No. 22A902

IN THE
Supreme Court of the United States

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

Applicants,

v.

ALLIANCE FOR HIPPOCRATIC MEDICINE ET AL.,

Respondents.

APPLICATION TO STAY THE ORDER ENTERED BY THE UNITED STATES DISTRICT COURT FOR THE NORTHERN DISTRICT OF TEXAS AND FOR AN ADMINISTRATIVE STAY

BRIEF OF MEDICAL AND PUBLIC HEALTH SOCIETIES AS *AMICI CURIAE* IN SUPPORT OF APPLICANTS

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INTEREST OF *AMICI CURIAE*[1]

Amici curiae are leading medical and public-health societies representing physicians, clinicians, and public-health professionals who serve patients in Texas and nationwide. They include: (1) The American College of Obstetricians and Gynecologists ("ACOG"). Representing more than 90% of board-certified OB/GYNs in the United States, ACOG is the nation's premier professional membership organization for obstetrician-gynecologists dedicated to access to high-quality, safe, and equitable obstetric and gynecologic care. ACOG maintains the highest standards of clinical practice and continuing education of its members, promotes patient education, and increases awareness among its members and the public of the changing issues facing women's health care. ACOG is committed to ensuring access for all people to the full spectrum of evidence-based quality reproductive health care, including abortion care, and is a leader in the effort to confront the maternal mortality crisis in the United States; (2) The American Medical Association ("AMA"), the largest professional association of physicians, residents, and medical students in the country. Through state and specialty medical societies and other physician groups seated in its House of Delegates, substantially all physicians, residents, and medical students in the United States are represented in the AMA's policy-making process. The AMA was founded in 1847 to promote the art and science of medicine and the betterment of public health, and these remain its core purposes; (3) The Society for

[1] Pursuant to United States Supreme Court Rule 37.6, counsel for *amici curiae* authored this brief in whole; no party's counsel authored, in whole or in part, this brief; and no person or entity other than *amici* and their counsel contributed monetarily to preparing or submitting this brief.

Maternal-Fetal Medicine ("SMFM"). Founded in 1977, SMFM is the medical professional society for maternal-fetal medicine subspecialists, who are obstetricians with additional training in high-risk pregnancies. SMFM represents more than 5,500 members who care for high-risk pregnant people and provides education, promotes research, and engages in advocacy to advance optimal and equitable perinatal outcomes for all people who desire and experience pregnancy. SMFM and its members are dedicated to ensuring that all medically appropriate treatment options are available for individuals experiencing a high-risk pregnancy; and (4) 13 other organizations whose members' work is impacted by the matter before this Court and who can offer a unique perspective not otherwise provided by the parties.

These organizations collectively represent hundreds of thousands of medical practitioners across the country, with deep expertise in both medical research and the treatment of patients in real-world settings. Courts frequently rely on *amici*'s medical and scientific expertise in cases involving pregnancy.[2] Ensuring robust access to evidence-based health care and promoting health care policy that improves patient health are central to *amici*'s missions. *Amici* believe that all patients are entitled to prompt, complete, and unbiased health care that is medically and scientifically sound. *Amici* submit this brief to explain that mifepristone is exceedingly safe and effective and that the Food and Drug Administration's ("FDA") decision to

[2] *See, e.g.*, *June Med. Servs. LLC v. Russo*, 140 S. Ct. 2103, 2131 (2020); *Whole Woman's Health v. Hellerstedt*, 579 U.S. 582, 612–13 (2016); *Whole Woman's Health v. Paxton*, 978 F.3d 896, 910 (5th Cir. 2000); *Stenberg v. Carhart*, 530 U.S. 914, 928 (2000); *Planned Parenthood Ctr. for Choice v. Abbott*, No. A-20-CV-323-LY, 2020 WL 1815587, at *4–5 (W.D. Tex. Apr. 9, 2020).

eliminate certain restrictions on mifepristone was and continues to be based on sound medical science.

Amici's ability to effectively care for patients often requires access to mifepristone, which has undergone rigorous testing and review and has been approved for use in the United States for more than twenty years. Accordingly, *amici* have a strong interest in preserving that access and ensuring that the science surrounding mifepristone's safety and efficacy is correctly understood.

Amici are the following organizations: ACOG; SMFM; AMA; American Academy of Family Physicians; American Academy of Nursing; American Academy of Pediatrics; American College of Nurse-Midwives; American Gynecological and Obstetrical Society; American Society for Reproductive Medicine; Council of University Chairs of Obstetrics and Gynecology; National Association of Nurse Practitioners in Women's Health; Society for Academic Specialists in General Obstetrics and Gynecology; Society of Family Planning; Society of General Internal Medicine; Society of Gynecologic Oncology; and Society of OB/GYN Hospitalists.

SUMMARY OF THE ARGUMENT

On behalf of the nation's leading medical organizations and the patients they serve, *Amici* urge this Court to preserve access to mifepristone under the conditions of use established by the FDA. Those conditions—set aside without proper basis by the decisions of the two courts below—are scientifically sound and supported by decades of evidence, and ensure access to an exceedingly safe and commonly used medication that is necessary to preserve the life and health of countless patients. The Fifth Circuit's decision to reimpose restrictions deemed unnecessary by the FDA will significantly limit access to mifepristone and have dramatic, harmful consequences for *amici* and their patients.

