Nos. 23-235, 23-236

IN THE

Supreme Court of the United States

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

v.

ALLIANCE FOR HIPPOCRATIC MEDICINE, ET AL.,
Respondents,

DANCO LABORATORIES, L.L.C.,
Petitioner,

v.

ALLIANCE FOR HIPPOCRATIC MEDICINE, ET AL.,
Respondents.

On Writs of Certiorari to the United States Court of Appeals for the Fifth Circuit

REPLY BRIEF FOR DANCO LABORATORIES, LLC

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INTRODUCTION

The lower courts' decision to enjoin FDA's 2016 and 2021 decisions was unprecedented. None of Respondents' contrary arguments proves otherwise.

Start with jurisdiction. Respondents do not deny that their claim to standing combines a statistical theory of future injury to unnamed members (contra *Summers* v. *Earth Island Institute*, 555 U.S. 488 (2009)) with claimed past injury by a few members (irrelevant under *City of Los Angeles* v. *Lyons*, 461 U.S. 95 (1983)) for parties unregulated by the

challenged action (discredited by *Clapper* v. *Amnesty International USA*, 568 U.S. 398 (2013)), without linking traceability or redressability to the challenged action (improper under *TransUnion LLC* v. *Ramirez*, 594 U.S. 413 (2021)). Respondents try to patch the holes in their theory by distorting FDA's documents and Respondents' declarations. But even on Respondents' expansive readings, those documents do not meet the requirements of this Court's standing precedents.

On the merits, Respondents' theme is that reversing here would equate to holding that FDA is above the law. That is wrong. Neither Danco nor FDA have *ever* suggested that FDA is above the law or that courts cannot check FDA's work. Respondents' view that FDA failed to adequately explain its actions is based on the wrong standard for REMS modifications, a theoretical "cumulative impact" they never asked FDA to address and have no evidence to support, and the revolutionary position that FDA may not make reasonable predictive judgments based on the evidence before the agency.

The Court should reverse.

ARGUMENT

I. RESPONDENTS LACK STANDING.

A. Respondents Do Not Allege A Concrete Injury To An Identified Member.

Respondents offer no direct response to Petitioners' explanation of why Respondents lack standing under this Court's precedents. Danco Br. 19-33. Instead, Respondents offer misquotes of FDA documents, declarations that don't say what Respondents claim, and alternative theories the court

below refused to endorse. None fills the gaps in Respondents' standing argument.

1. Respondents' Theory Of Injury Is Contradicted By The Record.

Respondents suggest (at 28) that they have standing because FDA acknowledged that ERs will play a role for some women after a medication abortion. That theory is untethered to the challenged 2016 and 2021 actions, *see* Danco Br. 32 (explaining traceability and redressability requirements), fails to distinguish the role of ERs here from the role that ERs play in any medical treatment, *see id*. at 34 (noting limitless nature of Respondents' theory), and elides the difference between the possibility that some doctor somewhere might treat a woman in an ER and the risk that a Respondent-association member will be required to do so, *see id*. at 20-21 (highlighting Respondents' failure to identify an injured member).

Respondents' theory is also belied—in every respect—by the FDA documents Respondents purport to rely upon.

First, Respondents wrongly suggest (at 25) that lack of access to emergency services is a "contraindication" for Mifeprex. In fact, FDA *removed* that contraindication from the labeling in the 2016 changes, *see* Mifeprex Prescribing Information 4-5 (2016),[1] which Respondents acknowledged when they complained about that change in their second citizen petition, J.A. 332, 391. Respondents did not challenge that change in this suit. Instead, the labeling directs certified prescribers to ensure "that the patient knows whom to call and what to do, including *potentially*

[1] https://perma.cc/7X2S-CKGG.

going to an emergency room," in the event of serious adverse events. J.A. 391 (emphasis added); *see also id.* (prescribers must be able to "provide surgical intervention" personally or assure access to that care and must "give the patient the name and phone number of a healthcare provider who will be handling emergencies").

Respondents also wrongly suggest (at 8-9) that FDA made ERs the "backstop" for mifepristone complications when it disagreed with their request for a formal study of mifepristone use by those "without access to emergency care." J.A. 411. The portions of the citizen petition denial that Respondents cite explain that certified prescribers must be able to "provide any necessary surgical intervention or have made arrangements for others to provide such care; *or* [can] assure patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary." J.A. 381 (emphasis added); *accord* J.A. 384, 411. FDA has not "spent decades directing women harmed by abortion drugs to emergency rooms." Resp. Br. 32.

