which method—if any—is used to make this determination. FDA has never denied that an ultrasound is the *most accurate* method to determine gestational age and identify ectopic pregnancies. *See* ECF No. 1-14 at 62. And the fact that other clinical methods can be used does not mean that all such methods are equal in their accuracy and reliability.[50] FDA did rely on a study showing that clinicians rarely underestimate gestational age. ECF No. 1-28 at 19 n.49. But this study does nothing to support FDA's view that a transvaginal ultrasound is not necessary to diagnose ectopic pregnancies. To this point, FDA merely argues that even transvaginal ultrasounds do not *guarantee* an existing ectopic pregnancy will be identified. *Id.* at 19. If that is the case, it does not follow that it should be left to the provider's discretion to employ less reliable methods—or no methods at all.

Correct diagnosis of gestational age and ectopic pregnancies is vital. The error in FDA's judgment is

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[50] Studies reflect that women recurrently miscalculate their unborn child's gestational age. *See* P. Taipale & V. Hiilesmaa, *Predicting delivery date by ultrasound and last menstrual period in early gestation*, 97 OBSTETRICS GYN. 189 (2001); David A. Savitz et al., *Comparison of pregnancy dating by last menstrual period, ultrasound scanning, and their combination*, 187 AM. J. OBSTETRICS GYN. 1660 (2002).

borne out by myriad stories and studies brought to the Court's attention. One woman alleged she did not receive an ultrasound or any other physical examination before receiving chemical abortion drugs from Planned Parenthood. ECF No. 1 at 22. "The abortionist misdated the baby's gestational age as six weeks, resulting in the at-home delivery of a 'lifeless, fullyformed baby in the toilet,' later determined to be around *30-36 weeks old*." *Id.*; *see also Patel v. State*, 60 N.E.3d 1041, 1043 (Ind. Ct. App. 2016) (woman who used chemical abortion drugs "delivered a live baby of approximately twenty-five to thirty weeks gestation who died shortly after birth"). Another woman was given chemical abortion drugs during an ectopic pregnancy because her ultrasound "was not even that of a uterus but was of a bladder."[51] ECF No. 31 at 5. The resulting rupture "led to massive infection and a collapse of her vital systems." *Id.* Amicus Human Coalition identified four of their clients who were unknowingly ectopic when they arrived at their clinic "with abortion pills in hand." ECF No. 96 at 20. And at least two women died from chemical abortion drugs last year. *See* ECF No. 120 at 30 n.5. One of those women was an estimated twenty-one weeks pregnant. *See id.* Presumably, the fact that the woman obtained chemical abortion drugs more than two months past FDA's gestational age cutoff suggests that no adequate procedures confirmed the gestational age in her case.

FDA has also reported at least ninety-seven cases where women with ectopic pregnancies took mifepris-

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[51] This incident also demonstrates that even where ultrasounds are used, only a qualified provider can assure they are done properly.

tone.[52] But these data are likely incomplete because FDA now only requires reporting on deaths. *See* ECF No. 1 at 4. And as noted above, hospitals often miscode complications from chemical abortions as miscarriages. Studies show that women are thirty percent more likely to die from a ruptured ectopic pregnancy while seeking abortions if the condition remains undiagnosed.[53] A woman may interpret the warning signs of an ectopic pregnancy—cramping and severe bleeding—as side effects of mifepristone. In reality, the symptoms indicate her life is in danger.[54] Another study revealed that of 5,619 chemical abortion visits, 452 patients had a pregnancy of "unknown location" and 31 were treated for ectopic pregnancy—including 4 that were ruptured.[55] Yet another study examined 3,197 unique, U.S.-only adverse event reports dated September 2000 to February 2019.[56] That study noted 20 deaths, 529 life-threatening events, and 1,957 *severe* adverse events before concluding that a pre-abortion ultrasound "should be required to rule out ectopic pregnancy and confirm gestational age."[57]

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[52] FDA, *Mifepristone US. Post-Marketing Adverse Events Summary Through 6/30/2022,* http://www.fda.gov/media/164331/download.

[53] H.K. Atrash et al., *Ectopic pregnancy concurrent with induced abortion: incidence and mortality*, 162 AM. J. OBSTETRICS GYN. 726 (1990).

[54] *Id.*

[55] Alisa B. Goldberg et al., *Mifepristone and Misoprostol for Undesired Pregnancy of Unknown Location*, 139 OBSTETRICS GYN. 771, 775 (2022).

[56] Aultman et al., *supra* note 44.

[57] *Id.*

The record confirms FDA once shared these concerns. After all, many tragedies could be avoided by auditing physician qualifications and requiring ultrasounds. In 1996, the FDA Advisory Committee expressed to the Population Council "serious reservations" on how the drugs were described "in terms of assuring safe and adequate credentialing of providers." ECF No. 1-14 at 51. Population Council initially committed to conducting post-approval studies in 1996, and FDA reiterated these requirements mere months before the September 2000 approval. *See* ECF No. 1-24 at 6 ("We remind you of your commitments dated September 16, 1996, to perform the . . . Phase 4 studies."). Those protocols would have required, *inter alia*, that the Population Council: (1) assess the long-term effects of multiple uses of mifepristone; (2) ascertain the frequency with which women follow the regimen and outcomes of those that do not; (3) study the safety and efficacy of chemical abortion in girls under the age of eighteen; and (4) ascertain the regimen's effects on children born after treatment failure.[58] ECF No. 1-28 at 32.

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[58] *See* 153 Cong. Rec. S5765 (daily ed. May 9, 2007) (statement of Sen. Coburn) ("I recently learned of a woman who was given RU-486 after she had a seizure. Her physicians assumed that the seizure was life-threatening to the baby she was carrying and gave her RU-486 for a therapeutic abortion. RU-486 was not effective in her case and the woman carried the baby to term. When the baby was born at a low birth weight, it also suffered from failure to thrive. That baby has had three subsequent brain surgeries due to hydrocephalus. The baby also suffers from [idiopathic lymphocytic colitis]—an inflammatory disease of the colon, which is extremely rare in children. It is clear that RU-486 not only is unsafe in women,

Similarly, on February 18, 2000—months before chemical abortion approval—FDA informed the Population Council that "adequate information ha[d] *not* been presented to demonstrate that the drug, when marketed in accordance with the terms of distribution proposed, is safe and effective for use as recommended." ECF No. 1-24 at 6 (emphasis added). FDA then stated the "restrictions on distribution will need to be amended." *Id.* Accordingly, FDA informed the Population Council that it would proceed under Subpart H—the *only* provision that could implement the requisite restrictions on distribution. *Id.* But as explained above, that was the improper regulation for the approval of chemical abortion. Regardless, the restrictions were insufficient to ensure safe use.

On June 1, 2000, FDA privately delivered to the Population Council a set of proposed restrictions to rectify the safety issues. Said proposal required physicians who were: (1) "trained and authorized by law" to perform surgical abortions; (2) trained in administering mifepristone and treating adverse events; and (3) allowed "continuing access (*e.g.*, admitting privileges) to a medical facility equipped for instrumental pregnancy termination, resuscitation procedures, and blood transfusion at the facility or [one hour's] drive from the treatment facility." *See* ECF No. 1- 14 at 53-54. When FDA's proposal was leaked to the press, a political and editorial backlash ensued.[59] In response, the Popula-

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but it is also not completely effective. And when it is not effective, the results are devastating.").

[59] Sheryl Gay Stolberg, *FDA Adds Hurdles in Approval of Abortion Pill*, THE NEW YORK TIMES (June 8, 2000), https://www.ny-

tion Council rejected the proposal and repudiated the restrictions the sponsor *itself* proposed in 1996—what FDA deemed a "very significant change" in the sponsor's position. *Id.* at 50. Because "[t]he whole idea of mifepristone was to increase access," abortion advocates argued that restrictions on mifepristone "would effectively eliminate" the drug's "main advantage" and would "kill[] the drug."[60]

In September 2000, FDA abandoned its safety proposals and acquiesced to the objections of the Population Council and Danco. Despite its "serious reservations" about mifepristone's safety, FDA approved a regimen that relied on a self-certification that a prescribing physician has the *ability* to diagnose ectopic pregnancies. *Id.* at 51, 62; *see also* ECF No. 1-28 at 21 ("[W]e concluded that there was no need for special certification programs or additional restrictions."). FDA later released the applicant *entirely* from its Phase 4 duties—*twelve years* after the 1996 commitment. ECF Nos. 1-24 at 6, 1-28 at 32; *see also* 21 C.F.R. § 314.510 ("Approval under this section will be subject to the requirement that the applicant study the drug further, to verify and describe its clinical benefit, where there is uncertainty . . . of the observed clinical benefit to ultimate outcome. Postmarketing studies would usually be studies *already underway*.") (emphasis added).

FDA *must* refuse to approve a drug if the agency determines there is "insufficient information to determine whether such drug is safe for use" or a "lack of

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times.com/2000/06/08/us/fda-adds-hurdles-in-approval-of-abortion-pill.html.

[60] *Id.*

substantial evidence that the drug will have the effect it purports or is represented to have" under the conditions of use in the proposed label. 21 U.S.C. § 355(d)(4)-(5); *see also* 21 C.F.R. § 314.125(b). FDA is therefore required to deny an NDA if it makes the exact findings FDA made in its 2000 review. "[A]n agency's decision to change course may be arbitrary and capricious if the agency ignores or countermands its earlier factual findings without reasoned explanation for doing so." *F.C.C. v. Fox Television Stations, Inc.*, 556 U.S. 502, 537 (2009). The agency must ordinarily "display awareness that it *is* changing position," and "must show that there are good reasons for the new policy." *Id.* at 515. And "if the agency's decision was in any material way influenced by political concerns it should not be upheld." *Earth Island Inst. v. Hogarth*, 494 F.3d 757, 768 (9th Cir. 2007). FDA's only acknowledgments of its prior proposals were that "FDA and the applicant were not always in full agreement about the distribution restrictions" and that fulfilling the Phase 4 commitments "would not be feasible." ECF No. 1-28 at 18, 32-33.

The Court does not second-guess FDA's decision-making lightly. But here, FDA acquiesced on its legitimate safety concerns—in violation of its statutory duty —based on plainly unsound reasoning and studies that did not support its conclusions. There is also evidence indicating FDA faced significant political pressure to forego its proposed safety precautions to better advance the *political* objective of increased "access" to chemical abortion —which was the "whole idea of mifepristone."[61] As President Clinton's Secretary for Health

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[61] Stolberg, *supra* note 59.

& Human Services ("HHS") explained to the White House, it was *FDA* that arranged the meeting between the French pharmaceutical firm—who owned the mifepristone patent rights —and the eventual drug sponsor Population Council. The purpose of the FDA-organized meeting was "to facilitate an agreement between those parties to work together to test [mifepristone] and file a new drug application." ECF No. 95 at 14. HHS also "initiated" another meeting "to assess how the United States Government"—*i.e.*, the Clinton Administration—"might facilitate successful completion of the negotiations" between the French firm and the American drug sponsor to secure patent rights and eventual FDA approval. *Id.* at 16. In fact, for their "negotiations [to be] successfully concluded," the HHS Secretary believed American pressure on the French firm was necessary.[62] *Id.*

Whether FDA abandoned its proposed restrictions because of political pressure or not, one thing is clear: the lack of restrictions resulted in many deaths and many more severe or life-threatening adverse reactions. Due to FDA's lax reporting requirements, the exact number is not ascertainable. But it is likely far higher than its data indicate for reasons previously

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[62] *See also* Lars Noah, *A Miscarriage in the Drug Approval Process?: Mifepristone Embroils the FDA in Abortion Politics*, 36 WAKE FOREST L. REV. 571, 576 (2001) ("The Clinton administration went to great lengths to bring mifepristone into the United States. From pressuring the hesitant manufacturer to apply for approval, and utilizing a specialized review procedure normally reserved for life-saving drugs, to imposing unusual restrictions on distribution, and promising to keep the identity of the manufacturer a secret, the FDA's approval process deviated from the norm in several respects.").

mentioned. Whatever the numbers are, they likely would be considerably lower had FDA not acquiesced to the pressure to increase access to chemical abortion at the expense of women's safety. FDA's failure to *insist* on the inclusion of its proposed safety restrictions was not "the product of reasoned decisionmaking." *State Farm*, 463 U.S. at 52. To hold otherwise would be "tantamount to abdicating the judiciary's responsibility under the [APA] to set aside agency actions that are 'arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law.'" *A.L. Pharma, Inc. v. Shalala*, 62 F.3d 1484, 1491 (D.C. Cir. 1995) (quoting 5 U.S.C. § 706(2)(A)). Finally, the 2000 Approval was also arbitrary and capricious because it violated Subpart H.[63]

b. The 2016 Changes

FDA made numerous substantial changes to the chemical abortion regimen in 2016. These changes include but are not limited to: (1) eliminating the requirement for prescribers to report *all* nonfatal serious adverse events; (2) extending the maximum gestational age from 49 days to 70 days; (3) eliminating the requirement that administration of misoprostol occurs in-

[63] As one scholar noted, "the agency took this route so that it could better justify imposing otherwise unauthorized restrictions on the use and distribution of the drug." *See* Noah, *supra* note 62, at 582. And "while agency action may generally be 'entitled to a presumption of regularity,' here FDA itself acknowledges that its action has not been regular: it failed to respond to the Citizen Petition for years." *Bayer*, 942 F. Supp. 2d at 25 (internal marks omitted). At the hearing, Defendants' leading argument for Subpart H was that "none of it really matters" because of the FDAAA. *See* ECF No. 136 at 100. "This is not the argument of an agency that is confident in the legality of its actions." ECF No. 100 at 15.

clinic; (4) removing the requirement for an in-person follow-up exam; and (5) allowing "healthcare providers" other than physicians to dispense chemical abortion drugs. ECF No. 1 at 53-54. Plaintiffs allege the 2016 Changes were also arbitrary and capricious "because *none* of the studies on which FDA relied were designed to evaluate the safety and effectiveness of chemical abortion drugs for use under the conditions prescribed, recommended, or suggested in the proposed labeling." ECF No. 7 at 24.