Without any form of evidentiary hearing and completely disregarding the overwhelming body of evidence proving that mifepristone is safe, the District Court's order (the "Order") purported to suspend the use of a treatment essential to *amici*'s patients, in order to further its own agenda and that of Respondents. The decision is rife with medically inappropriate assumptions and terminology. It disregards decades of unambiguous analysis supporting the use of mifepristone in miscarriage and abortion care. It relies on pseudoscience and on speculation, and adopts wholesale and without appropriate judicial inquiry the assertions of a small group of declarants who are ideologically opposed to abortion care and at odds with the overwhelming majority of the medical community and the FDA.

The Fifth Circuit agreed to temporarily stay the Order as to the FDA's initial 2000 approval, but embraced the same flawed and unscientific logic as the District Court: (i) that the FDA's decision to begin alleviating the Risk Evaluation and Miti-

gation Strategies ("REMS") for mifepristone in 2016 was arbitrary and capricious, and (ii) that reinstating those unnecessarily harsh restrictions would help patients, not hurt them. On the contrary, the decisions below endanger *amici*'s patients by depriving them of medically appropriate, safe access to an effective and important medicine. This Court should not uphold or ignore a decision that is so demonstrably at odds with the facts and so hostile to *amici*'s patients.

Each *amici* organization and its members adhere to a standard of ethics and practice centered on patient care, and on the bedrock principal to "do no harm." The erroneous decision to reintroduce unnecessary restrictions on the prescription and use of mifepristone threatens the very core of *amici*'s medical practice by preventing the provision of appropriate, safe, and standard care for their patients.

Amici urge this Court to uphold science and the rule of law. Mifepristone is extremely safe and effective. Hundreds of medical studies and vast amounts of data amassed over the course of more than two decades have confirmed it. When mifepristone is used in medication abortion, as part of a two-step, two-drug regimen with misoprostol, serious side effects are exceedingly rare compared to many commonly used medications, occurring in ***less than 1%*** of patients. Major adverse events—significant infection, blood loss, or hospitalization—occur in ***less than 0.3%*** of patients. The risk of death is almost non-existent.

Mifepristone is not just used for medication abortion—it has become an essential medicine for the treatment of miscarriage as well. Miscarriage[3] is common. It can be dangerous, even life-threatening. The District Court's order purporting to prevent the use of mifepristone harms these patients too. Limiting patients' access to standard, safe care that will protect their lives, health, and ability to carry future pregnancies to term is an extraordinary departure from the provision of evidence-based medicine and the patient-centered approach that *amici* and their members advocate and practice.

The Fifth Circuit took issue with the FDA's scientific judgment that certain previous restrictions on the use of mifepristone are not actually necessary. REMS programs do not apply by default and should be deployed only where necessary to keep patients safe—circumstances that do not exist here. The REMS at issue do nothing to protect patients given mifepristone's demonstrated safety, and instead act only as a barrier to access. Science proves that. The hundreds of studies conducted prior to 2016 were more than sufficient to justify the FDA's decision to begin lifting restrictions. And studies conducted since 2016 have shown ***no increase*** in adverse events. In concluding otherwise, the Fifth Circuit has supplanted the FDA's judgment with its own—a dangerous precedent that will lead to uncertainty and destabilize the drug approval process in the United States.

[3] *See* ACOG Practice Bulletin No. 200, *Early Pregnancy Loss* (Nov. 2018, *reaff'd* 2021) ("Early pregnancy loss is defined as a nonviable, intrauterine pregnancy with either an empty gestational sac or a gestational sac containing an embryo or fetus without fetal heart activity within the first 12 6/7 weeks of gestation. In the first trimester, the terms miscarriage, spontaneous abortion, and early pregnancy loss are used interchangeably[.]").

Limiting access to mifepristone will not make patients safer—it will actively jeopardize their health. Pregnancy can be dangerous. The risks of maternal mortality in the U.S. are alarmingly high, and drastically higher for Black women, poor women, and all those whose access to reproductive care has been historically and geographically limited. Pregnancy can cause hemorrhaging, infection, dangerously high blood pressure, and many other critical physiological conditions. These dangers directly impair the health and well-being of pregnant patients, often in material ways. Abortion, including medication abortion involving a regimen of mifepristone and misoprostol, is an essential component of reproductive care that is protected in many states. Despite the harrowing stories coming out of states that are banning or severely restricting abortion, it is essential that miscarriage management remain available and accessible in all states. Limiting access to mifepristone simply endangers patients, regardless of whether they are seeking abortion or miscarriage care.

The Fifth Circuit's assumption that broad access to mifepristone increases the burden on our health care system is also incorrect. Removing the in-person dispensing requirement actively ***reduces*** any burden, as patients in need of abortion care are able to take mifepristone at home following consultation with their health care provider. And because mifepristone is an effective treatment for miscarriage as well as a range of other pregnancy-related conditions, reducing access to mifepristone will ***increase*** the burden on patients, clinicians, and the health care system as a whole by depriving countless patients of an established and effective form of care.

Failing to stay the Order in full will cause profound and irreparable harm to patients across the country. These impacts will be most severe for people of color as well as low-income and rural patients, who are more likely to die or develop serious complications from pregnancy, and more likely to have limited access to alternative procedures (i.e., procedural abortion) or lack the ability to travel long distances for health care. The FDA's decision to remove certain restrictions on the use of mifepristone—just like its initial approval—is supported by law and the overwhelming weight of medical evidence. This Court should grant Applicants' request to stay the Order.