To the extent Respondents suggest (at 28, 30) that FDA's references to emergency care set Mifeprex apart, that's wrong, too. "It is common practice for healthcare providers to provide emergency care coverage for other healthcare providers' patients." J.A. 384. "Adverse drug events" from all FDA-approved drugs combined "cause approximately 1.3 million emergency department visits each year,"[2] and FDA-approved labeling regularly directs people to seek emergency medical care if they need it. For

[2] CDC, Adverse Drug Events in Adults, https://perma.cc/47U4-MRB3.

example, Viagra's labeling says patients "should seek emergency treatment if an erection lasts >4 hours,"[3] and Imitrex's labeling (a drug commonly used for migraines) directs patients to "get emergency medical help right away if you have any of [seven] symptoms."[4] Finding standing here "threatens limitless litigation" by inviting healthcare providers to challenge "*any* drug approval or subsequent change" they dislike, destabilizing the industry and harming patients. PhRMA Br. 3, 6.

Second, Respondents misrepresent (at 26, 28) Mifeprex's labeling in stating that it identifies a set percentage of women whom FDA has concluded will always "go to the emergency room" or "need emergency care" after taking mifepristone. The labeling merely notes that three studies reported "ER visit[s]" of 0%, 2.9%, and 4.6%, J.A. 533, but cautions that these data "may not reflect the rates observed in practice," J.A. 531, and notes that across all 10 studies referenced in that section of the label, "[s]erious adverse reactions were reported in <0.5% of women," J.A. 532.

Respondents quibble (at 28) with the number of non-serious adverse events reported in FAERS. Those include a host of "common side effects," like nausea, weakness, headaches, and dizziness, J.A. 544, for which prescriber reporting has always been voluntary, J.A. 230. Respondents do not dispute that during 15-plus years of mandatory reporting for *serious* adverse events, a vanishingly small number

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[3] Viagra Prescribing Information 1 (2017), https://perma.cc/9SXN-TYTV.

[4] Imitrex Prescribing Information 20-21 (2017), https://perma.cc/7ECW-WET9.

were reported. *See* Danco Br. 10 (citing J.A. 500-502). Respondents' lamentations about *voluntary* reporting of non-serious adverse events do nothing to undermine that estimate.

Third, Respondents have no factual basis for their assertion (at 26-27) that all women who go to the ER require "urgent treatment." For example, the Raymond study (cited at 11, 36, 53) reported that "half of [ER/urgent care] visits did not entail *any medical treatment*." J.A. 404 (emphasis added); *accord* Ushma D. Upadhyay et al., *Abortion-Related Emergency Department Visits In The United States: An Analysis Of A National Emergency Department Sample*, BMC Medicine (2018), https://perma.cc/X8SH-86JH (50.6% of abortion-related ER visits require observational care only).

2. Respondents' Declarations Do Not Support Their Alleged Injuries.

Even taking Respondents' declarations at face value, *but see* ACLU Br. 6-19 (detailing reasons not to), Respondents failed to identify a single member facing the imminent injury necessary for injunctive relief.

Conscience rights. No declarant describes being imminently forced to "participat[e] in an elective abortion," or even says that they were forced to do so in the past. Resp. Br. 19. This Court has repeatedly rejected that "some day" possibilities without "any specification of when the some day will be" can support a claim of imminent injury. *Summers*, 555 U.S. at 496 (citation omitted).

- Dr. Barrows (relinquished medical license in 2015), Dr. Harrison (stopped practicing in 2000),

and Mr. Dickerson (not a doctor) express "concern[]" that association members *could* be forced "to complete an unfinished elective abortion," J.A. 142, 121, 136; ACLU Br. 12, 18, 16, but don't say that actually happened.

- Dr. Francis describes once spending time with a patient who took non-FDA-approved drugs obtained from India (plainly not traceable to any FDA action), but never states she was "forced" to provide care. *Compare* Resp. Br. 19 *with* J.A. 153 ¶ 12 (not identifying who performed the surgery); *see* Danco Br. 28. Dr. Francis identifies only one procedure a specific person performed—and the person was her "partner," who is not described as an association member. *See* J.A. 154.
- Dr. Skop says she has "cared for at least a dozen women who have required surgery" across 30 years of practice, but says she performed only one (undated) procedure. J.A. 161-164; *see* Danco Br. 22, 28. Dr. Skop's sole reference to a conscience injury is her concern that FDA's actions "*could* force [her] to have to surgically finish an incomplete elective chemical abortion." J.A. 167 (emphasis added).
- Drs. Wozniak, Johnson, and Frost-Clark likewise describe no past or imminent conscience injury; the words "conscience injury" appear nowhere in their declarations. *See* J.A. 169-174, 177-181, 183-187.

