United States Court of Appeals for the Fifth Circuit

United States Court of Appeals
Fifth Circuit
FILED
August 16, 2023
Lyle W. Cayce
Clerk

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,

versus

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,

versus

DANCO LABORATORIES, L.L.C.,

Intervenor—Appellant.

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 judgment, 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 ac-

tions—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 application 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

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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.

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 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 peti-

tion 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 in-

jury 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 suffering 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 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 emer-

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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.

> gency 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 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.

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 sometimes it is placental tissue that has not been

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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.

> 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 required 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 insurance 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 is-

sue" 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 plaintiff 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 Treat-

ment 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

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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.

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 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-substantial 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 obstetrics 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 pre-

scriber 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. Wozniak 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 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 organiza-

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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).

tional 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 dis-

tinguish 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 partic-

ular 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 Amend-

ments 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.

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–

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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.

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 medi-

cal 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 (explaining 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 diminishes 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 identified in FAERS . . . ."). Five events[7] were reported during that

[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.

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 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 require-

> ments 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 . . . supported the conclusion that mife-

pristone 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 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

[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.

"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 injunction, 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 be-

cause 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 Federal 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 pedigree 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 birdwatchers 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 get-go, 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.

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

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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.

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]hoever 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 producing 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 statutory 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.