ARGUMENT

The most common method of medication abortion in the U.S. is a two-drug regimen in which mifepristone is used in conjunction with misoprostol to end an early pregnancy by emptying the contents of the uterus.[4] Mifepristone followed by misoprostol is used both to induce abortion,[5] and in the treatment of miscarriage or early pregnancy loss (which can be life threatening),[6] a term which includes spontaneous abortion, missed abortion, incomplete abortion, or inevitable abortion.

The overwhelming weight of the scientific evidence supports the FDA's finding that mifepristone is safe and effective and that the restrictions on its use that

[4] A combined mifepristone-misoprostol regimen is the preferred therapy for medication abortion because it is more effective than a misoprostol-only regimen. *See* ACOG Practice Bulletin No. 225, *Medication Abortion Up to 70 Days of Gestation*, 1, 4 (Oct. 2020, *reaff'd* 2023).

[5] *Id.*

[6] *See* ACOG Practice Bulletin No. 200, *Early Pregnancy Loss* (Nov. 2018, *reaff'd* 2021).

were imposed in 2000 and codified in the REMS are no longer necessary. Mifepristone is one of the most studied medications prescribed in the U.S. and has a safety profile comparable to ibuprofen. Hundreds of studies and more than two decades of medical practice show that: (1) mifepristone is safe and effective; (2) special restrictions on its use are not necessary to keep patients safe; and (3) imposing unnecessary restrictions will limit access to mifepristone and have serious consequences for patients across the country—for those seeking abortions *and* for those experiencing pregnancy loss.

Respondents provide no scientific evidence supporting their position. They rely instead on anecdotes, speculation, and theories untested by cross-examination. The so-called studies on which the District Court relied are not scientifically tested or sound; they are produced by anti-abortion advocacy groups or contain serious (and often well-documented) methodological flaws—or both. If the District Court and Fifth Circuit are going to disregard the well-supported and expert judgment of an executive agency and rule to upend the status quo, they should not be permitted to do so based on untested claims outside the realm of mainstream, modern medical practice. If the District Court's decision is not stayed in full, it will impair access to safe and effective medical care for millions of women—whether seeking miscarriage or abortion care. This decision endangers the health and well-being of *amici*'s patients, and disrupts the sound, evidence-based practice of medicine that is at the very core of *amici*'s missions.

I. Mifepristone Has Been Thoroughly Studied and Is Conclusively Safe.

Decades of evidence demonstrate that medication abortion is safe and effective, with exceptionally low rates of major adverse events. Mifepristone's safety profile is on par with common painkillers like ibuprofen, which more than 30 million Americans take in any given day.[7] The District Court was wrong to conclude otherwise—and the Fifth Circuit was wrong to supplant the FDA's judgment with its own opinion. REMS are simply not necessary to maintain that safety profile.[8]

The FDA first approved the use of mifepristone in 2000, basing its decision on multiple, extensive clinical trials and sound research.[9] The FDA's analysis included an independent and unbiased review of the manufacturer's preclinical research and clinical test results to ensure that mifepristone was safe and effective, and that the health benefits outweighed the known risks.[10] It considered trials conducted for more than a decade and involving thousands of women.

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[7] *See* Nat'l Acads. of Sci., Eng'g. & Med., *The Safety and Quality of Abortion Care in the United States*, NAT'L ACADS. PRESS 45, 79 (2018); *see also* R. Morgan Griffin, *Making the Decision on NSAIDs*, WEBMD (Oct. 17, 2005), https://www.webmd.com/arthritis/features/making-decision-on-nsaids.

[8] Memorandum Opinion and Order, 2:22-CV-00223, Apr. 7, 2023, ECF No. 137, at 47 [hereinafter Mem]. Again, the District Court adopts Plaintiff-Respondents' assertions at its own, including statements that are purposefully inflammatory, are not based on the reality of a medication abortion in accordance with FDA's approved labeling, and are made without so much as a factual inquiry or an evidentiary hearing.

[9] *See* U.S. Gov't Accountability Off., GAO-08-751, *Report to Congressional Requestors: Food and Drug Administration Approval and Oversight of the Drug Mifeprex*, 1, 15–16 (Aug. 2008); 2000 FDA Approval Memorandum, Compl. Ex. 24, ECF No. 1-25.

[10] *See* Development & Approval Process: Drugs, FDA (Aug. 08, 2008), https://www.fda.gov/drugs/development-approval-process-drugs. In contrast, five other drugs were approved under restrictive Subpart H with clinical sample sizes of "several hundred patients or less." U.S. Gov't Accountability Off., *supra* note 9, at 26.

In the two decades since mifepristone's approval, and the many years since the FDA's 2016 review, hundreds of additional studies have reaffirmed that medication abortion is safe for patients—safer than pregnancy and safer than countless other medical procedures. To date, mifepristone has been discussed in more than 780 medical reviews and used in more than 630 published clinical trials—of which more than 420 were randomized controlled studies (the gold standard in research design).[11] These studies have repeatedly concluded that even minor complications arising from medication abortion are rare.[12]

Major adverse events—which include hospitalization and serious infection or bleeding—are "exceedingly rare," occurring in approximately 0.3% of cases.[13] Studies have shown an even smaller number, finding between 0.015% and 0.07% of patients experience serious infection.[14] The FDA has made clear that the same complications can be observed following a miscarriage, procedural abortion, or medication abortion—i.e., any time the pregnant uterus is emptied—and that "[n]o

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[11] Based on a review of PubMed, the National Institutes of Health's sponsored database of research studies.