For similar reasons as the 2000 Approval, the Court agrees. Unlike the crucial studies FDA relied upon to extend the maximum gestational age, change the dosing regimen, and authorize a repeat dose of misoprostol, the labeling approved by FDA in 2016 did *not* require: (1) an ultrasound; (2) an in-person follow-up exam; or (3) the ability of abortionists to personally perform a surgical abortion if necessary. *Id.* Simply put, FDA built on its already-suspect 2000 Approval by removing *even more* restrictions related to chemical abortion drugs that were present during the final phase of the investigation. And it did so by relying on studies that included the very conditions FDA refused to adopt.[64] None of the studies compared the safety of the changes against the then-current regimen, nor under the labeled conditions of use. Moreover, FDA shirked any responsibility for the consequences of its actions by eliminating any requirement that non-fatal adverse events be reported. Thus, FDA took its chemical abortion regimen—which had already culminated in *thousands* of adverse events suffered by women and girls—and removed what little restrictions protected these women

[64] *See* ECF No. 1-35.

and girls, systematically ensuring that almost all new adverse events would go unreported or underreported.

Defendants aver that "Plaintiffs point to no statutory provision requiring the conditions of use in a drug's approved labeling to duplicate the protocol requirements used in the studies supporting its approval." ECF No. 28 at 32. "The [FFDCA] thus requires FDA to apply its scientific expertise in determining whether a drug has been shown to be safe and effective under particular conditions of use, and the application of that expertise is owed substantial deference." *Id.* But FDA does not have unfettered discretion to approve dangerous drugs under substantially different conditions than the tests, trials, and studies cited. To be clear, the Court does not hold that *any* difference between approval conditions and testing conditions—no matter how well-justified—means the approval fails as a matter of law. But the agency "must cogently explain why it has exercised its discretion in a given manner," and that explanation must be "sufficient to enable [the Court] to conclude that the [agency's action] was the product of reasoned decision-making." *A.L. Pharma*, 62 F.3d at 1491 (quoting *State Farm*, 463 U.S. at 52). Defendants have not done so here. FDA's 2016 Actions were not the product of reasoned decision-making.

c. The 2019 Generic Approval

The FFDCA allows a generic drug manufacturer to submit an ANDA for premarket review and approval. 21 U.S.C. § 355(j); 21 C.F.R. § 314.94. The generic sponsor must show that: (1) the conditions of use prescribed, recommended, or suggested in the labeling have been previously approved; and (2) the drug prod-

uct is chemically the same as the already approved drug—allowing it to rely on FDA's previous finding of safety and effectiveness for the approved drug. *Id.* On April 11, 2019, FDA approved GenBioPro, Inc.'s ANDA for a generic version of mifepristone. ECF No. 7 at 10. In doing so, FDA relied on Mifeprex's safety data. *Id.*

Plaintiffs argue the 2019 Approval was unlawful because FDA relied on the unlawful 2000 Approval and its unlawful 2016 Changes when approving generic mifepristone. ECF No. 7 at 27. If FDA withdraws the listed drug on which the ANDA-approved generic drug is based, the agency is generally required to withdraw the generic drug as well. 21 U.S.C. § 355(j)(6); 21 C.F.R. § 314.151. Because the Court agrees that Plaintiffs have a substantial likelihood of success in their challenges to the 2000 and 2016 Actions, the Court is inclined to agree with Plaintiffs on this claim as well.

E. There Is a Substantial Threat of Irreparable Harm

To satisfy the second element of the preliminary injunction standard, Plaintiffs "must demonstrate that if the district court denied the grant of a preliminary injunction, irreparable harm would result." *Janvey*, 647 F.3d at 600 (internal marks omitted). "In general, a harm is irreparable where there is no adequate remedy at law, such as monetary damages." *Id.* (internal marks omitted). "When determining whether injury is irreparable, it is not so much the magnitude but the irreparability that counts." *Texas v. U.S. Env't Prot. Agency*, 829 F.3d 405, 433-34 (5th Cir. 2016) (internal marks omitted). Where "the likelihood of success on the merits is very high, a much smaller quantum of injury

will sustain an application for preliminary injunction." *Mova Pharm. Corp. v. Shalala*, 955 F. Supp. 128, 131 (D.D.C. 1997), *aff'd,* 140 F.3d 1060 (D.C. Cir. 1998) (citing *Cuomo v. U.S. Nuclear Regul. Comm'n*, 772 F.2d 972, 974 (D.C. Cir. 1985) (per curiam)). Plaintiffs' Motion satisfies this standard.

For reasons already stated, Plaintiffs are likely to suffer irreparable harm if the Motion is not granted. At least two women died from chemical abortion drugs just last year. *See* ECF No. 120 at 30 n.5;[65] *Deerfield Med. Ctr. v. City of Deerfield Beach*, 661 F.2d 328, 338 (5th Cir. 1981) (finding irreparable harm to third-party pregnant women). "The physical and emotional trauma that chemical abortion inflicts on women and girls cannot be reversed or erased." ECF No. 7 at 28; *see also E.E.O.C. v. Chrysler Corp.*, 733 F.2d 1183, 1186 (6th Cir. 1984) (affirming irreparable harm for plaintiffs' "emotional distress"). "The crucial time that doctors need to treat these injured women and girls cannot be replaced." *Id.* "The mental and monetary costs to these doctors cannot be repaid." *Id.* "And the time, energy and resources that Plaintiff medical associations expend in response to FDA's actions on chemical abortion drugs cannot be recovered." *Id.*; *see also Whitman-Walker Clinic, Inc. v. U.S. Dep't of Health & Hum. Servs.*, 485 F. Supp. 3d 1, 56 (D.D.C. 2020) (obstacles that make it more difficult for an or-

[65] One of those women was reportedly twenty-one weeks pregnant, which is well past the cutoff for gestational age even after the 2016 Changes. *See id.* The other maternal death occurred while the woman was seven weeks pregnant, which falls within FDA's current restrictions. *Id.*

ganization to accomplish its mission provide injury for both standing *and* irreparable harm).

Defendants' respond that the drugs at issue have been on the market for more than twenty years. ECF No. 28 at 41. This argument ignores that many restrictions and safeguards—which no longer exist—were in place for most of that time. Defendants also argue "Plaintiffs' extreme delay" in filing suit shows they face no irreparable harm. *Id.* at 42. But the time between the allegedly unlawful actions and the filing of a suit "is not determinative" of whether relief should be granted. *Boire v. Pilot Freight Carriers, Inc.*, 515 F.2d 1185, 1193 (5th Cir. 1975). Here, eleven months does not constitute an "extreme" delay. *See, e.g.*, *Optimus Steel, LLC v. U.S. Army Corps of Eng'rs*, 492 F. Supp. 3d 701, 720 (E.D. Tex. 2020) (eleven-month delay did not militate against equitable relief because "the Court can presume that Plaintiff needed ample time to evaluate its claims").[66] "[T]emporary injunctive relief may still be of great value to protect against ongoing harms, even if the initial harm is in the distant past." *N.L.R.B. v. Hartman & Tyner, Inc.*, 714 F.3d 1244, 1252 (11th Cir. 2013).

The Court also disagrees that Plaintiffs' theories of injury "are too speculative to even show standing." ECF No. 28 at 42. Plaintiffs have credibly alleged past and future harm resulting from the removal of restrictions for chemical abortion drugs. "Although a court's analysis of likelihood of success in the context of an injunctive relief request is governed by the deferen-

[66] To clarify, the eleven months referenced here is the approximate time between FDA's "final agency action" in the December 2021 Denial of the 2019 Petition and the commencement of this case.

tial APA's arbitrary and capricious standard, a court does not always owe deference to federal agencies' positions concerning irreparable harm, balance of hardships, or public interest." *San Luis & Delta-Mendota Water Auth. v. Jewell*, 969 F. Supp. 2d 1211, 1215 (E.D. Cal. 2013); *see also R.J. Reynolds Vapor Co. v. FDA*, No. 23-60037 (5th Cir. Mar. 23, 2023)[67] (noting FDA's public interest argument was "obviously colored by the FDA's view of the merits"); *Sierra Forest Legacy v. Sherman*, 646 F.3d 1161, 1186 (9th Cir. 2011) ("If the federal government's experts were always entitled to deference concerning the equities of an injunction, substantive relief against federal government policies would be nearly unattainable, as government experts will likely attest that the public interest favors the federal government's preferred policy.").

F. Preliminary Injunction Would Serve the Public Interest

The third and fourth factors—assessing the harm to the opposing party and weighing the public interest—"merge when the Government is the opposing party." *Nken v. Holder*, 556 U.S. 418, 435 (2009). "[T]he public interest weighs strongly in favor of preventing unsafe drugs from entering the market." *Hill Dermaceuticals*, 524 F. Supp. 2d at 12. "[T]here is generally no public interest in the perpetuation of unlawful agency action." *State v. Biden*, 10 F.4th 538, 560 (5th Cir. 2021) (internal marks omitted). And "there is a strong public interest in meticulous compliance with the law by public officials." *Fund for Animals, Inc. v. Espy*, 814 F. Supp. 142, 152 (D.D.C. 1993); *see also State v. Biden*,

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[67] https://www.ca5.uscourts.gov/opinions/pub/23/23-60037-CV0.pdf.

10 F.4th at 559. "Indeed, the Constitution itself declares a prime public interest that the President and, by necessary inference, his appointees in the Executive Branch 'take Care that the Laws be faithfully executed.'" *Id.* (internal marks omitted). Additionally, Defendants' actions harm States' efforts to regulate chemical abortion "in the interests of life, health, and liberty." ECF No. 100 at 21. "The Court appreciates FDA's institutional interest but, given its long-standing disregard of [Plaintiffs'] Citizen Petition[s], its argument has a hollow center." *Bayer HealthCare*, 942 F. Supp. 2d at 26. To the extent Defendants and third parties would be harmed by an injunction, the Court still balances these factors in favor of ensuring that women and girls are protected from unnecessary harm and that Defendants do not disregard federal law.

For these reasons, a preliminary injunction would serve the public interest. Defendants maintain that *unaborted* children of the women "who seek but are unable to obtain an abortion" are "expected to do worse in school," "to have more behavioral and social issues, and ultimately to attain lower levels of completed education." ECF No. 28-2 at 7. "They are also expected to have lower earnings as adults, poorer health, and an increased likelihood of criminal involvement." *Id.* But "[u]sing abortion to promote eugenic goals is morally and prudentially debatable." *Planned Parenthood of Ind. & Ky., Inc. v. Comm'r of Ind. State Dep't of Health*, 917 F.3d 532, 536 (7th Cir. 2018) (Easterbrook, J., dissenting); *see also Box v. Planned Parenthood of Ind. & Ky., Inc.*, 139 S. Ct. 1780, 1790 (2019) (Thomas, J., concurring) ("[A]bortion has proved to be a disturbingly effective tool for implementing the discriminatory preferences that undergird eugenics."). Though eugenics

were once fashionable in the Commanding Heights and High Court, they hold less purchase after the conflict, carnage, and casualties of the *last* century revealed the bloody consequences of Social Darwinism practiced by would-be Übermenschen. *Cf. Buck v. Bell*, 274 U.S. 200, 207 (1927) ("It is better for all the world, if instead of waiting to execute degenerate offspring for crime, or to let them starve for their imbecility, society can prevent those who are manifestly unfit from continuing their kind. The principle that sustains compulsory vaccination is broad enough to cover cutting the Fallopian tubes.").

Defendants are correct that one purpose of injunctive relief is to preserve the status quo. *See, e.g.*, *City of Dallas v. Delta Air Lines, Inc.*, 847 F.3d 279, 285 (5th Cir. 2017). But the "status quo" to be restored is "the last peaceable uncontested status existing between the parties before the dispute developed." *Texas v. Biden*, No. 2:21-CV-067-Z, 2022 WL 17718634, at *9 (N.D. Tex. Dec. 15, 2022) (internal marks omitted); *see also Texas v. United States*, 40 F.4th 205, 220 (5th Cir. 2022) (the relevant status quo is the one "absent the unlawful agency action"); *Wages & White Lion*, 16 F.4th at 1144 ("In other words, 'the relief sought here would simply suspend *administrative* alteration of the *status quo*.'") (quoting *Nken*, 556 U.S. at 430 n.1); *Callaway*, 489 F.2d at 576 ("If the currently existing status quo itself is causing one of the parties irreparable injury, it is necessary to alter the situation so as to prevent the injury."). "[P]arties could otherwise have no real opportunity to seek judicial review except at their peril." Mila Sohoni, *The Power to Vacate a Rule*, 88 GEO. WASH. L. REV. 1121, 1157-58 (2020). Chemical abortion is only the status quo insofar as Defendants' unlawful

actions and their delay in responding to Plaintiffs' petitions have made it so. The fact that injunctive relief could upset this "status quo" is therefore an insufficient basis to deny injunctive relief.

G. A Stay Under Section 705 of the APA Is More Appropriate Than Ordering Withdrawal or Suspension of FDA's Approval

The Motion asks for injunctive relief but goes as far as requesting the Court to order Defendants to "withdraw or suspend the approvals of chemical abortion drugs, and remove them from the list of approved drugs." ECF No. 7 at 7. Singular equitable relief is "commonplace" in APA cases and is often "necessary to provide the plaintiffs" with "complete redress." *E. Bay Sanctuary Covenant v. Biden*, 993 F.3d 640, 681 (9th Cir. 2021) (internal marks omitted). Although the Court finds Plaintiffs have a substantial likelihood of prevailing on the merits, the Court instead exercises its authority under the APA to order less drastic relief. Section 705 of the APA provides:

> When an agency finds that justice so requires, it may postpone the effective date of action taken by it, pending judicial review. On such conditions as may be required and to the extent necessary to prevent irreparable injury, the reviewing court, including the court to which a case may be taken on appeal from or on application for certiorari or other writ to a reviewing court, *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.