Respondents speculate (at 20-21, 31) that a Respondent-doctor might not have "time to invoke" conscience rights, a "non-objecting" doctor might not be available, or a doctor could feel a conscience injury

just from "refer[ring]" a patient to someone else.[5] But the declarations do not assert that these things have ever happened—let alone provide a factual basis to find a substantial risk they will happen to a specific doctor in the near future.

Time and resources. No case supports finding that the mix of patients a doctor might see in the ER during a given shift is a cognizable Article III injury. This may be why Respondents misrepresent (at 21) their sole citation through a bracketed alteration. That case referred to "wasted time" as a concrete harm, but Respondents have not suggested that treating someone in the ER is wasted time. *Losch* v. *Nationstar Mortg. LLC*, 995 F.3d 937, 943 (11th Cir. 2021); *cf. Diamond* v. *Charles*, 476 U.S. 54, 66 (1986) (no standing where pediatrician speculated that enforcing anti-abortion law would increase his "hoped-for fees"). In any event, the fact that "most" Respondent doctors do not work in an ER and see ER patients there only when "at times pulled into" it, as Respondents emphasize (at 22), hurts their standing claim—by introducing yet another layer of attenuation.

Stress and pressure. Relying on language about "[a]esthetic and environmental well-being," *Sierra Club* v. *Morton*, 405 U.S. 727, 734 (1972), and a footnote "tak[ing] no position on whether or how * * * emotional or psychological harm could suffice for Article III purposes," *TransUnion*, 594 U.S. at 436 n.7, Respondents claim standing by virtue of the stress and pressure they experience as doctors, Resp.

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[5] Respondents do not dispute that state conscience protections apply and would provide comparable or greater protection than federal law. *See, e.g.*, Ind. Code §§ 16-34-1-4, -5, -6 (1993).

Br. 23. The Fifth Circuit recognized that such claims "do[] not provide a separate basis for Article III standing," Pet. App. 35a,[6] and the cases from this Court that Respondents cite (at 22-23) bolster that correct conclusion. *Morton*, *Summers*, and *Lujan* rejected standing theories that would open the floodgates to suits by those who "seek to do no more than vindicate their own value preferences through the judicial process." *Morton*, 405 U.S. at 735, 738, 740; *see Summers*, 555 U.S. at 493-497; *Lujan* v. *Defs. of Wildlife*, 504 U.S. 555, 562-567 (1992). And *TransUnion* held only that emotional harm "with a 'close relationship' to * * * defamation" can establish standing. 594 U.S. at 432-433.

Increased liability. No declarant provides any factual basis to find a certainly impending increase to insurance premiums or liability from FDA's actions, particularly given that ER doctors regularly treat patients in emergency situations and OB/GYNs can be consulted for any number of situations that might bring someone to an ER. Nor is it unusual for doctors to lack "a prior relationship with" individuals seeking ER care or "access to the patient's medical history"—the reasons Respondents give for fearing increased liability. J.A. 121; *see* J.A. 142, 180, 185-186.

B. Respondents Cannot Show Traceability Or Redressability.

Respondents must show that the injuries they assert result from the way FDA's 2016 and 2021 actions altered Mifeprex's approval and conditions of use. *See* FDA Br. 29; Danco Br. 30-31. They cannot.

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[6] Citations are to FDA's Petition Appendix.

1. Most problematically for Respondents, FDA's 2016 changes *decreased* the need for subsequent interventions generally (including in an ER) by *increasing* the effectiveness of medication abortion. Danco Br. 7-8. Respondents' speculation (at 39) that women are nevertheless more likely to need "emergency care" because FDA "eliminated [three] critical safeguards" in 2016 is contradicted by the facts and Respondents' own citations.

First, Respondents cite nothing to suggest that FDA discourages women from following up with their prescriber. *Contra* Resp. Br. 40. Even today, the labeling says "[p]atients should follow-up with their healthcare provider," and emphasizes that this is "very important." J.A. 529. And the clinical studies FDA discussed showed that follow-up modalities other than in-person visits were safe and effective. J.A. 482-485.

Second, Respondents cite nothing to suggest an increased rate of ER care for women prescribed mifepristone by advanced-practice clinicians; Respondents instead assume that (1) such clinicians cannot provide follow-up care and (2) patients must seek ER treatment instead. *See* Resp. Br. 40. But FDA-reviewed studies found equivalent or greater efficacy of mifepristone when prescribed by advanced-practice clinicians compared to physicians, J.A. 461, Reproductive Health Researchers Br. 6-7; advanced-practice clinicians can and do safely prescribe mifepristone and provide surgical abortions and other follow-up care, Nat'l Ass'n Nurse Practitioners Br. 13-20, 24-28; and, like physician-prescribers, advanced-practice clinicians "refer patients to the ER only * * * [as] a last resort," *id.* at 27 (citation omitted).