[12] *See*, *e.g.*, Advancing New Standards in Reproductive Health ("ANSIRH"), *Analysis of Medication Abortion Risk and the FDA Report: Mifepristone US Post-marketing Adverse Events Summary through 6/30/2021*, UNIV. OF CAL., S.F. at 2 (Nov. 2022) [hereinafter "ANSIRH, Adverse Events 2021"]; ANSIRH, *Analysis of Medication Abortion Risk and the FDA Report: Mifepristone U.S. Post-Marketing Adverse Events Summary through 12/31/2018*, UNIV. OF CAL., S.F. (April 2019) [hereinafter "ANSIRH, Adverse Events 2018"]; ANSIRH, *Safety of Abortion in the United States*, UNIV. OF CAL., S.F. (Dec. 1, 2014) [hereinafter "ANSIRH, Abortion Safety"]; Nat'l Acads. of Sci., Eng'g. & Med., *supra* note 7.

[13] FDA Ctr. For Drug Eval. & Research, *Medical Review, Application No. 020687Orig1s020* at 56 (Mar. 29, 2016) [hereinafter "2016 FDA Medical Review"]; Ushma D. Upadhyay, et al., *Incidence of Emergency Department Visits and Complications After Abortion*, 125 OBSTET. & GYNECOL. 175, 175 (2015).

[14] 2016 FDA Medical Review, *supra* note 13, at 53–54.

causal relationship between the use of MIFEPREX and misoprostol and [infections and bleeding] has been established."[15]

The risk of death from medication abortion is near zero.[16] A 2019 analysis of FDA data examining potentially mifepristone-related deaths over an 18-year period by the University of San Francisco Medical Center found that only 13 deaths were possibly or probably related to medication abortion, yielding an approximate mortality rate of 0.00027%.[17] Even when considering deaths that followed a medication abortion but did not appear to be related to mifepristone use, that number rises to only 0.00053%.[18] While the District Court claims that "at least two women" died from medication abortion last year, this is demonstrably false—and underscores the danger of limiting access to mifepristone before a hearing on the merits.[19]

The mifepristone safety profile is similar to that of procedural abortion—and both are comparatively low compared to other common medications and procedures.[20] There is a greater risk of complications or mortality from procedures like

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[15] Mifeprex Prescribing Information, FDA at 2, 5 (Mar. 2016) https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/020687s020lbl.pdf.

[16] *See* Katherine Kortsmit, et al., *Abortion Surveillance – United States, 2019*, 70 CDC MORBIDITY & MORTALITY WKLY. REP. at 29, tbl. 15 (2021).

[17] ANSIRH, Adverse Events 2021, *supra* note 12, at 1–2.

[18] *Id.*

[19] Mem. at 53, 61; PPGNHAIK Statement on Incorrect Indiana Data, PLANNED PARENTHOOD (April 11, 2023), https://www.plannedparenthood.org/planned-parenthood-great-northwest-hawaii-alaska-indiana-kentuck/press/ppgnhaik-statement-on-incorrect-indiana-data.

[20] ANSIRH, Adverse Events 2021, *supra* note 12, at 2 ("[t]he safety profile [of medication abortion with mifepristone and misoprostol] is similar to that of vacuum aspiration abortion, and medication abortion is safer than continuing a pregnancy to term or using other common medications"); *see also* ANSIRH, *U.S. Studies on Medication Abortion without In-Person Clinician Dispensing of Mifepristone*, UNIV. OF CAL., S.F. (Oct. 2021); Elizabeth Raymond & Hillary Bracken, *Early Medical Abortion Without Prior Ultrasound*, 92 CONTRACEPT. 212 (2015); Upadhyay, et al. (2015), *supra* note 13.

wisdom-tooth removals, tonsillectomies, colonoscopies, and plastic surgeries, than by any abortion method (medication or procedural).[21] Using Viagra is more dangerous than using mifepristone. Studies have shown Viagra to be associated with 4.9 deaths per 100,000 prescriptions,[22] death by colonoscopy occurs in about 0.03% of cases,[23] and the "risk of death associated with childbirth [is] approximately 14 times higher" than the risk associated with an abortion.[24] Every drug has side effects, and every procedure has risks—but medication abortion is among the safest medical interventions in any category, pregnancy-related or not.[25]

The District Court did not consider these facts. Instead, it selectively relied on a narrow minority of biased and flawed studies in an attempt to set aside decades of safe, FDA-approved use. For example, it recites statistics on emergency room visits from a study whose author is an employee of an anti-abortion organiza-

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[21] *Compare* ANSIRH, Abortion Safety, *supra* note 12 (complication rate for wisdom-tooth extraction is approximately 3.5x higher than abortions; complication rate for tonsillectomies is approximately 4x higher than abortions) *with* ASGE Standards of Practice Comm., *Complications of Colonoscopy*, 74 AM. PLASTIC & RECONSTR. SURGERY 745, 745 (2011) (up to 33% of colonoscopies result in minor complications); Frederick M. Grazer & Rudolph H. de Jong, *Fatal Outcomes from Liposuction: Census Survey of Cosmetic Surgeon*s, 105 PLASTIC & RECONSTR. SURGERY 436, 441 (2000) (mortality rate from liposuction was 20 deaths per 100,000 patients).

[22] *See* Mike Mitka, *Some Men Who Take Viagra Die—Why?*, 283 JAMA, 590, 590–93 (Feb. 2, 2000).