5 U.S.C. § 705 (emphasis added).

The Fifth Circuit has acknowledged "meaningful differences between an injunction, which is a 'drastic and extraordinary remedy,' and vacatur, which is 'a less drastic remedy.'" *Texas v. Biden*, 2022 WL 17718634 at *7 (quoting *Texas v. United States*, 40 F.4th at 219). Whereas an injunction "tells someone what to do or not to do," a vacatur only reinstates "the status quo absent the unlawful agency action and neither compels nor restrains further agency decision-making." *Id.* (internal marks omitted). A Section 705 stay can "be seen as an interim or lesser form of vacatur under Section 706." *Id.* "Just as a preliminary injunction is often a precursor to a permanent injunction, a stay under Section 705 can be viewed as a precursor to vacatur under Section 706." *Id.*; *see also Nken*, 556 U.S. at 428-29 (a stay "temporarily suspend[s] the source of authority to act —the order or judgment in question —not by directing an actor's conduct"). "Motions to stay agency action pursuant to [Section 705] are reviewed under the same standards used to evaluate requests for interim injunctive relief." *Id.* at *10 (citing *Affinity Healthcare Servs., Inc. v. Sebelius*, 720 F. Supp. 2d 12, 15 n.4 (D.D.C. 2010)); *see also Nken*, 556 U.S. at 434; *Texas v. U.S. Env't Prot. Agency*, 829 F.3d at 435. Because the Court finds injunctive relief is generally appropriate, Section 705 plainly authorizes the lesser remedy of issuing "all necessary and appropriate process" to postpone the effective date of the challenged actions. "Courts—including the Supreme Court—routinely stay *already-effective* agency action under Section 705." *Id.* at *8 (emphasis added) (collecting cases).

Accordingly, the Court hereby **STAYS** the effective date of FDA's September 28, 2000, Approval of mifepristone and all subsequent challenged actions related

to that approval—*i.e.*, the 2016 Changes, the 2019 Generic Approval, and the 2021 Actions. This Court acknowledges that its decision in *Texas v. Biden* has been appealed to the Fifth Circuit. *See* 2:21-CV-067-Z, ECF No. 184 (Feb. 13, 2023). If the Fifth Circuit reverses this Court's Section 705 analysis, the Court clarifies that it alternatively would have ordered Defendants to suspend the chemical abortion approval and all subsequent challenged actions related to that approval until the Court can render a decision on the merits.

CONCLUSION

For the foregoing reasons, the Court **GRANTS** the Motion **IN PART**. FDA's approval of mifepristone is hereby **STAYED**. The Court **STAYS** the applicability of this opinion and order for seven (7) days to allow the federal government time to seek emergency relief from the United States Court of Appeals for the Fifth Circuit.

SO ORDERED

April 7, 2023

/s/ MATTHEW J. KACSMARYK
MATTHEW J. KACSMARYK
UNITED STATES DISTRICT JUDGE

APPENDIX C

UNITED STATES COURT OF APPEALS
FOR THE FIFTH CIRCUIT

No. 23-10362

ALLIANCE FOR HIPPOCRATIC MEDICINE; AMERICAN ASSOCIATION OF PRO-LIFE OBSTETRICIANS & GYNECOLOGISTS; AMERICAN COLLEGE OF PEDIATRICIANS; CHRISTIAN MEDICAL & DENTAL ASSOCIATIONS; SHAUN JESTER, D.O.; REGINA FROST-CLARK, M.D.; TYLER JOHNSON, D.O.; GEORGE DELGADO, M.D., PLAINTIFFS-APPELLEES

v.

FOOD & DRUG ADMINISTRATION; ROBERT M. CALIFF, COMMISSIONER OF FOOD AND DRUGS; JANET WOODCOCK, M.D., IN HER OFFICIAL CAPACITY AS PRINCIPAL DEPUTY COMMISSIONER, U.S. FOOD AND DRUG ADMINISTRATION; PATRIZIA CAVAZZONI, M.D., IN HER OFFICIAL CAPACITY AS DIRECTOR, CENTER FOR DRUG EVALUATION AND RESEARCH, U.S. FOOD AND DRUG ADMINISTRATION; UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES; XAVIER BECERRA, SECRETARY, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES,
DEFENDANTS-APPELLANTS

v.

DANCO LABORATORIES, L.L.C.,
INTERVENOR-APPELLANT

Filed: Apr. 12, 2023

Appeal from the United States District Court
for the Northern District of Texas
USDC No. 2:22-CV-223

UNPUBLISHED ORDER

Before HAYNES,* ENGELHARDT, and OLDHAM, *Circuit Judges*.

PER CURIAM:

For the reasons given below, IT IS ORDERED that defendants' motions for a stay pending appeal are GRANTED IN PART. At this preliminary stage, and based on our necessarily abbreviated review, it appears that the statute of limitations bars plaintiffs' challenges to the Food and Drug Administration's approval of mifepristone in 2000. In the district court, however, plaintiffs brought a series of alternative arguments regarding FDA's actions in 2016 and subsequent years. And the district court emphasized that its order separately applied to prohibit FDA's actions in and after 2016 in accordance with plaintiffs' alternative arguments. As to those alternative arguments, plaintiffs' claims are timely. Defendants have not shown that plaintiffs are unlikely to succeed on the merits of their timely challenges. For that reason, and as more fully

* JUDGE HAYNES concurs only in part: she concurs in the grant of the expedited appeal and the denial of the motion to dismiss. With respect to the request for a stay of the district court's order, as a member of the motions panel, she would grant an administrative stay for a brief period of time and defer the question of the stay pending appeal to the oral argument merits panel which receives this case.

explained below, defendants' motions for a stay pending appeal are DENIED IN PART. Defendants' alternative motions for an administrative stay are DENIED AS MOOT. Plaintiffs' motion to dismiss the appeal is DENIED. The appeal is EXPEDITED to the next available Oral Argument Calendar.

I.

A.

Congress delegated to the Food and Drug Administration ("FDA") the responsibility to ensure that "new drugs" are "safe and effective." 21 U.S.C. §§ 321(p), 355; *see also id.* § 393(b)(2)(B). When making its approval determination, FDA evaluates whether a new drug application ("NDA") includes scientific evidence demonstrating that the drug is safe and effective for its intended uses. *Id.* § 355(d); *see also* 21 C.F.R. §§ 314.50, 314.105(c). Similarly, when a sponsor submits a supplemental new drug application ("SNDA") proposing changes to the conditions of approval for a drug (such as changes to a drug's labeling or FDA-imposed restrictions), FDA reviews the scientific evidence to support the changes. *See* 21 C.F.R. § 314.70. To approve a generic version of a previously approved drug, FDA reviews whether an abbreviated new drug application ("ANDA") contains information showing that the proposed generic drug is materially the "same" as the approved drug. 21 U.S.C. § 355(j)(2).

In 1992, FDA promulgated the so-called "Subpart H" regulations. Subpart H accelerates approval of drugs "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 (*e.g.*, ability to treat patients unresponsive to, or intolerant of, available therapy, or improved patient response over available therapy)." 21 C.F.R. § 314.500. Originally, Subpart H was intended to promote rapid approval for life-saving HIV-AIDS drugs. But given that Subpart H approvals were accelerated, FDA recognized that it would need *post*-approval safety measures. These post-approval safety measures would "assure safe use" of the quickly approved Subpart H drugs. *Id.* § 314.520. In 2007, Congress ratified these post-approval safety measures as "risk evaluation and mitigation strategies" ("REMS"), which "ensure that the benefits of the drug outweigh the risks." 21 U.S.C. § 355-1(a)(1)-(2).

B.

In 2000, FDA approved mifepristone to be marketed with the brand name Mifeprex under Subpart H (the "2000 Approval"). *See* 21 C.F.R. § 314.500; FDA Add. 181.[1] In the 2000 Approval, FDA concluded that pregnancy is a "life-threatening illness," triggering an accelerated approval of mifepristone under Subpart H. FDA Add. 186. FDA also concluded that a variety of post-approval restrictions on Mifeprex were required "to assure safe use." 21 C.F.R. § 314.520. As noted in the previous section, today we call such post-approval restrictions "REMS." The 2000 Approval imposed several REMS, including: (1) limiting the drug to pregnant women and girls for use through 49 days gestation; (2) requiring three in-person office visits, the

[1] Citations to the addendum to FDA's emergency motion for a stay pending appeal are denoted "FDA Add." Citations to the appendix to plaintiffs' motion for a preliminary injunction are denoted "PI App."

first to administer mifepristone, the second to administer misoprostol, and the third to assess any complications and ensure there were no fetal remains in the womb; (3) requiring the supervision of a qualified physician; and (4) requiring the reporting of all adverse events from the drugs. FDA Add. 181-91. FDA granted Danco Laboratories, LLC, an exclusive license to manufacture, market, and distribute Mifeprex in the United States. FDA Add. 109.

In 2002, two of the plaintiff associations in this case filed a citizen petition challenging the 2000 Approval (the "2002 Citizen Petition"). *See* 21 C.F.R. § 10.25(a); PI App. 280-375. Roughly fourteen years later, FDA denied the 2002 Citizen Petition (the "2016 Petition Denial"). FDA Add. 804-36. And on the very same day in March 2016, FDA approved several major changes to mifepristone's approved conditions of use, including its REMS. Specifically, FDA removed four of the original safety restrictions by (1) increasing the maximum gestational age at which a woman can use the drug from 49 to 70 days; (2) reducing the number of required in-person office visits from three to one; (3) allowing non-doctors to prescribe and administer the chemical abortions drugs; and (4) eliminating the requirement for prescribers to report non-fatal adverse events from chemical abortion (the "2016 Major REMS Changes"). FDA Add. 777-802.

In March 2019, one of the plaintiff associations filed a second citizen petition challenging the 2016 Major REMS Changes (the "2019 Citizen Petition"). FDA Add. 192-217. That petition asked FDA to "restore" the 2000 Approval's REMS and "retain" a requirement

that mifepristone be dispensed to patients in person. FDA Add. 192.

In April 2019, FDA approved GenBioPro, Inc's ANDA for a generic version of mifepristone (the "2019 Generic Approval"). PI App. 694-708. GenBioPro's generic version of mifepristone has the same labeling and REMS requirements as Danco's Mifeprex.

In April 2021, FDA announced that it would "exercise enforcement discretion" to allow "dispensing mifepristone through the mail . . . or through a mail-order pharmacy" during the COVID-19 pandemic (the "2021 Mail-Order Decision"). PI App. 713-15. FDA took this action in response to a letter from the American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine. PI App. 710-11.

Later that year, in December 2021, FDA denied almost all of the 2019 Citizen Petition (the "2021 Petition Denial"). FDA Add. 837-76. In particular, FDA expressly rejected the 2019 Citizen Petition's request to keep the in-person dispensing requirements and announced that the agency had concluded that "the in-person dispensing requirement is no longer necessary." FDA Add. 842.

Finally, in January 2023, FDA approved a modified REMS for mifepristone lifting the in-person dispensing requirement. *See REMS Single Shared System for Mifepristone 200 mg* (Jan. 2023), https://perma.cc/MJT5- 35LF (the "2023 Mail-Order Decision").[2]

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[2] Danco suggests the 2023 Mail-Order Decision moots part of plaintiffs' claims. *See* Danco Stay App. 22. We disagree. The

C.

In November 2022, plaintiffs (physicians and physician organizations) filed this suit against FDA, HHS, and a several agency heads in the official capacities. Plaintiffs first challenged FDA's 2000 Approval of the drug. But they also requested multiple grounds of alternative relief for FDA's subsequent actions. Immediately after filing, plaintiffs moved for a preliminary injunction ordering FDA to withdraw or suspend (1) FDA's 2000 Approval and 2019 Generic Approval, (2) FDA's 2016 Major REMS Changes, and (3) FDA's 2021 Mail-Order Decision and its 2021 Petition Denial of the 2019 Citizen Petition. If that's confusing, we hope this chart helps:

Event	Citation	Description
2000 Approval	FDA Add. 181-91	Approved mifepristone with these REMS: (1) pregnancies under 50 days gestation; (2) three in-person office visits; (3) supervision of a qualified physician; and (4) reporting of all adverse events
2002 Citizen Petition	PI App. 280-375	Plaintiffs' challenge to 2000 Approval

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Supreme Court has explicitly instructed this court to review a new agency action finalized after litigation commenced and while the appeal was pending because this decision was a "final agency action" for purposes of 5 U.S.C. § 704. *Biden v. Texas*, 142 S. Ct. 2528, 2544-45 (2022) (quotation omitted).

2016 Petition Denial	FDA Add. 804-36	FDA denial of 2002 Citizen Petition
2016 Major REMS Changes	FDA Add. 768, 777-802	FDA changed four of the 2000 Approval's REMS: (1) increased maximum gestational age to 70 days; (2) reduced required in-person office visits to one; (3) allowed non-doctors to prescribe and administer mifepristone; and (4) eliminated reporting of nonfatal adverse events
2019 Citizen Petition	FDA Add. 192-217	Plaintiffs' challenge to 2016 Major REMS Changes
2019 Generic Approval	PI App. 694-708	FDA ANDA Approval Letter for mifepristone generic to GenBioPro, Inc.
2021 Mail-Order Decision	PI App. 713-15	FDA announces "enforcement discretion" to allow mifepristone to be dispensed through the mail during COVID-19
2021 Petition Denial	FDA Add. 837-76	FDA denial of almost all of the 2019 Citizen Petition, including plaintiffs' request to keep the in-person dispensing requirements

2023 Mail-Order Decision	https://perma.cc/MJT5-35LF	FDA permanently removed the in-person dispensing REMS

On April 7, 2023, the district court entered an order staying the effective date of the 2000 Approval and each of the subsequent challenged actions.[3] The district court stayed its own order for seven days to allow the defendants time to appeal.