Third, Respondents cite nothing to suggest that because the on-label gestational age increased to 10 weeks in 2016, more women will imminently seek ER care. More patients have a complete treatment at 10 weeks under the dosing regimen approved in 2016 than occurred in the studies supporting the initial 7-week approval. *See* J.A. 449-450 (92% required no intervention under pre-2016 labeling; 96.1% to 97.4% required no intervention under 2016 regimen). Respondents' contrary speculation (at 39) does not equate to traceability; for every drug, there will be patients for whom it is not effective. With Mifeprex, that number is very small.

2. Respondents' argument (at 35-36) that some additional number of women are likely to go to the ER as a result of FDA's 2021 decisions distorts the data. *Infra* pp. 21-23. But even if their description of the data were accurate, it says nothing about whether *these specific doctors* will be forced to treat *those specific women* as a result of *the 2021 decisions*. Since 2000, certified prescribers have been required to attest that they can accurately assess gestational age and diagnose ectopic pregnancies, and FDA has never required an ultrasound to do so. *See* J.A. 255-256, 383-384.

No declarant provides factual support for having to imminently treat (or having previously treated) a woman prescribed mifepristone despite having an ectopic pregnancy or after the prescriber miscalculated gestational age; nor does any declarant link any such nonexistent circumstances to FDA's 2021 decisions. And despite their speculation that FDA's 2021 decisions may increase "complications," J.A. 185, 171, Respondents point to no data showing

that actually happened after mandatory in-person dispensing was suspended.[7]

Respondents also ignore that many declarants practice in States that *do* mandate in-person dispensing or ultrasounds (when abortion isn't entirely banned), further undermining traceability of any asserted injury to the challenged actions. Danco Br. 23 & n.9.

C. Respondents' Alternative Standing Theories Are Meritless.

Respondents lack organizational standing. Complaining (at 43) that FDA "downplays the potential dangers of [abortion] drugs" does not show a significant or perceptible impairment to their goal of "[e]ducat[ing] the public * * * about the potential risks of abortion drugs"—a non-cognizable, abstract social interest in any event. *See Havens Realty Corp.* v. *Coleman*, 455 U.S. 363, 379 (1982). This Court requires "far more than simply a setback to the organization's abstract social interests" for organizational standing. *Id.* An "association's self-serving observation that it has expended resources to educate its members and others regarding challenged [agency actions] does not present an injury in fact."

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[7] Recent data suggest the opposite. *E.g.*, Ushma D. Upadhyay et al., *Effectiveness And Safety Of Telehealth Medication Abortion In The USA*, Nat. Med. (Feb. 15, 2024), https://perma.cc/75WX-ZBDH (of 4,454 medication abortions via telehealth, 97.7% had complete abortions, with only 1.4% requiring aspiration or surgical treatment; the serious-adverse-event rate was 0.34%; and only 1.8% of abortions were followed by an ER visit, 38.3% of which resulted in no treatment); *see also* Reproductive Health Researchers Br. 29-30.

Nat'l Ass'n of Home Builders v. *EPA*, 667 F.3d 6, 12 (D.C. Cir. 2011) (citation omitted).

And Respondents cannot "spend [their] way to standing through" pre-litigation activities like a "citizen petition." *Children's Health Def.* v. *FDA*, No. 23-50167, 2024 WL 244938, at *5 (5th Cir. Jan. 23, 2024) (citation omitted); *accord Home Builders*, 667 F.3d at 11-12. Especially not where, as here, Respondents' "mission includes advocating on behalf of its members, including in litigation." J.A. 139, 152. Respondents are not being diverted from their mission: This case is helping them fulfill it.

Nor can Respondents save their claims by invoking (at 45) third-party standing based on the rights of individuals who sought and obtained a medication abortion from another provider, or labor and delivery patients who Respondent-doctors might supposedly be called away from treating. Respondents fail all "three important criteria" for third-party standing. *Powers* v. *Ohio*, 499 U.S. 400, 411 (1991). Litigants must "have satisfied Article III" themselves before attempting to "raise the rights of others." *Kowalski* v. *Tesmer*, 543 U.S. 125, 129 (2004). Respondents do not even recognize that requirement, let alone meet it. Nor have Respondents shown a "close relation" to third parties unable to "protect" their "own interests." *Powers*, 499 U.S. at 411-412.