[23] ASGE Standards of Practice Comm., *supra* note 21, at 747.

[24] Elizabeth G. Raymond & David A. Grimes, *The Comparative Safety of Legal Induced Abortion and Childbirth in the United States*, 119 OBSTET. & GYNECOL. 215, 215 (2012).

[25] Respondents also inaccurately claim that mifepristone acts as an "endocrine-disruptor" in adolescents. *See* Compl. ¶¶ 54, 60. Nothing suggests that medication abortion has any effect on adolescent development.

tion.[26] *Amici* strongly disagree with the District Court's approach and conclusions, and the Fifth Circuit's partial approval of that decision.

The District Court's unquestioning endorsement of Respondents' view that medication abortion causes emotional and physical harm is again unsupported by scientific fact. Studies show that patients who seek an abortion, including medication abortion, do not suffer from emotional distress or negative mental-health outcomes, and experience better long-term outcomes than those who seek abortion care but are denied it.[27] For example, participants who received abortion care confirmed in one study that they believed it had been the "right decision for them" in the years that followed.[28]

The District Court chose to rely on studies that served an agenda, including one cited "study" authored by an anti-abortion research group that was based on blog posts made on an anti-abortion website,[29] and on studies that have been widely critiqued by researchers and scholars for their serious methodological flaws.[30] The

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[26] *See, e.g.*, Mem. at 47 n.44-45. Study authors James Studnicki and Kathi Aultman are listed on the website of the Charlotte Lozier Institute as the Director of Analytics and as an Associate Scholar, respectively. The Charlotte Lozier Institute describes itself as the "research and education institute of Susan B. Anthony Pro-Life America." Charlotte Lozier Institute, *About Us*, https://lozierinstitute.org/about/, *see* Charlotte Lozier Institute, *Leadership and Staff*, https://lozierinstitute.org/leadership-and-staff.

[27] M. Antonia Biggs et al., *Women's Mental Health and Well-being 5 Years After Receiving or Being Denied an Abortion: A Prospective, Longitudinal Cohort Study*, 74 JAMA PSYCHIATRY 169, 177 (2017).

[28] Corrine H. Rocca et al., *Decision Rightness and Emotional Responses to Abortion in the United States: A Longitudinal Study*, 10 PLOS ONE, 1, 7 (2015).

[29] *See* Mem. at 46 n. 40-41.

[30] *Id.* at 11 (citing David C. Reardon et al., *Deaths Associated with Pregnancy Outcome: A Record Linkage Study of Low Income Women*, 95 S. MED. J. 834 (2002); Priscilla K. Coleman, *Abortion and Mental Health: Quantitative Synthesis and Analysis of Research Published 1995–2009*, 199 BRIT. J. PSYCHIATRY 180 (2011)).

District Court's selective reliance on pseudoscience endangers *amici*'s patients and their ability to provide safe, effective reproductive care. It purports to suspend the use of a common and safe medicine based on studies that are directly contradicted by the *vast* majority of research—research that demonstrates overwhelmingly and conclusively that there is no association between medication abortion and adverse physical or psychological outcomes.[31] This Court should not endorse that dangerous result.

II. REMS Restrictions Are Not Necessary to Ensure Patients' Safety.

When it revisited its guidance on mifepristone use in 2016, the FDA had exceptionally broad and strong confirmation of mifepristone's safety and efficacy. It therefore concluded that it could revisit certain aspects of the REMS put in place sixteen years prior. Each change to the REMS since 2016 has been fully supported by scientific evidence and has not changed mifepristone's safety profile.

The FDA's safety analysis relied on 11 independent clinical studies conducted between 2005 and 2015, covering "well over 30,000 patients,"[32] a randomized control trial,[33] and several observational studies,[34] all of which demonstrated the safety and

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[31] *See*, *e.g.*, Brenda Major et al., *Abortion and Mental Health: Evaluating the Evidence*, 64(9) AM. PSYCH. 863 (2009); M. Antonia Biggs, et al., *Mental Health Diagnoses After Receiving or Being Denied an Abortion in the United States* 105(12) AM. J. OF PUB. HEALTH 2557 (2015); Vignetta E. Charles, et al., *Abortion and Long-term Mental Health Outcomes: A Systematic Review of the Evidence*, 78(6) CONTRACEPT. 436 (2008).

[32] 2016 FDA Medical Review, *supra* note 13, at 50.

[33] *See id.* at 79.

[34] *See, e.g.*, *id.* at 18, 35–38.

effectiveness of mifepristone up to the ten-week gestational period.[35] Those studies conclusively demonstrated that "serious adverse events . . . are rarely reported . . . with rates ***generally far below 1.0%***."[36] This medicine is safer than countless other drugs on the market. Based on this sound, scientific evidence, the FDA determined that it was appropriate to adjust the heavy restrictions on mifepristone's use, and began unwinding previously mandated ultrasound requirements and other unnecessary barriers.