II.

FDA and Danco ("stay applicants" or "applicants") ask us to stay the district court's order pending appeal. Our power to grant a stay is inherent. *See In re McKenzie*, 180 U.S. 536, 551 (1901); *Scripps-Howard Radio v. FCC*, 316 U.S. 4, 10-14 (1942). It's also statutory. *See* Fed. R. App. P. 8; 28 U.S.C. § 1651; 5th Cir. R. 27.3; *see also* 16A CHARLES ALAN WRIGHT & ARTHUR R. MILLER, FEDERAL PRACTICE & PROCEDURE § 3954 (5th ed. Apr. 2022 update).

But we grant stays "only in extraordinary circumstances." *Williams v. Zbaraz*, 442 U.S. 1309, 1311

[3] As both parties recognize, this order would have the practical effect of an injunction because it would remove mifepristone from the market. Plaintiffs filed a motion to dismiss applicants' appeal on the theory that § 705 stays are not sufficient to trigger our interlocutory appellate jurisdiction under 28 U.S.C. § 1292(a). We disagree. *See Abbott v. Perez*, 138 S. Ct. 2305, 2319-20 (2018) (explaining that the "practical effect" test of 28 U.S.C. §§ 1292(a)(1) and 1293 "prevents [the] manipulation" that could occur "if the availability of interlocutory review depended on the district court's use of the term 'injunction'").

(1979) (Stevens, J., in chambers); *see also Graves v. Barnes*, 405 U.S. 1201, 1203 (1972) (Powell, J., in chambers) (same); *Ruckelshaus v. Monsanto Co.*, 463 U.S. 1315, 1316 (1983) (Blackmun, J., in chambers) (same). This rule reflects the fact that "a stay is not a matter of right, even if irreparable injury might otherwise result." *Virginian Ry. Co. v. United States*, 272 U.S. 658, 672 (1926). Instead, a stay requires "an exercise of judicial discretion." *Ibid.* A "decree creates a strong presumption of its own correctness," which often counsels against a stay. *Id.* at 673.

The Supreme Court has prescribed "four traditional stay factors" that govern this equitable discretion in most civil cases. *Ala. Ass'n of Realtors v. HHS*, 141 S. Ct. 2485, 2487 (2021) (quotation omitted); *see also Hilton v. Braunskill*, 481 U.S. 770, 776-77 (1987); *Rose v. Raffensperger*, 143 S. Ct. 58, 59 (2022) (reversing stay of an injunction after the court of appeals failed to analyze the traditional stay factors). Those factors are:

> (1) whether the stay applicant has made a strong showing that he is likely to succeed on the merits; (2) whether the applicant will be irreparably injured absent a stay; (3) whether issuance of the stay will substantially injure the other parties interested in the proceeding; and (4) where the public interest lies.

Nken v. Holder, 556 U.S. 418, 426 (2009) (quoting *Hilton*, 481 U.S. at 776); *see also Whole Woman's Health v. Jackson*, 141 S. Ct. 2494, 2495 (2021). Although no factor is dispositive, the likelihood of success and irreparable injury factors are "the most critical." *Nken*, 556 U.S. at 434. Success on either factor requires that the

stay seeker make a strong not merely "possib[le]" showing. *Ibid.*

In these respects, stays might appear identical to preliminary injunctions. Similar factors govern both and both require an "extraordinary" deployment of judicial discretion. *Winter v. Nat. Res. Def. Council*, 555 U.S. 7, 24 (2008). But the two are not "one and the same." *Nken*, 556 U.S. at 434. A stay "operates upon the judicial proceeding itself," not on the conduct of a particular actor. *Id.* at 428. And, once one party has won an injunction, proof burdens reverse. It is the enjoined party who seeks a stay, or FDA and Danco here, who must carry the burden of proving that the *Nken* factors command us to issue one. *See Landis v. N. Am. Co.*, 299 U.S. 248, 255 (1936).

If the stay applicants show that circumstances require a stay of some but not all of the district court's order, we may, in our discretion, "tailor a stay so that it operates with respect to only some portion of the proceeding." *Trump v. Int'l Refugee Assistance Project*, 137 S. Ct. 2080, 2087 (2017) (per curiam) (quoting *Nken*, 556 U.S. at 428).

We find that FDA and Danco succeed only in part.

III.

Regarding likelihood to succeed on the merits, the stay applicants raise four arguments. They contend (A) plaintiffs are unlikely to defend the district court's stay because they lack standing. They next contend (B) plaintiffs' claims are untimely. Then they claim (C) plaintiffs' claims are unexhausted. Finally, applicants contend (D) FDA's actions are not arbitrary, ca-

pricious, or otherwise contrary to law. We consider each in turn.

A.

We begin with Article III standing. To bring their claims in federal court, plaintiffs must satisfy the familiar tripartite test: they must show they suffered an injury in fact, that's fairly traceable to the defendants, and that's likely redressable by a favorable decision. *See Lujan v. Nat'l Wildlife Fed'n*, 497 U.S. 871 (1990). Importantly, only one plaintiff needs to have standing to present a valid case or controversy. *See Rumsfeld v. Forum for Acad. & Institutional Rts., Inc.*, 547 U.S. 47, 52 n.2 (2006).

Plaintiffs and the district court offered numerous theories of standing. At this preliminary, emergency stage, we are unpersuaded by applicants' contentions that all of these theories fail to create a justiciable case or controversy. We need only consider two: (1) injuries to doctors and (2) injuries to the plaintiff medical associations.[4]

1.

First, it appears that the individual plaintiffs and doctors in plaintiff associations have standing to challenge FDA's actions.

To allege an injury in fact, these doctors must show they have suffered an "invasion of a legally protected

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[4] We are cognizant of the fact that the Supreme Court has disavowed the theories of third-party standing that previously allowed doctors to raise patients' claims in abortion cases. *See Dobbs v. Jackson Women's Health Org.*, 142 S. Ct. 2228, 2275 & n.61 (2022). So we express no opinion on plaintiffs' third-party standing theories.

interest" that is both "concrete and particularized" and "actual or imminent, not conjectural or hypothetical." *Spokeo, Inc. v. Robins*, 578 U.S. 330, 339 (2016) (quotation omitted). Plaintiffs must identify specific injuries that go beyond "general averments" or "conclusory allegations." *Friends of the Earth, Inc. v. Laidlaw Env't Servs. (TOC), Inc.*, 528 U.S. 167, 184 (2000) (quoting *Lujan*, 497 U.S. at 888). Where a plaintiff seeks prospective relief and hence points to future injuries, the Supreme Court has emphasized that "threatened injury must be *certainly impending* to constitute injury in fact, and that allegations of *possible* future injury are not sufficient." *Clapper v. Amnesty Int'l USA*, 568 U.S. 398, 409 (2013) (quotation omitted).

Here, FDA-approved the "Patient Agreement Form," which is part of the REMS for mifepristone, provides:

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**: _____

2023 Mail-Order Decision at 10. FDA thus cannot deny that serious complications from mifepristone are certainly impending. Those complications are right there on the "Patient Agreement Form" that FDA itself approved and that Danco requires every mifepristone user to sign. According to the applicants, more than

5,000,000 women have taken this drug since the 2000 Approval. FDA Stay App. 1. That means that, again according to the applicants' own information, between 100,000 (2%) and 350,000 (7%) of mifepristone users had unsuccessful chemical abortions and had to "talk with [their] provider[s] about a surgical procedure to end [their] pregnanc[ies]." 2023 Mail-Order Decision at 10. And where did those hundreds of thousands of women go for their "surgical procedures"? Again, we need not speculate because the 2016 Major REMS Changes, the 2021 Petition Denial, and the 2023 Mail-Order Decision all allow non-doctors to prescribe mifepristone. The women who use this drug cannot possibly go back to their non-doctor-prescribers for surgical abortions, so again, as the "Patient Agreement Form" itself says, they must instead seek "emergency care" from a qualified physician.

The plaintiff emergency room doctors have a concrete, particularized injury since they have provided—and with certainty will continue to provide—the "emergency care" that applicants specified in the "Patient Agreement Form." PI App. 167, 169, 194, 206. Mifepristone users who present themselves to the plaintiffs have required blood transfusions, overnight hospitalization, intensive care, and even surgical abortions. PI App. 205-06. As one doctor testified:

> For example, in one month while covering the emergency room, my group practice admitted three women to the hospital. Of the three women admitted in one month due to chemical abortion complications, one required admission to the intensive care unit for sepsis and intravenous antibiotics, one required a blood transfusion for hemorrhage, and one

> required surgical completion for the retained products of conception (*i.e.*, the doctors had to surgically finish the abortion with a suction aspiration procedure).

PI App. 206.

> Another doctor testified:
>
> [O]ne of my patients had obtained mifepristone and misoprostol from a website, without an in-person visit. . . . After taking the chemical abortion drugs, she began having very heavy bleeding followed by significant abdominal pain and a fever. When I saw her in the emergency room, she had evidence of retained pregnancy tissue along with endometritis, an infection of the uterine lining. She also had acute kidney injury, with elevate creatinine. She required a dilation and curettage (D&C) surgery to finish evacuating her uterus of the remaining pregnancy tissue and hospitalization for intravenous (IV) antibiotics, IV hydration, and a blood transfusion. I spent several hours with her the day of her surgery/hospital admission, keeping me from my primary patient responsibilities in the labor and delivery unit and requiring me to call in an additional physician to help cover those responsibilities.

PI App. 194-95. As a result of FDA's failure to regulate this potent drug, these doctors have had to devote significant time and resources to caring for women experiencing mifepristone's harmful effects. This harm is sufficiently concrete.

A second independent injury from the adverse effects of mifepristone is the "enormous stress and pressure" physicians face in treating these women. PI

App. 215. One doctor said the strain "is some of the most emotionally taxing work I have done in my career." PI App. 880. Thus, this is an independent injury because FDA's actions "significantly affect[]" the doctors' "quality of life." *Sierra Club v. Morton*, 405 U.S. 727, 734-35 (1972).

The doctors offered specific facts to explain this stress. Women who take these drugs are susceptible to "torrential bleeding." PI App. 170, 215. In fact, "the risk of severe bleeding with chemical abortion is five times higher than from surgical abortion." PI App. 879. And these situations can quickly go from bad to worse. As one doctor testified:

> One of my patients, who was about nine weeks pregnant, had previously been treated by hospital staff for a pulmonary embolism with anti-coagulants. She was advised that she could not seek a chemical abortion because it was contraindicated due to the medications; yet the woman left the hospital and sought an abortion at Planned Parenthood of Indiana. The woman was given mifepristone by the doctor at Planned Parenthood and took the drug. The woman called an Uber for a ride home from Planned Parenthood. The woman began to experience bleeding and other adverse effects from the mifepristone. The woman's Uber driver did not take her home because she was so ill and instead brought her to the hospital's emergency department. At the hospital, the woman came under my care. The woman had not yet taken the second abortion drug, misoprostol. I treated the patient for the adverse effects she suffered and told her not to take the misoprostol given to her by Planned

> Parenthood because of the grave risk that she could bleed out and die.

PI App. 216-17. Another doctor recounted an experience where he treated a patient—who "suffered from two weeks of moderate to heavy bleeding, and then developed a uterine infection"—by providing her "with intravenous antibiotics" and performing a D&C procedure. PI App. 886. If the patient waited a few more days to go to the hospital, the doctor predicted that "she could have been septic and died." PI App. 886. Another doctor testified that he has encountered "at least a dozen cases of life-threatening complications" from these drugs, and the frequency of these emergency situations has only increased over time. PI App. 865.

The risks are only exacerbated for women who have ectopic pregnancies. PI App. 207. This occurs in approximately two percent of pregnancies. PI App. 539. As one doctor explained:

> Chemical abortion drugs will not effectually end an ectopic pregnancy because they exert their effects on the uterus, which leaves women at risk of severe harm from hemorrhage due to tubal rupture, in need of emergent surgery or potentially at risk of death. Failure to perform an ultrasound prior to prescribing abortion drugs will cause some women to remain undiagnosed and at high risk for these adverse outcomes.

PI App. 208. The risks are greater under FDA's relaxed standards. That is because "without an in-person examination, it is impossible to rule out an ectopic pregnancy," placing a woman "at an increased risk of rupture or even death." PI App. 886.

The doctors also face an injury from the irreconcilable choice between performing their jobs and abiding by their consciences. These doctors structured their careers so they would not have to administer abortions. And yet, because women often come to hospitals when they experience complications from these drugs, these doctors sometimes have no other choice but to perform surgical abortions. As one doctor testified:

> The FDA's expansion of chemical abortions also harms my conscience rights because it could force me to have to surgically finish an incomplete elective chemical abortion. I object to abortion because it ends a human life. My moral and ethical obligation to my patients is to promote human life and health. But the FDA's actions may force me to end the life of a human being in the womb for no medical reason.