II. RESPONDENTS' MERITS ARGUMENTS ALSO FAIL.

A. Respondents Cannot Obtain Relief Without The Administrative Record.

Respondents do not explain how a court could fault FDA's decisional process without reviewing all of

FDA's reasoning. This is not a case where review could be based on "those parts of [the record] cited by a party," Resp. Br. 63 (quoting 5 U.S.C. § 706), "after both sides had fully reviewed the complete record" and agreed to submit "particular portions," *Walter O. Boswell Memorial Hospital* v. *Heckler*, 749 F.2d 788, 793 (D.C. Cir. 1984). Preliminary relief in APA cases is not a shell game, with the incentive for plaintiffs to try to get a ruling of unreasonableness before anyone can see what the full record shows. This matters particularly to a party like Danco, which has no access to the agency documents necessary to defend itself but will directly bear the harms from a preliminary injunction.

Respondents attempt (at 64) to distinguish Danco's cases as relying on post-hoc affidavits and the parties' representations, but the courts below did the same here, *e.g.*, Pet. App. 60a-61a, in addition to relying on extra-record "junk science," ACLU Br. 19-22, like articles retracted for "lack of scientific rigor" and undisclosed conflicts of interest, Retraction Notice, Sage J. (Vol. 11, Feb. 5, 2024), https://perma.cc/9ZAP-5TE2; *e.g.*, Pet. App. 119a & n.9, 167a & n.37, 210a. And although the lower courts had *some* decisional documents, like "FDA's approval letter[s]," preliminary relief is inappropriate because there is no way to know whether the analysis in those documents *fully reveals* "the basis on which the FDA acted," *Am. Bioscience, Inc.* v. *Thompson*, 243 F.3d 579, 581-582 (D.C. Cir. 2001)—a point Respondents do not dispute.[8]

[8] Respondents' attempt to avoid these problems comes too late. They not only waived waiver by failing to raise it in opposing certiorari, S. Ct. R. 15.2, Respondents *agreed* the "administrative record * * * is particularly crucial here," Br. in Opp'n 17-18.

B. FDA's 2016 And 2021 Decisions Complied With The APA.

Respondents accuse Danco and FDA of "barely defend[ing]" FDA's decisions on the merits, Resp. Br. 2, but nothing could be further from the truth. *See* Danco Br. 38-52; FDA Br. 34-44. Their challenge is a policy dispute dressed up as an APA claim. They ask this Court to adopt non-statutory standards, second-guess FDA's measured decisions, and endorse arguments not presented to FDA or the courts below.

1. FDA Thoroughly Considered And Adequately Explained Its 2016 Changes.

The Fifth Circuit faulted FDA for not "consider[ing] the cumulative effect" of *all* the 2016 changes, "includ[ing] * * * switching the method of administration * * * and changing the dos[ing]." Pet. App. 53a. In this Court, however, Respondents expressly disclaim challenging FDA's "dosing, timing, or route of administration" changes. Resp. Br. 41. *But see* Appellee Br. 53 n.9 (5th Cir. May 8, 2023). That disclaimer undercuts their "cumulative-effects" argument and the court of appeals' acceptance of it. Respondents' argument now seems to be that FDA failed to address the potential cumulative effect of a *subset* of the 2016 changes, even though Respondents never identified that subset or asked the agency to address it. This new formulation is as meritless as its predecessor.

1. There is no basis in law or logic for Respondents' theory that FDA cannot approve changes to a drug's approval and conditions of use unless the manufacturer presents FDA with *one* clinical study whose protocol addresses *every* proposed change and

whose methodology *does not deviate in any way* from the proposed labeling.

Start with law. Respondents' position (at 59, 62) seems to be that by referencing a drug's "proposed labeling," 21 U.S.C. § 355(d), Congress mandated that FDA deny any application not including a clinical study precisely matching the "proposed labeling." But Section 355(d) doesn't say that; it tasks FDA with making predictive judgments about whether the applicant has submitted, or FDA otherwise has before it, "adequate tests" and other "information" that allow the agency to "find[]" the drug will be safe under "the conditions prescribed, recommended, or suggested in the proposed labeling." *Id.* §§ 355(d)(1), (4).[9]

Then, consider logic. Respondents' imagined study-match requirement is not how clinical trials work. FDA Br. 37-38; Pharm. Cos. Br. 16-19. Respondents' proposed requirement "would be at minimum impractical and at worst impossible to effectuate" due to its "economic and temporal costs," "practical complexity," PhRMA Br. 23, and questionable ethics, Pharm. Cos. Br. 17.

2. Respondents' argument that FDA did not adequately explain its decision to approve the 2016 changes is equally meritless. FDA relied on numerous studies that "support[ed] multiple changes," individually and in combination. J.A. 298; Danco Br. 40-44; FDA Br. 34-39. Respondents' contrary argument again depends on misrepresenting the factual record.

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[9] Section 355(d)(5) separately requires "substantial evidence" of efficacy—not safety. *Contra* Resp. Br. 49. Respondents challenge only FDA's safety finding. *See, e.g.*, Resp. Br. i, 60.