The agency concluded that mifepristone's safety profile was "well-characterized" and it could therefore remove the adverse reporting requirement imposed on Danco Labs from the REMS.[37] Contrary to what the District Court believes, this does *not* "ensur[e] that almost all new adverse events [will] go unreported or underreported."[38] As the FDA recognized in its 2016 Medical Review, Danco is still bound by 21 CFR § 314.80 to report serious, unexpected adverse events within 15 days, and all others on an annual basis.[39] The suggestion that recent safety data is somehow tainted by this decision or materially different from the data gathered

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[35] *See, e.g.*, Dina Abbas et al., *Outpatient Medical Abortion is Safe and Effective Through 70 Days Gestation*, 92 CONTRACEPT. 197 (2015); A.A. Boersma, et al., *Mifepristone Followed by Home Administration of Buccal Misoprostol for Medical Abortion Up to 70 Days of Amenorrhoea in a General Practice in Curacao*, 16 EUR. J. CONTRACEPT. REPROD. HEALTH CARE 61 (2011); E.V. Gouk, *Medical Termination of Pregnancy at 63 to 83 Days Gestation*, 106 BR. J. OBSTET. GYNAECOL. 535 (1999); Beverly Winikoff et al., *Extending Outpatient Medical Abortion Services Through 70 Days of Gestational Age*, 120 OBSTET. & GYNECOL. 1070 (2012). More recent studies have again confirmed these results. For example, a 2020 evidence review recognized that medication abortion can safely and effectively be used up to at least 70 days of gestation. *See* ACOG Practice Bulletin No. 225, *Medication Abortion Up to 70 Days of Gestation* at 1, 4 (Oct. 2020, *reaff'd* 2023).

[36] 2016 FDA Medical Review, *supra* note 13, at 56 (emphasis added).

[37] *Id.* at 8.

[38] Mem. at 59.

[39] *See* 2016 FDA Medical Review, *supra* note 13, at 8.

between 2000 and 2016 is simply incorrect. Adverse events are still being reported and mifepristone continues to be used safely and effectively.

The Fifth Circuit's conclusion that mifepristone's safety must have been a *result* of the REMS fundamentally misunderstands the science, and shows exactly why these decisions are best left to agency experts. For example, the ultrasound requirement was removed because, although an ultrasound *can* help determine gestational age and identify ectopic pregnancies, these goals can be accomplished *just as effectively* by discussing the patient's medical history—and that holds true even if the medical history is collected via telemedicine rather than in person.[40] The decision of which method to use should be left to the provider's reasonable judgment, based on the facts before them.

The District Court's purported concern that the FDA was abdicating its responsibilities and "assum[ing] physicians will ascertain gestational age"[41] fundamentally misunderstands the practice of medicine—which is not predicated solely on FDA medication approvals. To ensure the safety and wellbeing of their patients, physicians, and other practitioners follow clinical guidance and use their years of

[40] Compl. Ex. 24, ECF No. 1-25 at 6 ("In practice, dating pregnancies occurs through using other clinical methods, as well as through using ultrasound."); Raymond & Bracken, *supra* note 20, at 214 (noting that gestational dating using last monthly period rather than ultrasound may be reasonable for selected patients before medication abortion); *see also* Ushma D. Upadhyay et al., *Outcomes and Safety of History-Based Screening for Medication Abortion: A Retrospective Multicenter Cohort Study*, 182 JAMA INTERNAL MED. 482, 489 (2022) (finding that mifepristone labels could be revised to state that "if pregnancy duration can be reasonably estimated by history and if no symptoms or risk factors for ectopic pregnancy are present," ultrasonography should not be required); Holly Anger et al., *Clinical and Service Delivery Implications of Omitting Ultrasound before Medication Abortion Provided via Direct-to-Patient Telemedicine and Mail in the U.S.*, 104 CONTRACEPT. 659 (2021).

[41] Mem. at 51.

training, expertise, and experience to treat patients, which before prescribing mifepristone, require them to determine gestational age.[42]

Similarly, mifepristone's in-person dispensing requirement was removed in 2021 based on scientific evidence that doing so would not pose any additional harm to patients. In response to the COVID-19 pandemic, the FDA initially exercised its enforcement discretion to suspend the in-person dispensing requirement—but only after determining that the science "[did] not appear to show" that doing so would result in any "increases in serious safety concerns (such as hemorrhage, ectopic pregnancy, or surgical interventions)."[43] Months later, the FDA denied a Citizens Petition by anti-abortion organizations seeking to reinstate that constraint[44]—having confirmed that eliminating the in-person requirement had no effect on mifepristone's safety profile based on a comparison of adverse events data from before and during the suspension of this requirement, which revealed no significant change in safety profile.[45]

Given these facts and the dearth of accessible in-person health care in large portions of this country, there is no logical reason to declare the FDA's reasoned judgment arbitrary and capricious, or to create a precedent allowing a court to sub-

[42] ACOG Practice Bulletin No. 225, *Medication Abortion Up to 70 Days of Gestation* at 1, 4 (Oct. 2020, *reaff'd* 2023).

[43] Letter from Janet Woodcock, Acting Comm'r, FDA, to Maureen G. Phipps, Chief Exec. Officer, Am. Coll. of Obstetricians and Gynecologists, and William Grobman, President, Soc'y for Maternal-Fetal Med. at 2 (Apr. 12, 2021), https://www.aclu.org/wp-content/uploads/legal-documents/fda_acting_commissioner_letter_to_acog_april_12_2021.pdf.

[44] *See* Response Letter from FDA Ctr. For Drug Evaluation & Rsch. Amer. Ass'n of Pro-Life Obstetricians and Gynecologists and Amer. Coll. of Pediatricians, Docket No. FDA-2019-P-1534 (Dec. 16, 2021), https://www.regulations.gov/document/FDA-2019-P-1534-0016.

[45] *Id.* at 26–27.

stitute its judgment and reinstate requirements that have been shown, time and again, to provide no meaningful health benefits to patients.