PI App. 209-10. And this harm is not speculative. Several doctors confirmed that they have had to surgically complete an abortion or remove an unborn child. PI App. 886, 205. As one doctor testified: "In my practice, I have cared for at least a dozen women who have required surgery to remove retained pregnancy tissue after a chemical abortion. Sometimes this includes the embryo or fetus, and sometimes it is placental tissue that has not been completely expelled." PI App. 205. That same doctor described how she had to "perform[] a suction aspiration procedure" on one patient who took the pill but needed surgery to complete the abortion. PI App. 206. Others have seen it firsthand. One doctor recounted a time where a woman came to the emergency room "with heavy vaginal bleeding and unstable vital signs as a result of taking chemical abortion drugs." PI App. 195. When the woman ar-

rived in the emergency room, the baby in her womb was not dead; the doctors were "able to detect a fetal heartbeat." PI App. 195. But due to the mother's unstable condition, the doctors "had no choice but to perform an emergency D&C." PI App. 196. The doctor testified that her colleague "felt as though she was forced to participate in something that she did not want to be a part of—completing the abortion." PI App. 196.

And not only have these doctors suffered injuries in the past, but it's also inevitable that at least one doctor in one of these associations will face a harm in the future. *Cf. City of Los Angeles v. Lyons*, 461 U.S. 95 (1983). Here, the plaintiff-doctors have "'set forth' by affidavit or other evidence 'specific facts'" that they are certain to see more patients. *Clapper*, 568 U.S. at 411 (quoting *Lujan v. Defs. of Wildlife*, 504 U.S. 555, 561 (1992)). That's because FDA has removed almost all of mifepristone's REMS and thus enabled women to (1) get the drug without *ever* talking to a physician, (2) take the drug without *ever* having a physical exam to ensure gestational age and/or an ectopic pregnancy, and (3) attempt to complete the chemical abortion regimen at home; FDA has also (4) directed the hundreds of thousands of women who have complications to seek "emergency care" from the plaintiffs and plaintiffs' hospitals. Several doctors testified that they have seen an increasing number of women coming to the emergency room with complications from chemical abortions due to FDA's virtual elimination of controls on the dispensing and administration of the drugs. PI App. 194, 205, 215, 866. And given how many women these doctors have seen in emergency departments in the past, these doctors quite reasonably know with sta-

tistical certainty—again, a statistic estimated on Mifeprex's own "Patient Agreement Form"—that women will continue needing plaintiffs' "emergency care." *See* PI App. 205, 215, 868. The crisis is "concededly ongoing." *Friends of the Earth*, 528 U.S. at 184. Accordingly, plaintiffs face a "substantial risk" of recurrence. *Susan B. Anthony List v. Driehaus*, 573 U.S. 149, 158 (2014) (quotation omitted).

And even if one of the named doctors never sees another patient, it's inevitable that one of the thousands of doctors in plaintiff associations will. For example, one of the plaintiff associations, the American Association of Pro-Life Obstetricians & Gynecologists, "is the largest organization of prolife obstetricians and gynecologists" and has "more than 7,000 medical professionals nationwide." PI App. 165. The Christian Medical and Dental Association has "more than 600 physicians and approximately 35 OBGYNs." PI App. 179. The American College of Pediatricians has a membership of "more than 600 physicians and other healthcare professionals." PI App. 187. These associations presented affidavits from individual members, elucidating the various harms discussed herein. *See Friends of the Earth*, 528 U.S. at 183-84. Thus, they have associational standing to sue on behalf of their members. *See N.Y. State Club Ass'n, Inc. v. City of New York*, 487 U.S. 1, 9 (1988); *Hunt v. Wash. State Apple Advertising Comm'n*, 432 U.S. 333, 343 (1977). That means that so long as one doctor among the thousands of members in these associations faces an injury, Article III is satisfied. *See Rumsfeld*, 547 U.S. at 52 n.2.

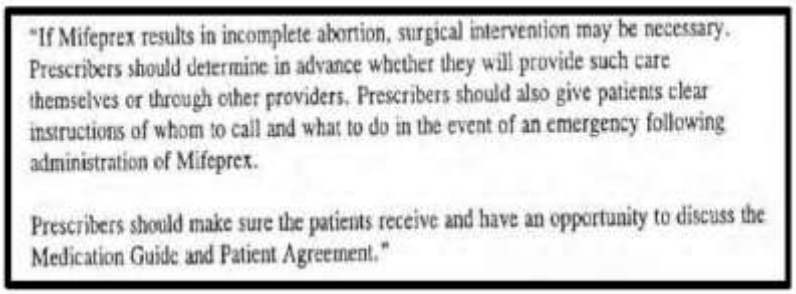
The doctors can also show that these injuries are traceable to FDA regulations and redressable by this court. *See Defs. of Wildlife*, 504 U.S. at 560-61. That's because the 2016 Major REMS Changes, the 2021 Petition Denial, and the 2023 Mail-Order Decision all empower *non-doctors* to prescribe mifepristone and thus shift the costs of the drug onto the plaintiff physicians who must manage the aftermath. *See, e.g.*, PI App. 218 ("I spent a significant amount of time that day working to save her life from unnecessary complications due to the irresponsible administration and use of mifepristone and misoprostol. As a result of the significant time that I devoted to that patient, my time and attention was taken away from other patients, who also need my care."); PI App. 867 ("Because more women [who take mifepristone] are unnecessarily presenting in the emergency department, more of my time and attention is taken away from other patients who need it."). In this way, "[t]he FDA's actions have created a culture of chaos for emergency room physicians." PI App. 867. And we're capable of redressing plaintiffs' injuries by restoring the 2000 Approval's REMS. Accordingly, at this stage, applicants have not shown that all of the plaintiffs lack standing.

We hasten to emphasize the narrowness of this holding. We do not hold that doctors necessarily have standing to raise their patients' claims. *See supra* n.4. We do not hold that doctors have constitutional standing whenever they're called upon to do their jobs. And we do not hold that doctors have standing to challenge FDA's actions whenever the doctor sees a patient experiencing complications from an FDA-approved drug. Rather, we hold that on the record

before us applicants know that hundreds of thousands of women *will*—with applicants' own statistical certainty—need emergency care on account of applicants' actions. And because applicants chose to cut out doctors from the prescription and administration of mifepristone, plaintiff doctors and their associations will necessarily be injured by the consequences. This is an exceedingly unusual regime. In fact, as far as the record before us reveals, FDA has not structured the distribution of any comparable drug in this way.

FDA's principal contention to the contrary is that mifepristone is comparable to "ibuprofen." FDA Stay App. 1. The theory appears to be that we cannot recognize plaintiffs' standing here without opening a pandora's box in which doctors have standing to litigate everything at all times, including the banalities of over-the-counter Advil.

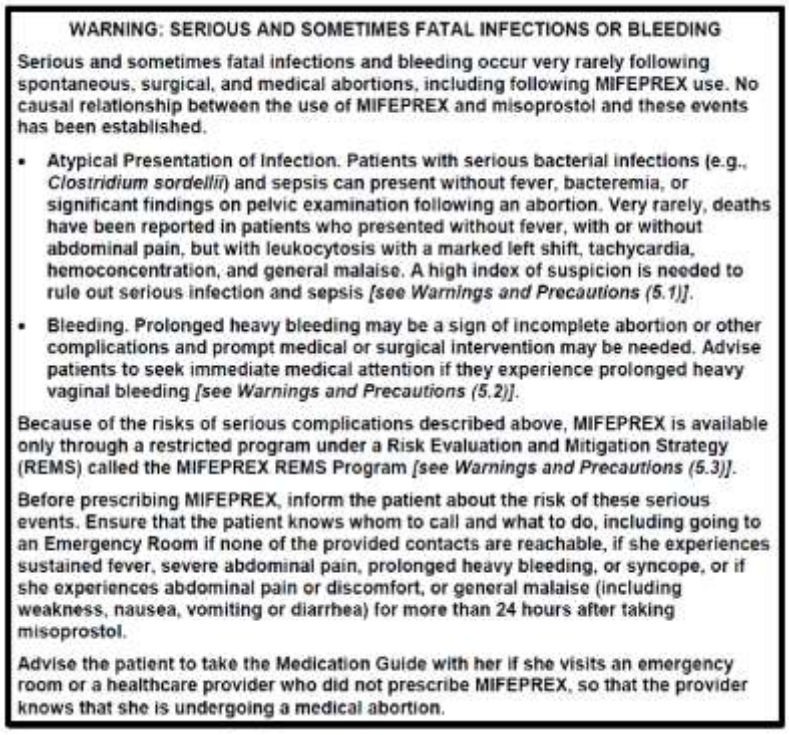
We disagree because FDA's own documents show that mifepristone bears no resemblance to ibuprofen. In the 2000 Approval, FDA imposed a "Black Box" warning on mifepristone. FDA requires "Black Box" warnings when a drug "may lead to death or serious injury." 21 C.F.R. § 201.57(c)(1). In its 2000 Approval, FDA conditioned its approval of mifepristone on the inclusion of this "Black Box" warning:



"If Mifeprex results in incomplete abortion, surgical intervention may be necessary. Prescribers should determine in advance whether they will provide such care themselves or through other providers. Prescribers should also give patients clear instructions of whom to call and what to do in the event of an emergency following administration of Mifeprex.

Prescribers should make sure the patients receive and have an opportunity to discuss the Medication Guide and Patient Agreement."

FDA Add. 182. The 2016 Major REMS Changes relaxed many of the requirements for marketing and using mifepristone. But it retained this "Black Box" warning:



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 MIFEPREX 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 she experiences sustained fever, severe abdominal pain, prolonged heavy bleeding, or syncope, or if she experiences abdominal pain or discomfort, or general malaise (including weakness, nausea, vomiting or diarrhea) for more than 24 hours after taking misoprostol.

Advise the patient to take the Medication Guide with her if she visits an emergency room or a healthcare provider who did not prescribe MIFEPREX, so that the provider knows that she is undergoing a medical abortion.

https://perma.cc/R56J-BHW4.

Ibuprofen's label, which FDA helpfully provided in its stay addendum, obviously bears no resemblance to the "Black Box" warning on mifepristone's label. FDA Add. 465-68. To the contrary, FDA has a special regulation regarding ibuprofen so all manufacturers of that over-the-counter medicine include the same information on their labels. *See* 21 C.F.R. § 201.326. It says nothing about REMS, surgery, emergencies, Emergency Rooms, or death.

In sum, applicants' own documents—from the "Patient Agreement Form" to the "Black Box" warning that have accompanied mifepristone ever since the 2000 Approval up to and including today—prove that emergency room care is statistically certain in hundreds of thousands of cases. Plaintiff doctors have provided that emergency room care and are statistically certain to provide it in the future.

2.

Second, the associations have standing. As previously discussed, they have associational standing to sue on behalf of their members. *See N.Y. State Club Ass'n, Inc.*, 487 U.S. at 9; *Hunt*, 432 U.S. at 343. The associations presented affidavits from individual member doctors who have suffered harms. *See Friends of the Earth*, 528 U.S. at 183-84. Accordingly, they have standing to sue on their members' behalf.

Plaintiff associations have also suffered independent injuries because FDA's actions have frustrated their organizational efforts to educate their members and the public on the effects of mifepristone. *See Havens Realty Corp. v. Coleman*, 455 U.S. 363, 379 (1982) (holding that housing non-profit had standing to challenge racial

steering practices that impaired its ability "to provide counseling and referral services for low-and-moderate-income homeseekers"). As a result, plaintiff associations have expended "time, energy, and resources to compensate for this lack of information by conducting their own studies and analyses of available data" to "the detriment of other advocacy and educational efforts." PI App. 174. The Supreme Court has previously stated that such a "concrete and demonstrable injury to the organization's activities—with the consequent drain on the organization's resources—constitutes far more than simply a setback to the organization's abstract social interests," *Havens*, 455 U.S. at 379, even where the organizational interest is purely "noneconomic," *id.* at 379 n.20. Rather, under these circumstances, "there can be no question that the organization has suffered an injury in fact." *Id.* at 379.

This injury is also traceable to FDA's elimination of non-fatal adverse events in the 2016 Major REMS Changes. And it's redressable by an order vacating those changes. Accordingly, these associations also have standing.

B.

Next we turn to timeliness.

Everyone acknowledges that 28 U.S.C. § 2401(a)'s six-year limitations period applies to all of this case's challenged actions. And plaintiffs' right of action against the lion's share of the challenged actions are squarely within the six-year window. That includes all of plaintiffs' alternative arguments challenging the 2016 Major REMS Changes, the 2019 Generic Approval, the 2021

Mail-Order Decision, and the 2021 Petition Denial of the 2019 Citizen Petition.

True, FDA's March 2016 Major REMS Changes were promulgated more than six years before plaintiffs filed suit in November 2022. But Section 2401(a) instructs that the six-year period begins when "the right of action first accrues." "And '[t]he right of action first accrues on the date of the final agency action.'" *Texas v. Biden*, 20 F.4th 928, 951 n.3 (5th Cir. 2021), *rev'd on other grounds*, 142 S. Ct. 2528 (2022) (quoting *Wash. All. of Tech. Workers v. DHS*, 892 F.3d 332, 342 (D.C. Cir. 2018)). Though FDA promulgated the Major REMS Changes in 2016, the Agency didn't respond to plaintiffs' 2019 Petition challenging those changes until December 16, 2021. So plaintiffs' right of action against FDA's final decision first accrued in December of 2021. *See* 21 C.F.R. § 10.45. That's less than a year before plaintiffs sued, which is well within the limitations period.

Next, applicants claim that plaintiffs' primary challenges to the 2000 Approval and FDA's 2016 Petition Denial to their 2002 Citizen Petition are time-barred. Though admittedly a close question, we ultimately agree with applicants at this preliminary juncture.

Plaintiffs' right of action against the 2000 Approval and 2016 Petition Denial first accrued on March 29, 2016—the date FDA issued its final decision rejecting their 2002 Petition challenging the 2000 Approval. *See* 21 C.F.R. § 10.45. But plaintiffs didn't file suit until November 18, 2022, more than six months beyond the statute of limitations. The district court nevertheless found timely the plaintiffs' challenges to the 2000 Ap-

proval and the 2016 Petition Denial. How? First, the district court held that FDA "reopened" those decisions in 2016 and 2021, thus restarting the statute of limitations. Second—and alternatively—the district court decided plaintiffs were entitled to equitable tolling.