For example, Respondents mischaracterize the Winikoff study. The ultrasound and in-person follow-up components of that study were *not* "safety measures." *Contra* Resp. Br. 6-7. The researchers said they used ultrasounds to confirm study eligibility (because they focused on 57-70 days gestational age) and to determine group assignments (because they compared outcomes of 57-63 days with 64-70 days). ROA 728. And the study protocol requested participants return at 7-14 days, but "[i]f a participant failed to return for a follow-up visit," researchers conducted their "assessment of abortion status and the interview * * * by telephone." *Id.*

Respondents are also wrong to suggest (at 60) that providers are unable to address complications absent mandatory in-person follow-up visits. The self-serving say-so of Respondents—who have never prescribed mifepristone or followed-up with patients after doing so—does not outweigh FDA's assessment, after reviewing multiple scientific studies, that "alternatives to in-clinic follow-up are effective." J.A. 484; *see* J.A. 482-485, 462.

Nor is this case a redux of *State Farm*. Based on evidence that seatbelts could be disabled, the agency there eliminated a passive-restraint requirement for vehicles that could be met by either a seatbelt or an airbag, without considering record evidence that continuing to require airbags would save thousands of lives. *Motor Vehicle Mfrs. Ass'n* v. *State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 35, 51-54 (1983). That's a far cry from FDA comprehensively reviewing dozens of studies covering tens of thousands of women, all of which *supported* the agency's conclusion.

3. Finally, FDA cannot be faulted for failing to offer a detailed answer to a question Respondents never asked. Respondents point (at 61) to J.A. 328 as proof that they "raised objections to the interrelated changes" in their citizen petition. That page does no such thing. It explains Respondents' view that "three office visits" is a better approach than one. Respondents did not use the term "cumulative" on this page—or anywhere else in the citizen petition—and did not reference an interaction between office visits and any other challenged change that FDA approved in 2016. Nothing in the petition gave FDA an opportunity to address Respondents' "cumulative-effects" argument. *See Vt. Yankee Nuclear Power Corp.* v. *NRDC*, 435 U.S. 519, 553-554 (1978).

2. FDA Appropriately Relaxed Adverse-Event Reporting Requirements In 2016.

FDA also acted lawfully in aligning adverse-event reporting for mifepristone more closely with adverse-event reporting for other drugs. FDA cogently explained that after 15 years of mandatory reporting of all serious adverse events by prescribers, mifepristone's safety profile was "well-characterized," and that data demonstrated the 2016 changes would not alter that benefit-risk profile. J.A. 506; *see* Danco Br. 45-48. In these circumstances, nothing in the FDCA or APA required FDA to continue requiring prescribers to report all serious adverse events.

Respondents suggest (at 51) that FDA should have continued to require reporting because Mifeprex had boxed warnings and a REMS. But Respondents cite no rule requiring prescriber reporting for such drugs; indeed, FDA does not require that for other drugs with

boxed warnings and REMS. *E.g.*, Copiktra,[10] Aveed,[11] Sublocade.[12] Respondents also suggest causality where there is none. Respondents say (at 12) the warning is "require[d] * * * *because the drug can cause* 'serious and sometimes fatal infections and bleeding,'" (emphasis added); yet the label says only that such events "occur very rarely following *spontaneous*, *surgical*, *and* medical abortions, including following MIFEPREX use," and that "*[n]o causal relationship* between the use of MIFEPREX and misoprostol and these events has been established." J.A. 527 (emphases added). In other words, the label says that infections and bleeding can (rarely) result from *all* pregnancy losses, including miscarriage.

Respondents also complain (at 63) that adverse-event reporting by sponsors like Danco is never sufficient—apparently for any drug. That is no basis to enjoin FDA's action here. *No currently effective REMS* requires mandatory reporting of the type that applied to mifepristone from 2000-2016. Danco Br. 45. Fatality reporting by prescribers remains mandatory under the Mifepristone REMS—one of just seven REMS for which that is the case, Danco Br. 45-46—and anyone (including Respondents' members) can report any adverse event via phone call, email, or

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[10] Copiktra Prescribing Information (2021), https://perma.cc/UQB7-FQM5; Copiktra REMS (2022), https://perma.cc/9P2K-462L.

[11] Aveed Prescribing Information (2021), https://perma.cc/AB3F-4RBZ; Aveed REMS (2022), https://perma.cc/9TM5-ZGE9.

[12] Sublocade Prescribing Information (2023), https://perma.cc/8MEU-A5K4; Sublocade REMS (2023), https://perma.cc/3S5B-YRSQ.

online submission to Danco or FDA. Per FDA rules, Danco tracks and reports all adverse events to FDA. 21 C.F.R. §§ 314.80, 314.81.