III. Limiting Access to Mifepristone Will Harm Pregnant Patients and Have Severe Negative Impacts on the Broader Health Care System.

The Fifth Circuit's judicial expansion of the REMS will impose a severe cost on pregnant patients, their providers, and the health care system as a whole.

A. Expanding the REMS Will Harm Patients.

Even temporary lack of access to mifepristone—caused by a medically unnecessary expansion of the current REMS program—will cause patients to suffer serious physical harm, and even death. And because mifepristone has many uses outside of medication abortion, limiting access, even temporarily will also cause irreparable harm to patients who depend on this drug for miscarriage management and other conditions.

Abortion care can be lifesaving, especially for people suffering from serious health conditions or experiencing early pregnancy loss. Medication abortion's relative availability makes it more accessible to patients with limited access to medical care, including low-income patients and patients of color[46]—the very people who are most likely to experience severe maternal morbidity and more likely to die from

[46] *See* Christine Dehlendorf & Tracy Weitz, *Access to Abortion Services: A Neglected Health Disparity*, 22 J. HEALTH CARE FOR THE POOR & UNDERSERVED 415, 416 (2011); Jenna Jerman et al., *Characteristics of U.S. Abortion Patients in 2014 and Changes Since 2008*, GUTTMACHER INST. at 11 (May 2016); Rachel K. Jones et al., *COVID-19 Abortion Bans and Their Implications for Public Health*, 52 PERSPECTIVES ON SEXUAL & REPROD. HEALTH 65–67 (2020); *see also* Ctrs. for Medicare & Medicaid Servs., *CMS Rural Health Strategy* at 2 (2018), https://www.cms.gov/About-CMS/Agency-Information/OMH/Downloads/Rural-Strategy-2018.pdf.

pregnancy-related complications.[47] Indeed, 75% of those seeking abortion care are living at or below 200% of the federal poverty level, a majority of whom identify as people of color.[48] Pregnant people of color are also more likely to experience early pregnancy loss or miscarriage, the treatment for which can include procedural or medication abortion.[49] Restricting the use of mifepristone would only harm these patients by making an entirely safe treatment less available in the marketplace—resulting in the denial of medical care to many.

Substantial evidence demonstrates that the *denial* of abortion care alone causes harm. Patients who are denied abortions are more likely to experience intimate partner violence compared with patients who were able to have an abortion.[50] Studies have shown that being denied an abortion also exacerbated patients' economic hardships, revealing "large and statistically significant differences in the socioeconomic trajectories of women who were denied wanted abortions compared with women who received abortions—with women denied abortions facing more economic hardships."[51]

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[47] *See* Ctrs. for Medicare & Medicaid Servs., *Advancing Rural Maternal Health Equity* at 1 (May 2022), https://www.cms.gov/files/document/maternal-health-may-2022.pdf; *see also* Juanita Chinn, et al., *Health Equity Among Black Women in the United States*, 30 J. WOMEN'S HEALTH 212, 215 (2021).

[48] ACOG Committee Opinion No. 815, *Increasing Access to Abortion* (Dec. 2020).

[49] *See* Lyndsey S. Benson et al., *Early Pregnancy Loss in the Emergency Department, 2006–2016*, 2 J. AM. COLL. EMERGENCY PHYSICIANS OPEN e12549 at 2 (2021).

[50] *See* Sarah Roberts et al., *Risk of Violence from the Man Involved in the Pregnancy After Receiving or Being Denied an Abortion*, 12 BMC MEDICINE 1, 6 (2014).

[51] Diana Greene Foster et al., *Socioeconomic Outcomes of Women Who Receive and Women Who Are Denied Wanted Abortions in the United States*, 108 AM. J. PUB. HEALTH 407, 412 (2018).

Respondents' claim that continuing a pregnancy is a safer alternative—specifically, that "[p]regnancy rarely leads to complications that threaten the life of the mother or the child"[52]—is not based on science. Empirical evidence shows that women are at least 14 times more likely to die during childbirth than during any abortion procedure[53] and are at an increased risk of experiencing hemorrhage, infection, and injury to other organs during pregnancy and childbirth as well.[54] Even under the best of circumstances, pregnancy and childbirth impose significant physiological changes that can exacerbate underlying conditions and can severely compromise health, sometimes permanently.[55] Pregnancy, particularly when coupled with preexisting conditions, can quickly evolve into a life-threatening situation necessitating critical care, including abortion. Reverting to medically unnecessary restrictions will do nothing to alleviate those risks.

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[52] *See* Compl. ¶ 51.

[53] *See* Raymond & Grimes, *supra* note 24, at 216–17, fig. 1. The U.S. mortality rate associated with live births from 1998 to 2005 was 8.8 deaths per 100,000 live births. *Id.* at 216. Rates have sharply increased since then. *See, e.g.*, David Boulware, *Recent Increases in the U.S. Maternal Mortality Rate: Disentangling Trends from Measurement Issues*, 128 OBSTET. & GYNECOL. 447 (2016). By contrast, the mortality rate associated with legal abortions performed from 1998 to 2005 was 0.6 deaths per 100,000 procedures. *See* Raymond & Grimes, *supra* note 24, at 216. A committee of the National Academies in a 2018 peer-reviewed, evidence-based report similarly concluded that abortion is safer than pregnancy; Specifically, "the risk of death subsequent to a legal abortion (0.7 [deaths] per 100,000 [patients]) is a small fraction of that for childbirth (8.8 [deaths] per 100,000 [patients])." Nat'l Acads. of Sci., Eng'g. & Med., *supra* note 7, at 7.