We consider each justification in turn.

First, reopening. "The reopen[ing] doctrine allows an otherwise untimely challenge to proceed where an agency has—either explicitly or implicitly—undertaken to reexamine its former choice." *Nat'l Biodiesel Bd. v. EPA*, 843 F.3d 1010, 1017 (D.C. Cir. 2016) (quotation omitted). Put simply, the purpose of the reopening doctrine is "to pinpoint an agency's final action in cases where the agency has addressed the same issue multiple times." *Texas v. Biden*, 20 F.4th at 951. The limitations period runs from the agency's earlier decision unless the later decision "opened the issue up anew." *Ibid.* (quotation omitted). This makes good sense: Because a key step in the timeliness inquiry is determining when an agency action became final, it's sometimes necessary to determine whether an agency's subsequent action "actually reconsidered" its former action, *Growth Energy v. EPA*, 5 F.4th 1, 21 (D.C. Cir. 2021) (per curiam) (quotation omitted), or merely "reaffirm[ed] its prior position," *Sierra Club v. EPA*, 551 F.3d 1019, 1024 (D.C. Cir. 2008) (quotation omitted); *see also Texas v. Biden*, 20 F.4th at 951 ("If the agency opened the issue up anew, and then reexamined and reaffirmed its prior decision, the agency's second action (the reaffirmance) is reviewable. . . . But if the agency merely reaffirmed its decision without *really* opening the decision back up and reconsidering it, the

agency's initial action is the only final agency action to review." (quotation omitted)).

Courts have articulated various tests for determining whether an agency has reopened a prior decision. These tests fall into two general categories.

Under the first, courts look "to the entire context of the [relevant agency action] including all relevant proposals and reactions of the agency to determine whether an issue was in fact reopened." *Pub. Citizen v. Nuclear Regul. Comm'n*, 901 F.2d 147, 150 (D.C. Cir. 1990); *see also, e.g.*, *id.* at 150-53; *Growth Energy*, 5 F.4th at 21-22; *Nat'l Ass'n of Reversionary Prop. Owners v. Surface Transp. Bd.*, 158 F.3d 135, 141-46 (D.C. Cir. 1998). An agency can reopen an earlier decision in many ways, but the quintessential example of this type of reopening is when an agency "hold[s] out [its prior rule] as a proposed regulation, offer[s] an explanation for its language, solicit[s] comments on its substance, and respond[s] to the comments in promulgating the regulation in its final form." *Am. Iron & Steel Inst. v. EPA*, 886 F.2d 390, 397 (D.C. Cir. 1989). Under the second reopening category, courts consider whether an agency "constructively reopened" its prior decision. *Kennecott Utah Copper Corp. v. DOI*, 88 F.3d 1191, 1214-15 (D.C. Cir. 1996). They do so by evaluating whether "the revision of accompanying regulations significantly alters the stakes of judicial review as the result of a change that could have not been reasonably anticipated." *NRDC v. EPA*, 571 F.3d 1245, 1266 (D.C. Cir. 2009) (quotation omitted).

Although a close call, we are unsure at this preliminary juncture and after truncated review that FDA re-

opened the 2000 Approval in its 2016 Major REMS Changes and its 2021 Petition Denial.

As for the first reopening test, neither the 2016 Major REMS Changes nor the 2021 Petition Denial appears to "substantive[ly] reconsider[]" FDA's 2000 Approval. *Growth Energy*, 5 F.4th at 21. FDA's 2016 decision to relax many of the REMS was issued in response to Danco's supplemental application requesting as much. *See* PI App. 615-52. And FDA's 2021 Petition Denial was issued in response to plaintiffs' 2019 Citizen Petition asking FDA to "restore" the pre-2016 REMS—not revoke or reconsider FDA's underlying 2000 Approval. *See* PI App. 667-93. Therefore neither of the "relevant proposals" prompted FDA to reopen and reconsider its 2000 Approval. *Pub. Citizen*, 901 F.2d at 150.

That said, the district court correctly noted that FDA nevertheless "undertook a full review of the Mifepristone REMS Program" when it reviewed plaintiffs' 2019 Citizen Petition—even though the plaintiffs only asked FDA to restore the pre-2016 status quo ante. *See* PI App. 735-76; FDA Add. 22. In FDA's words:

> In 2021, FDA also undertook a full review of the Mifepristone REMS Program. 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[.]

PI App. 735. And after conducting this unrequested "full review" of the REMS Program, FDA (*inter alia*) added two modifications to the REMS Program that plaintiffs never even mentioned in their 2019 Citizen Petition, including "a requirement that pharmacies that dispense the drug be specially certified." PI App. 736; *see also id.* at 735 n.11 (acknowledging that "this was not raised in your Petition"). All of this suggests FDA went back to the beginning, including its very first REMS report, and conducted an independent review that far exceeded the issues raised in the 2019 Citizen Petition.

Especially because the dangerousness of a drug is grounds to withdraw its approval, *see* 21 U.S.C. § 355(e)—and REMS are required to "ensure that the benefits of the drug outweigh the risks," *id.* § 355-1(a)(1)-(2)—plaintiffs reasonably argue that FDA's 2021 "full review" of the entire REMS Program was in effect a reconsideration of FDA's 2000 Approval. Indeed, plaintiffs might very well prevail on that claim later in this litigation. But at this early juncture—and in light of our necessarily truncated review—we are not yet confident enough to say that viewed in "the entire context," FDA "has undertaken a serious, substantive reconsideration of the [2000 Approval]" rather than "incremental adjustments to existing regulations." *Texas v. Biden*, 20 F.4th at 952-93 (quotation omitted).

The result is the same under the second reopening test. Recall that under the second test, "[a] constructive reopening occurs if the revision of accompanying regulations significantly alters the stakes of judicial re-

view as the result of a change that could have not been reasonably anticipated." *Sierra Club*, 551 F.3d at 1025 (quotation omitted).

Sierra Club is the seminal case. In 1994, EPA adopted a rule that exempted major sources of air pollution from the Clean Air Act's emission standards during startups, shutdowns, and malfunctions (the "SSM exemption"). *Id.* at 1022. But the 1994 rule also required sources to develop an SSM plan in order to receive the benefit of the SSM exemption. *Ibid.* An SSM plan required "the source to demonstrate how it will do its reasonable best to maintain compliance with the standards, even during SSMs." *Ibid.* (quotation omitted). SSM plans were publicly available and were incorporated into the sources' permits under Title V of the Clean Air Act. *Ibid.*

In a series of rulemakings between 2002 and 2006, EPA substantially weakened the requirement that sources maintain and follow an SSM plan in order to benefit from the SSM exemption. It removed the requirement that a source's Title V permit incorporate its SSM plan; it stopped making SSM plans publicly available; and it ultimately retracted the requirement that sources implement their SSM plans during SSM periods. *Id.* at 1023.

The Sierra Club filed suit in 2007. But the Sierra Club did not challenge the changes to the SSM plan requirements that EPA had adopted in its 2002, 2003, and 2006 rulemakings. Instead, it challenged the legality of the SSM exemption itself. *Id.* at 1024. EPA had adopted that exception in 1994 and had not considered rescinding it in any of its rulemakings during the 2000s. Rather, those rulemakings had treated the SSM exemp-

tion as a given—in fact, they had strengthened it by weakening the SSM plan requirements. *See id.* at 1022-23.

The D.C. Circuit nonetheless held that the Sierra Club's challenge to the SSM exemption was timely. Even though EPA had not expressly reopened its decision to create a SSM exemption, it had constructively reopened that decision "by stripping out virtually all of the SSM plan requirements that it created to contain that exemption." *Id.* at 1025 (quotation omitted). Because EPA had allegedly abandoned these "necessary safeguards" limiting the SSM exemption, its rulemakings had "changed the calculus for petitioners in seeking judicial review and thereby constructively reopened consideration of the exemption." *Id.* at 1025-26 (quotation omitted).

Sierra Club thus establishes that an agency can constructively reopen a decision if it removes essential safeguards that had previously limited or contained the impact of that decision. In making this determination, the D.C. Circuit looks to the extent to which the agency has "alter[ed] th[e] regulatory framework" and whether the agency has "work[ed] a change that [plaintiffs] could not have reasonably anticipated." *Nat'l Biodiesel Bd.*, 843 F.3d at 1017.

Under *Sierra Club* and its progeny, FDA's 2016 Major REMS Changes and 2021 Petition Denial seemingly reopened its 2000 Approval decision. Of course, FDA did not expressly reconsider its mifepristone approval. But it eliminated the "necessary safeguards," *Sierra Club*, 551 F.3d at 1025, that had accompanied and limited the impact of that approval for two decades. The in-person dispensing requirement, for example, was

critical to FDA's initial approval of mifepristone in 2000, which relied on the in-person dispensing requirement to dismiss concerns about provider qualifications, improper use, illicit distribution, and detection of adverse events. *See* PI App. 519-23. And the in-person dispensing requirement was also the cornerstone of the REMS for mifepristone that FDA approved in 2011 and then relied on in its 2016 rejection of plaintiffs' 2002 Citizen Petition. *See* PI App. 578-82, 605, 608.

Thus FDA's elimination of the in-person distribution requirement—not to mention various other REMS—arguably worked a "sea change" in the legal framework governing mifepristone distribution that plaintiffs "could not have reasonably anticipated" and that "significantly alters the stakes of judicial review." *Nat'l Biodiesel Bd.*, 843 F.3d at 1017 (quotation omitted). That's because the in-person dispensing requirement was FDA's primary tool for ensuring the safe distribution and use of mifepristone, so plaintiffs arguably had little reason to anticipate this important change before 2021. FDA does not argue otherwise, appearing to concede that its 2021 announcement was a stark departure from previous regulatory approaches. And because this change eliminates a major safeguard against complications and adverse effects arising from improper mifepristone use, it can be said to "significantly alter[] the stakes of judicial review" for plaintiff doctors who treat patients with these complications. *Ibid.* (quotation omitted).

Even so, we ultimately hold at this early and emergency stage that these alterations didn't constructively reopen the 2000 Approval for review. That's because there's at least a colorable argument that plaintiffs

"could have . . . reasonably anticipated" changes like those in 2016 and 2021 by dint of the statutorily defined supplemental application process and other similar revision mechanisms. *NRDC v. EPA*, 571 F.3d at 1266 (quotation omitted); *see, e.g.*, 21 C.F.R. § 314.71(b). We also recognize that it's somewhat of a strain to say that the 2016 Major REMS Changes and 2021 Petition Denial (and related changes) altered the regulatory landscape to such a degree that the prior rule is only now "worth challenging" when it otherwise might "not have been." *Sierra Club*, 551 F.3d at 1025-26 (quotation omitted). After all, plaintiffs *did* challenge the 2000 Approval well before the 2016 and 2021 changes were even proposed. But again, plaintiffs could very well prevail on this reopening claim.

In the alternative, the district court held that plaintiffs were entitled to equitable tolling of the statute of limitations. FDA Add. 23-25. We are unpersuaded. "[A] litigant is entitled to equitable tolling of a statute of limitations only if the litigant establishes two elements: '(1) that he has been pursuing his rights diligently, and (2) that some extraordinary circumstance stood in his way and prevented timely filing.'" *Menominee Indian Tribe of Wis. v. United States*, 577 U.S. 250, 255 (2016) (quoting *Holland v. Florida*, 560 U.S. 631, 649 (2010)). Here, no "extraordinary circumstance" prevented plaintiffs from filing within six years of FDA's 2016 Petition Denial. The district court is of course correct that FDA took "13 years, 7 months, and 9 days" to render that March 2016 ruling, FDA Add. 24, but that delay had no impact on the length of the statute-of-limitations period or plaintiffs' capacity to challenge the 2016 Petition Denial.

C.

Next exhaustion. Stay applicants contend they are likely to succeed on the merits because plaintiffs failed to exhaust their claims before FDA. We disagree.

"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); *cf. United States v. L.A. Tucker Truck Lines*, 344 U.S. 33, 37 (1952). For challenges to FDA actions, the general administrative exhaustion requirement is codified at 21 C.F.R. § 10.45(b). Section 10.45(b) states that a "request that the [FDA] Commissioner take or refrain from taking any form of administrative action must first be the subject of a final administrative decision based on a petition submitted under § 10.25(a)." *See id.* § 10.25(a) ("An interested person may petition the [FDA] Commissioner to issue, amend, or revoke a regulation or order, or to take or refrain from taking any other form of administrative action.").

No one disputes that every argument the plaintiffs raised in their 2019 Citizen Petition is exhausted. That includes all of plaintiffs' challenges to the 2016 Major REMS Changes and everything fairly embraced by those challenges. For example, the 2019 Citizen Petition argued explicitly that FDA should "[c]ontinue limiting the dispensing of Mifeprex to patients in clinics, medical offices, and hospitals." FDA Add. 193, 209-16. When FDA rejected that request in the 2021 Petition Denial, it expressly reaffirmed its commitment to mail-order abortion drugs. As such, plaintiffs have properly exhausted their challenge to FDA's by-mail dis-

tribution regime by raising it in the 2019 Citizen Petition.

Even if plaintiffs failed to exhaust their claims, courts retain "discretion to waive exhaustion" where one of the "traditionally recognized" exceptions applies. *Wash. Ass'n for Television & Child.*, 712 F.2d at 681-82. Two exceptions are relevant here: futility and administrative abuse of process.