3. FDA's 2021 Decisions Were Not Arbitrary And Capricious.

Contrary to Respondents' claim (at 57), FDA did not "permanently remove[] the in-person dispensing requirement" in 2021; rather, FDA declined to enforce that requirement until FDA modified the REMS in 2023. Danco Br. 11-12. And Respondents do not contest that they never challenged the 2023 REMS modification. Even as to those earlier (no longer operative) non-enforcement decisions, Respondents' argument fails.

1. Respondents fault (at 49-55) FDA's 2021 decisions as lacking "'adequate tests,' test 'results,' or '[]sufficient information'" to determine safety under 21 U.S.C. § 355(d). But *§ 355-1* applies to FDA's decisions, not § 355(d); FDA can decide on its own "initiative" to require a REMS modification where an element of the existing REMS is no longer necessary to "ensure the benefits of the drug outweigh the risks," or to "minimize the burden on the health care delivery system." *Id.* §§ 355-1(g)(4)(B)(i), (ii). Those are precisely the reasons FDA gave for its decisions in 2021. J.A. 397, 407; *see* FDA Scholars Br. 5-6, 11-14.

Relying on the wrong legal standard, Respondents manufacture a new prohibition on FDA using FAERS data to support a REMS modification. The fact that FAERS does not include "every adverse event," Resp. Br. 50 (quoting J.A. 417), and sometimes has "duplicate" reports or reports of events not "caus[ed]" by the product is why FDA says FAERS data cannot be used to calculate the *specific incidence rate* of a

given adverse event. J.A. 416-417. But that data is "a useful tool" that FDA regularly relies on as part of its "post-marketing safety surveillance program." J.A. 414; *see* Pharm. Cos. Br. 18-20; FDA Scholars Br. 24-25. And there is *no drug* for which prescribers must report *every* adverse event, as Respondents suggest was necessary before FDA could use FAERS data. Even for Mifeprex pre-2016, FDA required reporting of only "*serious* events." J.A. 230 (emphasis added). Respondents' made-up standard would invalidate or undermine virtually every modification for every drug on the market with a REMS. *See* Pharm. Cos. Br. 20-21; FDA Scholars Br. 25 & n.20.

Here, FDA reasonably relied on the mifepristone FAERS data—which showed no "new safety concerns * * * during the time when in-person dispensing was not enforced," J.A. 398—and other post-marketing assessments, "supported by" the published literature, to conclude that in-person dispensing was "no longer necessary to ensure that the benefits of the drug outweigh the risk," J.A. 397, and should be modified "to reduce the burden on the health care delivery system," J.A. 394.

Respondents strain to come up with alternative explanations for the absence of real-world serious adverse events, arguing (at 51) that the lack of FAERS data proves more stringent reporting for mifepristone is required. But the most likely explanation for the relatively limited number of FAERS reports is that—consistent with decades of data (including 15 years of *mandatory* serious-adverse-event-reporting data) and numerous clinical studies—serious adverse events are simply not occurring at the rate Respondents claim.

See ACOG Br. 14-16; Reproductive Health Researchers Br. 22-31; J.A. 501.

2. Respondents urge this Court to reweigh the scientific literature. Even if this Court were inclined to engage in such scientific "second-guess[ing]," *Cytori Therapeutics, Inc.* v. *FDA*, 715 F.3d 922, 927 (D.C. Cir. 2013) (Kavanaugh, J.), that argument goes nowhere: The articles Respondents cite (at 53) do not suggest that in-person dispensing remained necessary.

For example, it is apples and oranges to compare (as Respondents do at 53-54) data referenced in the labeling about ER visits in three studies to other studies that lump together "ED/urgent care center encounters" or evaluated "unplanned clinical encounters," which includes follow-ups outside of the ER/urgent care context. J.A. 404. Moreover, one of those studies specifically stated that "half of the ED/urgent care visits did not entail any medical treatment." *Id.* So although more women might seek some sort of follow-up, which could be for observation, pain medication, or something else, none of the studies provided evidence that more women experienced serious adverse events. J.A. 406.

Respondents make the same error in arguing (at 35-38) that women are more likely to go to the ER as a result of FDA's 2021 decisions. They conflate in-person dispensing with "physical[]" examinations, "ultrasound[s]," and "sonograms." But assessing gestational age and ectopic pregnancy "does not necessarily require direct physical contact," J.A. 384; screening questions and menstrual history can suffice, ACOG Br. 23 & n.41, and FDA leaves the manner of assessment "to the professional judgment of each provider," J.A. 383. Reimposing in-person

dispensing would thus not mandate the procedures Respondents urge—a point they tacitly concede in complaining (at 36-37) about a lost "opportunity" for a physical examination, rather than any requirement that one be conducted.