[54] Raymond & Grimes, *supra* note 24, at 215, 216–17, fig.1.

[55] *See, e.g.*, ACOG Practice Bulletin No. 190, *Gestational Diabetes Mellitus* (Feb. 2018); ACOG Practice Bulletin No. 222, *Gestational Hypertension and Preeclampsia* (June 2020); ACOG Practice Bulletin No. 183, *Postpartum Hemorrhage* (Oct. 2017); ACOG Obstetric Care Consensus No. 7, *Placenta Accreta Spectrum* (July 2012, *reaff'd* 2021); ACOG Practice Bulletin No. 198, *Prevention and Management of Obstetric Lacerations at Vaginal Delivery* (Sept. 2018); ACOG Clinical Consensus No. 1, *Pharmacologic Stepwise Multimodal Approach for Postpartum Pain Management* (Sept. 2021).

Patients experiencing early pregnancy loss, miscarriage, and other maternal-health issues will also suffer. As with many medications, mifepristone also has many critical off-label uses beyond abortion.[56] Mifepristone is already widely prescribed for management and treatment of miscarriages, including spontaneous, missed, inevitable, and incomplete abortions.[57] Studies have also examined its use for a range of other maternal-health purposes, including treatment of uterine fibroids (tumorous growths of uterine muscle) and treatment of endometriosis (abnormal tissue growth outside the uterus, which can cause severe pain and infertility).[58] Mifepristone is also used off-label to reduce the duration of bleeding or hemorrhaging during certain serious pregnancy complications, and may have beneficial effects on the cervix in full-term pregnancies, which in turn may affect the likelihood of successful labor.[59] Restricting the use of mifepristone will harm patients seeking a prescription for reasons unrelated to abortion.

B. Physicians and the Health Care System Will Be Harmed by Expanded REMS.

Limiting access to mifepristone through restrictions the FDA has previously deemed unnecessary will harm physicians, and, at a macro level, increase the bur-

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[56] *See* Christopher M. Wittich et al., *Ten Common Questions (and Their Answers) About Off-Label Drug Use*, 87 MAYO CLINIC PROC. 982 (2012).

[57] *See* Mara Gordon & Sarah McCammon, *A Drug that Eases Miscarriages is Difficult for Women to Get*, NPR (Jan. 10, 2019), https://www.npr.org/sections/health-shots/2019/01/10/666957368/a-drug-that-eases-miscarriages-is-difficult-for-women-to-get.

[58] *See* Mario Tristan et al., *Mifepristone for Uterine Fibroids*, COCHRANE DATABASE SYST. REV. (2012); Y. X. Zhang, *Effect of Mifepristone in the Different Treatments of Endometriosis*, CLIN. AND EXP. OBSTET. & GYNECOL. 350 (2016).

[59] *See* Yanxia Cao et al., *Efficacy of Misoprostol Combined with Mifepristone on Postpartum Hemorrhage and its Effects on Coagulation Function*, 13 INT. J. CLIN. EXP. MED. 2234 (Apr. 30, 2020).

den on the nation's health care system, particularly women's health and OBGYN care. Medical facilities will experience an increased strain on already-limited resources.[60] Medication abortion allows patients to ingest their prescriptions safely at home after consultation with their health care providers, freeing clinicians and inpatient resources to focus on providing other needed care. The FDA's lifting of the REMS in 2016 had the same effect—which previously required physicians to dispense the medication to patients in person and required patients to travel for medically unnecessary follow-up appointments. Reinstating those restrictions without compelling justification—and against the FDA's sound scientific judgment—will not only harm individual patients, but unnecessarily strain practitioners and health care system as a whole.

Imposing medically unnecessary REMS also raises serious medical ethics concerns for providers. Physicians are required to ensure their patients have access to demonstrably safe and effective drugs, like mifepristone—particularly when that medication serves as a safe and effective alternative to other more invasive treatments. At their core, medical ethics require that "the welfare of the patient . . . form the basis of all medical judgments."[61] Revisiting the REMS the FDA has already determined, based on a wide range of medical studies and years of data, are no

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[60] *Cf.* Alexander Janke, *An Emergency in U.S. Emergency Care: Two Studies Show Rising Strain*, U. MICH. INST. OF HEALTHCARE POL'Y & INNOVATION (Oct. 7, 2022), https://ihpi.umich.edu/news/emergency-us-emergency-care-two-studies-show-rising-strain.

[61] ACOG, *Code of Professional Ethics* at 2 (Dec. 2018); AMA, Code of Medical Ethics Opinion 1.1.1 ("The relationship between a patient and a physician is based on trust, which gives rise to physicians' ethical responsibility to place patients' welfare above the physician's own self-interest or obligations to others, to use sound medical judgment on patients' behalf, and to advocate for their patients' welfare.").

longer beneficial to patients, undermines this principle, improperly inserts the courts in the doctor–patient relationship, and allows a court to supplant the FDA and a clinician's scientific and medical judgments regarding what is in the patients' best interests with a court's non-expert decision regarding whether and when physicians may provide routine, safe, and essential healthcare.

CONCLUSION

For the reasons explained above and outlined more fully in the Applicants' submissions, *Amici* respectfully urge the Court to grant Applicants' requested relief.

Respectfully submitted,

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