Start with futility. Plaintiffs need not exhaust claims where they can demonstrate "the futility or inadequacy of administrative review." *Gardner v. Sch. Bd. Caddo. Par.*, 958 F.2d 108, 112 (5th Cir. 1992); *see also Honig v. Doe*, 484 U.S. 305, 327 (1988). The futility exception applies when exhaustion would be "clearly useless" and "it is certain [a] claim will be denied." *Tesoro Refin. & Mktg. Co. v. FERC*, 552 F.3d 868, 874 (D.C. Cir. 2009) (quotation omitted); *see also Carr v. Saul*, 141 S. Ct. 1352, 1361 (2021) ("[T]his Court has consistently recognized a futility exception to exhaustion requirements.").

Given FDA's 2016 Petition Denial and its 2021 Petition Denial, it would have been futile for plaintiffs to include a challenge to the 2000 Approval in their 2019 Citizen Petition. FDA rejected this exact challenge in its 2016 Petition Denial. So it would have been "clearly useless" to raise the precise challenge again in the 2019 Citizen Petition. Further, this exact reasoning applies with equal force to plaintiffs' challenge to the 2019 Generic Approval because it's entirely dependent on the underlying 2000 Approval. Thus, plaintiffs' challenges to the 2000 Approval and the 2019 Generic Approval are not barred by exhaustion.

Next, administrative abuse of process. It's well-established that where an agency fails to follow its own regulations, exhaustion may not be required. *See Way of Life Television Network, Inc. v. FCC*, 593 F.2d 1356, 1359-60 (D.C. Cir. 1979); *see also Wash. Ass'n for Television & Child.*, 712 F.2d at 681. That's especially true "where the obvious result would be a plain miscarriage of justice." *Hormel v. Helvering*, 312 U.S. 552, 558 (1941). Here, FDA was required by its own regulations to respond to citizen petitions within 180 days. *See* 21 C.F.R. § 10.30(e)(2). Instead of timely responding, FDA responded to plaintiffs' first petition fourteen years after it was filed. And it responded to the second petition over two years after it was filed. FDA plainly and repeatedly refused to follow its own regulations here. Even assuming any of plaintiffs' challenges were unexhausted and that it wasn't futile to raise them before FDA, FDA's repeated failure to follow its own regulations indicates that the district court did not abuse its "discretion to waive exhaustion." *Wash. Ass'n for Television & Child.*, 712 F.2d at 681.

D.

As applicants recognize, FDA's actions are constrained by the APA's arbitrary-and-capricious standard. *See* 5 U.S.C. § 706(2)(A). Under that standard, "the 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." *Motor Vehicle Mfrs. Ass'n of U.S., Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983) (quotation omitted); *see also Sw. Elec. Power Co. v. EPA*, 920 F.3d 999, 1013 (5th Cir. 2019) (judicial review of agency action "is not toothless"). We must "con-

sider whether the decision was based on a consideration of the relevant factors and whether there has been a clear error of judgment." *State Farm*, 463 U.S. at 43 (quotation omitted). An agency's action is "arbitrary and capricious" if it "entirely failed to consider an important aspect of the problem, offered 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." *Ibid.*

When an agency acts, it must "reasonably consider[] the relevant issues and reasonably explain[]" its actions. *FCC v. Prometheus Radio Project*, 141 S. Ct. 1150, 1158 (2021); *see also ibid.* ("The APA's arbitrary-and-capricious standard requires that agency action be reasonable and reasonably explained."); *Michigan v. EPA*, 576 U.S. 743, 750, 752 (2015) ("[A]gency action is lawful only if it rests on a consideration of the relevant factors" and "important aspect[s] of the problem." (quotation omitted)). Of course, we cannot "substitute" our "own policy judgment for that of the agency." *Prometheus*, 141 S. Ct. at 1158. We nonetheless must still carefully ensure that "the agency has acted within a zone of reasonableness and, in particular, has reasonably considered the relevant issues and reasonably explained the decision." *Ibid.* The upshot is that we "must set aside any action premised on reasoning that fails to account for 'relevant factors' or evinces 'a clear error of judgment.'" *Univ. of Tex. M.D. Anderson Cancer Ctr. v. HHS*, 985 F.3d 472, 475 (5th Cir. 2021) (quoting *Marsh v. Or. Nat. Res. Council*, 490 U.S. 360, 378 (1989)).

Here, applicants have failed to carry their burden at this preliminary stage to show that FDA's actions[5] were not arbitrary and capricious. We have two principal concerns in that regard. First, FDA failed to "examine the relevant data" when it made the 2016 Major REMS changes. *State Farm*, 463 U.S. at 43. That's because FDA eliminated REMS safeguards based on studies that *included those very safeguards.* FDA Add. 59, 122-23, 171. Imagine that an agency compiles studies about how cars perform when they have passive restraint systems, like automatic seatbelts. *See State Farm*, 463 U.S. at 34-36. For nearly a decade, the agency collects those studies and continues studying how cars perform with passive safety measures. Then one day the agency changes its mind and *eliminates* passive safety measures based only on existing data of how cars perform *with* passive safety measures. *Cf. id.* at 47-49. That was obviously arbitrary and capricious in *State Farm*. And so too here. The fact that mifepristone might be safe when used with the 2000 Approval's REMS (a question studied by FDA) says nothing about whether FDA can eliminate those REMS (a question not studied by FDA).

True, FDA studied the safety consequences of eliminating one or two of the 2000 Approval's REMS in *isolation*. But it relied on zero studies that evaluated the safety-and-effectiveness consequences of the 2016 Major REMS Changes *as a whole*. This deficiency shows

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[5] Here we limit our discussion to FDA's decisions in the 2016 Major REMS Changes and its subsequent agency actions. As described above in Part III.B, it appears at this preliminary juncture that plaintiffs' challenges to the 2000 Approval and 2016 Petition Denial are untimely.

that FDA failed to consider "an important aspect of the problem" when it made the 2016 Major REMS Changes. *Michigan v. EPA*, 576 U.S. at 752 (quotation omitted).

Second, the 2016 Major REMS Changes eliminated the requirement that non-fatal adverse events must be reported to FDA. After eliminating that adverse-event reporting requirement, FDA turned around in 2021 and declared the absence of non-fatal adverse-event reports means mifepristone is "safe." *See, e.g.*, FDA Add. 861-76 (explaining that FDA's FAERS database, which collates data on adverse events, indicated that the 2016 Major REMS Changes hadn't raised "any new safety concerns"). This ostrich's-head-in-the-sand approach is deeply troubling—especially on a record that, according to applicants' own documents, necessitates a REMS program, a "Patient Agreement Form," and a "Black Box" warning. *See supra* Part III.A. And it suggests FDA's actions are well "outside the zone of reasonableness." *Prometheus*, 141 S. Ct. at 1160. 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.

These actions make it unlikely that plaintiffs' arbitrary-and-capricious challenges will fail on the merits, at least as far as they challenge FDA's decisions including and following the 2016 Major REMS Changes.

IV.

Beyond likelihood of success on the merits, we also must consider the other three factors for granting a stay. Those are "[A] whether the applicant will be irreparably injured absent a stay; [B] whether issuance of the stay will substantially injure the other parties in-

terested in the proceeding; and [C] where the public interest lies." *Nken*, 556 U.S. at 434 (quotation omitted). We address each in turn. And we (D) discuss how the Comstock Act, 18 U.S.C. §§ 1461, 1462 affects the stay inquiry. Outside of the 2000 Approval, we find that the applicants fail to make a strong showing on any of these factors for a stay.

A.

Of the remaining three factors, irreparable injury matters most. *See Nken*, 556 U.S. at 434. FDA argues that the plaintiffs fail to show irreparable injury. But the irreparable injury factor asks whether "*the [stay] applicant* will be irreparably injured" absent a stay, not whether the plaintiff would be irreparably injured absent an injunction. *Ibid.* (emphasis added) (quotation omitted). Similarly, FDA's assertion that the district court's injunction will harm pregnant women or other members of the public does not speak to the irreparable injury factor (although it may speak to other factors), because those persons are not stay applicants in this case.

Since FDA does not articulate any irreparable harm that *FDA* will suffer absent a stay, it makes no showing on this "critical" prong. *Ibid.* We may not need to address the merits of the applicants' stay request any further, because failure to show irreparable injury often "decides the [stay] application." *Whalen v. Roe*, 423 U.S. 1313, 1318 (1975) (Marshall, J., in chambers).

Danco by contrast does claim it will suffer irreparable injury, albeit in just one paragraph. Danco notes that mifepristone is its sole product and argues that it may have to shut down absent relief. We have held

that catastrophic financial losses "*may* be sufficient to show irreparable injury." *Wages & White Lion Investments, LLC v. FDA*, 16 F.4th 1130, 1142 (5th Cir. 2021) (emphasis added) (quotation omitted). Of course, irreparable injury alone does not entitle Danco to a stay. *See Virginian Ry. Co.*, 272 U.S. at 672.

And even if it did, neither FDA nor Danco articulates why this, or any other, injury would require a stay of *all* of the district court's order, rather than only part. Recall that we may narrowly "tailor a stay" to impact "only some portion of the proceeding." *Int'l Refugee Assistance Project*, 137 S. Ct. at 2087 (quotation omitted). The applicants' arguments suggest, at best, that they require relief only from the district court's treatment of the 2000 Approval. They make no argument as to why the district court's treatment of the 2016 Major REMS Changes and later FDA activity irreparably harms anyone.

Applicants' forfeiture of this contention is understandable because the world operated under the 2000 Approval for sixteen years, apparently without problems. And neither applicant contends that it'll be irreparably injured without a stay so long as the 2000 Approval and its associated REMS remain in effect. Thus, the irreparable injury factor counsels against a stay.

B.

The next *Nken* factor asks whether "issuance of the stay will substantially injure the other parties interested in the proceeding." 556 U.S. at 434 (quoting *Hilton*, 481 U.S. at 776); *see also Ala. Ass'n of Realtors*, 141 S. Ct. at 2487 (same); *Planned Parenthood v. Abbott*,

134 S. Ct. 506, 506-08 (2013) (mem.) (opinions of seven Justices using the same standard). This language again focuses on harm from the *stay*, not the injunction. *Cf. Whole Woman's Health*, 141 S. Ct. at 2495 (using less specific "balance of the equities" language). To succeed on this prong, applicants must show that the requested stay will not harm the opposing appellees or other interested parties.

Applicants discuss at length their view that *the district court's order* might harm various persons, but mostly decline to address the apposite question, which is why *the requested stay* would not harm relevant persons. What points the applicants do make on this relevant question distill down to two arguments.

First, applicants briefly argue that the injuries the plaintiffs would suffer from a stay are speculative or minimal. But we have already addressed why plaintiffs' injuries are non-speculative. *See supra* Part III.A. We have also addressed the specific risks impacting women and the plaintiffs that stem from the 2016 Major REMS Changes and other post-2016 FDA decisions that the district court enjoined. *See supra* Part III.A, D. The applicants' abbreviated argument focuses on consequences flowing from the district court's treatment of the 2000 Approval and largely ignores plaintiffs' alternative arguments regarding the 2016 Major REMS Changes and what followed.

Second, the applicants argue that the plaintiffs' failure to bring litigation sooner undercuts any contention that they would be harmed from a stay. That contention is untenable given FDA's *fourteen-year delay* in adjudicating the 2002 Citizen Petition. But, even setting aside FDA's own delays, the applicants do not explain

why the plaintiffs' alleged procrastination warrants a stay of the entirety of the district court's order, rather than just the portion of the order impacted by long litigation delay (the 2000 Approval).

To the extent applicants make any showing that the third *Nken* factor favors a stay, they do so only with respect to the 2000 Approval and do not address plaintiffs' alternative arguments.

C.

The last *Nken* factor asks "where the public interest lies." 556 U.S. at 434 (quotation omitted). The stay applicants make three principal arguments.

First, the applicants argue that "procedural irregularity" in the court below favors relief. But the applicants do not explain why any specific alleged irregularity necessarily speaks to public (versus their own private) interest. Even if we assume away that problem, it is not clear to us, on our accelerated review, that any litigation below was irregular. And even if we assume, which we do not, that the district court or the plaintiffs departed from acceptable procedure, it's unclear on this record that applicants have embraced "the principles of equity and righteous dealing" in the twenty-one years since the filing of the 2002 Citizen Petition. *Binh Hoa Le v. Exeter Fin. Corp.*, 990 F.3d 410, 416 (5th Cir. 2021) (quotation omitted) (noting that a party's own imperfect conduct can prejudice their request for equitable relief).

Second, Danco argues that avoidance of "judicial conflict" warrants a stay given the order of an out-of-circuit district court. Comity between federal courts is a cognizable interest. *See Def. Distrib. v. Platkin*,

55 F.4th 486, 495-96 (5th Cir. 2022). We have every respect for fellow federal courts. But we cannot embrace an argument that would, in effect, allow the decision of an out-of-circuit district court to impel us towards "extraordinary" relief that would be otherwise inappropriate. *Williams*, 442 U.S. at 1311 (quotation omitted).

Third, the stay applicants warn us of significant public consequences should the district court's order result in the withdrawal of mifepristone from the market. These consequences, the applicants say, include injury to pregnant women, to public healthcare systems, and to the sense of order that governs FDA drug approvals. But these concerns center on the district court's removal of mifepristone from the market. The applicants make no arguments as to why the 2016 Major REMS Changes, the 2019 Generic Approval, or the 2021 and 2023 Mail Order Decisions are similarly critical to the public even though they were on notice of plaintiffs' alternative requests for relief. And it would be difficult for applicants to argue that the 2016 Major REMS Changes and subsequent FDA activity were 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.

The applicants have made some showing that the public interest warrants equitable relief from the district court's treatment of the 2000 Approval. Motivated in part by the accelerated posture of our review, we credit their showing.

D.