3. Respondents say FDA could not exercise its predictive judgment here because, unlike the statute in *FCC* v. *Prometheus Radio Project*, 592 U.S. 414 (2021), the FDCA is not sufficiently "broad and open-ended." Resp. Br. 54-55 (citation omitted). *Prometheus* never said that—hence why Respondents cite a different case. And Respondents' argument that FDA gets *less* deference because its decision involves science, rather than policy, gets things precisely backwards. "When FDA makes scientific judgments, this Court owes the agency the 'most deferential' review." *Takeda Pharms. U.S.A., Inc.* v. *Burwell*, 691 F. App'x 634, 637 (D.C. Cir. 2016) (per curiam) (Kavanaugh, Wilkins, Silberman, JJ) (quoting *Baltimore Gas & Electric Co.* v. *NRDC*, 462 U.S. 87, 103 (1983)).

Unable to defend the Fifth Circuit's merits analysis, Respondents say—for the first time—that it was arbitrary for FDA to "change[] its longstanding position" on in-person dispensing. Resp. Br. 48. That newfound claim is forfeit. *United States* v. *Galletti*, 541 U.S. 114, 120 n.2 (2004); S. Ct. R. 15.2. It also fails on its own terms. Even if FDA's 2020 "litigation position" somehow binds the agency, *cf. Bowen* v. *Georgetown Univ. Hosp.*, 488 U.S. 204, 213 (1988), this was not a silent reversal. At the time of that statement in August 2020, in-person dispensing had been suspended for only one month. J.A. 398. By the time of FDA's December 2021 decision, months of data

and several new studies provided new data for FDA to assess. J.A. 398-399, 402-406. FDA explained why this new evidence warranted a new approach.

4. Finally, Respondents (at 56) ask this Court to address the Comstock Act, though the Fifth Circuit did not. Pet. App. 63a n.8. Respondents have never explained why it was arbitrary and capricious for FDA not to address a law that Respondents never raised to the agency, that FDA is not charged with enforcing, and that does not alter the governing standards for FDA's decisions. In any event, the courts of appeals have uniformly held that the Comstock Act does not bar the distribution in interstate commerce of items not intended for unlawful abortions or contraception. *See* Former DOJ Offs. Br. 10.

C. The Equities Favor Danco.

1. The Fifth Circuit erred in ordering a return to pre-2016 labeling and conditions of use as preliminary-injunction relief. Pet. App. 71a. Where "[t]here is a serious possibility" an agency can remedy any concerns, and "the disruptive consequences of vacating are substantial," remand without vacatur is the appropriate remedy even at the end of an APA suit. *Apache Corp.* v. *FERC*, 627 F.3d 1220, 1223 (D.C. Cir. 2010) (Kavanaugh, J.) (citation omitted). And even at the end of this case, no vacatur could extend beyond the challenged portions of FDA's 2016 and 2021 decisions, which is why ordering a return to the pre-2016 REMS and labeling makes no sense. Danco Br. 53-54.

2. Respondents take a head-in-the-sand approach to the many significant harms an injunction would cause. Respondents ignore the inevitable gap in access pending FDA's approval of revised labeling,

documentation, and a REMS. Danco Br. 53; FDA Br. 46. They are mum as to the million-plus patients experiencing "miscarriage" annually for whom "mifepristone is often a critical component of care," ACOG Br. 12, or how restricting medication abortion would "significantly increase the burden on public health-care systems" by "shift[ing] towards" more "resource-intensive" surgical abortions, N.Y.C. Br. 13-16. Nor do Respondents address the interests of States seeking to preserve abortion access within their borders. *See* New York Br. 3.

Respondents wave away concerns of industry-wide destabilization, but not a *single* industry member is on Respondents' side. As the leading industry association and nearly 350 pharmaceutical companies, executives, associations, and investors explained, the decision below "poses a serious threat to the health and stability of the nation's biopharmaceutical industry," PhRMA Br. 3, and "threatens a seismic shift in the clinical development, drug approval, and post-approval processes," Pharm. Cos. Br. 24.

In short, affirming the decision below would dramatically alter this Court's standing and APA jurisprudence; reversing would maintain principles and precedents that have long governed these inquiries. The choice is clear. The judgment should be reversed and remanded with instructions to dismiss for lack of standing, *see Munaf* v. *Geren*, 553 U.S. 674, 691-692, 705 (2008), or reversed on the merits.[13]

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[13] Missouri, Idaho, and Kansas's contrary arguments are wrong for the reasons set out in Danco's Intervention Opposition at 7-9.

CONCLUSION

The Fifth Circuit's judgment should be reversed.

Respectfully submitted,

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