The parties vehemently dispute how their competing interpretations of the Comstock Act of 1873 might impact the validity of the district court's order. The Comstock Act prohibits the carriage in interstate commerce of "any drug, medicine, article, or thing designed, adapted or intended for producing abortion." 18 U.S.C. § 1462. It similarly prohibits the mailing of any "article, instrument, substance, drug, medicine, or thing which is advertised or described in a manner calculated to lead another to use or apply it for producing abortion." *Id.* § 1461.

Both statutory provisions specify a *mens rea* of "knowingly." *Id.* §§ 1461-62. The plain text does not require that a user of the mails or common interstate carriage intend that an abortion actually occur. Rather, a user of those shipping channels violates the plain text merely by knowingly making use of the mail for a prohibited abortion item.

The applicants' principal defense against the Comstock Act is that FDA was not required to consider it. After all, say the applicants, 21 U.S.C. §§ 355 and 355-1 guide FDA's discretion over drug approval and REMS, and those statutes do not explicitly require consideration of other statutes like 14 U.S.C. § 1462.

Even assuming that's true, however, the Comstock Act nevertheless undermines applicants' showing on the final three *Nken* factors. For example, if the Comstock Act is construed in-line with its literal terms, then Danco cannot say it is irreparably harmed by the district court's order, because Danco has no interest in continuing to violate the law, which (under a plain view

of the Act) it does every time it ships mifepristone. For further example, if the Comstock Act is strictly understood, then applicants may lose the public interest prong entirely, because there is no public interest in the perpetuation of illegality. *See Louisiana v. Biden*, 55 F.4th 1017, 1035 (5th Cir. 2022).

The applicants raise other defenses. For example, they argue that the Food and Drug Administration Amendments Act, Pub. L. No. 110-85, 121 Stat. 823 (2007) ("FDAAA") *sub silentio* repealed the Comstock Act, at least where mifepristone is concerned. That's because the FDAAA in 2007 created a statutory framework governing REMS and drugs with then-existing distribution restrictions. *See id.* § 909(b). Mifepristone was one such drug. So, say applicants, the FDAAA acted to legalize shipment of mifepristone, regardless of what the Comstock Act might say. But "repeals by implication are not favored." *Maine Cmty. Health Options v. United States*, 140 S. Ct. 1308, 1323 (2020) (quotation omitted). We regard each of Congress's statutes as effective unless either "intention to repeal" one of them is "clear and manifest" or the two laws are "irreconcilable." *Ibid.* (quotation omitted). Section 909(b) did not expressly legalize mifepristone; agency action (not statute) did that. Section 909(b)'s brief text makes no mention of mifepristone at all. So, there is no "irreconcilable" conflict. And we hesitate to find "clear and manifest" intention to repeal a 150-year-old statute that Congress has otherwise repeatedly declined to alter in the far reaches of a single section of the cavernous FDAAA.

Failing all else, the applicants argue that the Comstock Act does not mean what it says it means. Or ra-

ther, that judicial gloss and lax enforcement over the past century act to graft relevant exceptions onto it. The applicants rely on a memo authored by the Office of Legal Counsel to press this position. *See* FDA Add. 258-78. That memo's thorough exploration of this topic notes that a variety of aging out-of-circuit opinions and a single footnote within one Supreme Court dissent favor the applicants' position. FDA Add. 262-68).

The speed of our review does not permit conclusive exploration of this topic. To the extent the Comstock Act introduces uncertainty into the ultimate merits of the case, that uncertainty favors the plaintiffs because the applicants bear the burden of winning a stay. *See Landis*, 299 U.S. at 255. Since plaintiffs already prevail on most *Nken* factors concerning most of the agency items effectively enjoined by the district court's order, we need not definitively interpret the Comstock Act to resolve this stay application.

* * *

As the stay applicants, defendants bear the burden of showing why "extraordinary circumstances" demand that we exercise discretion in their favor. To the extent the defendants make any such showing, they do so *only* with respect to the 2000 Approval—*not* the plaintiffs' alternative arguments challenging FDA's 2016 Major REMS Changes and all subsequent actions. Our decision to grant partial relief does not reflect our view on any merits question. The defendants' motions to stay the district court's order are GRANTED IN PART and DENIED IN PART. The appeal is EXPEDITED to the next available Oral Argument Calendar.

APPENDIX D

SUPREME COURT OF THE UNITED STATES

No. 22A901

DANCO LABORATORIES, LCC

v.

ALLIANCE FOR HIPPOCRATIC MEDICINE, ET AL.
ON APPLICATION FOR STAY

No. 22A902

FOOD AND DRUG ADMINISTRATION, ET AL.

v.

ALLIANCE FOR HIPPOCRATIC MEDICINE, ET AL.
ON APPLICATION FOR STAY

[April 21, 2023]

The applications for stays presented to JUSTICE ALITO and by him referred to the Court are granted. The April 7, 2023 order of the United States District Court for the Northern District of Texas, case No. 2:22-cv-223, is stayed pending disposition of the appeal in the United States Court of Appeals for the Fifth Circuit and disposition of a petition for a writ of certiorari, if such a writ is timely sought. Should certiorari be denied, this stay shall terminate automatically. In the event certiorari is granted, the stay shall terminate upon the sending down of the judgment of this Court.

JUSTICE THOMAS would deny the applications for stays.

JUSTICE ALITO, dissenting from grant of applications for stays.

In recent cases, this Court has been lambasted for staying a District Court order "based on the scanty review this Court gives matters on its shadow docket," *Merrill v. Milligan*, 595 U.S. ___, ___ (2022) (KAGAN, J., dissenting) (slip op., at 2). In another, we were criticized for ruling on a stay application while "barely bother[ing] to explain [our] conclusion," a disposition that was labeled as "emblematic of too much of this Court's shadow-docket decisionmaking—which every day becomes more unreasoned." *Whole Woman's Health v. Jackson*, 594 U.S. ___, ___-___ (2021) (KAGAN, J., dissenting from denial of application for injunctive relief) (slip op., at 1-2). And in a third case in which a stay was granted, we were condemned for not exhibiting the "restraint" that was supposedly exercised in the past and for not "resisting" the Government's effort to "shortcut" normal process. *Barr v. East Bay Sanctuary Covenant*, 588 U. S. ___, ___ (2019) (SOTOMAYOR, J., dissenting) (slip op., at 5). Cf. Does 1-3 v. Mills, 595 U. S. ___, ___ (2021) (BARRETT, J., concurring in denial of application for injunctive relief) (slip op., at 1) (warning that the Court should not act "on a short fuse without benefit of full briefing and oral argument" in a case that is "first to address the questions presented").

I did not agree with these criticisms at the time, but if they were warranted in the cases in which they were made, they are emphatically true here. As narrowed by the Court of Appeals, the stay that would apply if we failed to broaden it would not remove mifepristone from

the market. It would simply restore the circumstances that existed (and that the Government defended) from 2000 to 2016 under three Presidential administrations. In addition, because the applicants' Fifth Circuit appeal has been put on a fast track, with oral argument scheduled to take place in 26 days, there is reason to believe that they would get the relief they now seek—from either the Court of Appeals or this Court—in the near future if their arguments on the merits are persuasive.

At present, the applicants are not entitled to a stay because they have not shown that they are likely to suffer irreparable harm in the interim. The applicants claim that regulatory "chaos" would occur due to an alleged conflict between the relief awarded in these cases and the relief provided by a decision of the United States District Court for the Eastern District of Washington. It is not clear that there actually is a conflict because the relief in these cases is a stay, not an injunction, but even if there is a conflict, that should not be given any weight. Our granting of a stay of a lower-court decision is an equitable remedy. It should not be given if the moving party has not acted equitably, and that is the situation here. The Food and Drug Administration (FDA) has engaged in what has become the practice of "leverag[ing]" district court injunctions "as a basis" for implementing a desired policy while evading both necessary agency procedures and judicial review. *Arizona v. City and County of San Francisco*, 596 U. S. ___, ___ (2022) (ROBERTS, C. J., concurring) (slip op., at 2).

The Washington District Court enjoined the FDA from altering its current practice regarding

mifepristone—something that the FDA had never hinted it was contemplating. The FDA did not appeal that appealable order, and when seven States that might take such an appeal asked to intervene, the FDA opposed their request. This series of events laid the foundation for the Government's regulatory "chaos" argument.

Once this argument is put aside, the applicants' argument on irreparable harm is largely reduced to the claim that Danco could not continue to market mifepristone because the drug would be mislabeled and that distribution could not resume until Danco jumped through a series of regulatory steps that would be largely perfunctory under present circumstances. That would not take place, however, unless the FDA elected to use its enforcement discretion to stop Danco, and the applicants' papers do not provide any reason to believe the FDA would make that choice. The FDA has previously invoked enforcement discretion to permit the distribution of mifepristone in a way that the regulations then in force prohibited, and here, the Government has not dispelled legitimate doubts that it would even obey an unfavorable order in these cases, much less that it would choose to take enforcement actions to which it has strong objections.

For these reasons, I would deny the stay applications. Contrary to the impression that may be held by many, that disposition would not express any view on the merits of the question whether the FDA acted lawfully in any of its actions regarding mifepristone. Rather, it would simply refuse to take a step that has not been shown as necessary to avoid the threat of any real harm during the presumably short period at issue.

APPENDIX E

1. 5 U.S.C. 705 provides:

Relief pending review

When an agency finds that justice so requires, it may postpone the effective date of action taken by it, pending judicial review. On such conditions as may be required and to the extent necessary to prevent irreparable injury, the reviewing court, including the court to which a case may be taken on appeal from or on application for certiorari or other writ to a reviewing court, 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.

2. 21 U.S.C. 355 provides in relevant part:

New drugs

(a) Necessity of effective approval of application

No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) is effective with respect to such drug.

* * * * *

(d) Grounds for refusing application; approval of application; "substantial evidence" defined

If the Secretary finds, after due notice to the applicant in accordance with subsection (c) and giving him an opportunity for a hearing, in accordance with said sub-

section, that (1) the investigations, reports of which are required to be submitted to the Secretary pursuant to subsection (b), do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; (2) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions; (3) the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity; (4) upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions; or (5) evaluated on the basis of the information submitted to him as part of the application and any other information before him with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof; or (6) the application failed to contain the patent information prescribed by subsection (b); or (7) based on a fair evaluation of all material facts, such labeling is false or misleading in any particular; he shall issue an order refusing to approve the application. If, after such notice and opportunity for hearing, the Secretary finds that clauses (1) through (6) do not apply, he shall issue an order approving the application. As used in this subsection and subsection (e), the term "substantial evidence" means evidence consisting of adequate and well-controlled in-

vestigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof. If the Secretary determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the Secretary may consider such data and evidence to constitute substantial evidence for purposes of the preceding sentence. The Secretary shall implement a structured risk-benefit assessment framework in the new drug approval process to facilitate the balanced consideration of benefits and risks, a consistent and systematic approach to the discussion and regulatory decisionmaking, and the communication of the benefits and risks of new drugs. Nothing in the preceding sentence shall alter the criteria for evaluating an application for marketing approval of a drug.

3. 21 U.S.C. 355-1 provides in relevant part:

Risk evaluation and mitigation strategies

(a) Submission of proposed strategy

(1) Initial approval

If the Secretary, in consultation with the office responsible for reviewing the drug and the office responsible for postapproval safety with respect to the drug, determines that a risk evaluation and mitiga-

tion strategy is necessary to ensure that the benefits of the drug outweigh the risks of the drug, and informs the person who submits such application of such determination, then such person shall submit to the Secretary as part of such application a proposed risk evaluation and mitigation strategy. In making such a determination, the Secretary shall consider the following factors:

(A) The estimated size of the population likely to use the drug involved.

(B) The seriousness of the disease or condition that is to be treated with the drug.

(C) The expected benefit of the drug with respect to such disease or condition.

(D) The expected or actual duration of treatment with the drug.

(E) The seriousness of any known or potential adverse events that may be related to the drug and the background incidence of such events in the population likely to use the drug.

(F) Whether the drug is a new molecular entity.

(2) Postapproval requirement

(A) In general

If the Secretary has approved a covered application (including an application approved before the effective date of this section) and did not when approving the application require a risk evaluation and mitigation strategy under paragraph (1), the Secretary, in consultation with the offices de-

scribed in paragraph (1), may subsequently require such a strategy for the drug involved (including when acting on a supplemental application seeking approval of a new indication for use of the drug) if the Secretary becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks of the drug.

(B) Submission of proposed strategy

Not later than 120 days after the Secretary notifies the holder of an approved covered application that the Secretary has made a determination under subparagraph (A) with respect to the drug involved, or within such other reasonable time as the Secretary requires to protect the public health, the holder shall submit to the Secretary a proposed risk evaluation and mitigation strategy.

* * * * *

(g) Assessment and modification of approved strategy

(4) Modification

(A) On initiative of responsible person

After the approval of a risk evaluation and mitigation strategy by the Secretary, the responsible person may, at any time, submit to the Secretary a proposal to modify the approved strategy. Such proposal may propose the addition, modification, or removal of any goal or element of the approved strategy and shall include an adequate rationale to support such proposed addition, modifi-

cation, or removal of any goal or element of the strategy.

(B) On initiative of Secretary

After the approval of a risk evaluation and mitigation strategy by the Secretary, the Secretary may, at any time, require a responsible person to submit a proposed modification to the strategy within 120 days or within such reasonable time as the Secretary specifies, if the Secretary, in consultation with the offices described in subsection (c)(2), determines that 1 or more goals or elements should be added, modified, or removed from the approved strategy to—

(i) ensure the benefits of the drug outweigh the risks of the drug;

(ii) minimize the burden on the health care delivery system of complying with the strategy; or

(iii) accommodate different, comparable aspects of the elements to assure safe use for a drug that is the subject of an application under section 355(j) of this title, and the applicable listed drug.

* * * * *