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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF HAWAIʻI

HEIDI PURCELL, M.D., FACOG, *et al.*

Plaintiffs,

v.

XAVIER BECERRA, J.D., *in his official capacity as* SECRETARY, U.S. D.H.H.S., *et al.*,

Defendants.

CIVIL ACTION

Case No. 1:17-cv-00493-JAO-RT

CORRECTED SECOND AMENDED AND SUPPLEMENTAL COMPLAINT

Plaintiffs, by and through their undersigned attorneys, bring this complaint against the above-named Defendants, their employees, agents, and successors in office, and in support thereof allege the following:

PRELIMINARY STATEMENT

1. Mifepristone is a prescription medication that U.S. patients have used for decades to end an early pregnancy by initiating a process very similar to a miscarriage.[1] As the U.S. Food and Drug Administration ("FDA" or "the Agency") observed in 2016, mifepristone "has been increasingly used as its efficacy and safety have become well-established by both research and experience, and serious complications have proven to be extremely rare."[2]

2. Indeed, safety data from mifepristone's 5.6 million uses in the United States confirm that it is far safer than many other common medications, including Tylenol and Viagra.[3]

3. Moreover, FDA has never concluded that any very rare serious complications were actually caused by mifepristone. To the contrary, mifepristone's FDA-approved labeling notes that the serious risks identified in mifepristone's labeling

[1] Plaintiffs use "mifepristone" to refer to both the brand-name drug, Mifeprex®, and its generic, mifepristone, which are subject to identical regulations.

[2] FDA 0539.

[3] U.S. Food & Drug Admin., Mifepristone U.S. Post-Marketing Adverse Events Summary through 06/30/2022, 2023 SUPP 001052–53.

are the same risks arising any time the pregnant uterus is emptied, whether through childbirth, miscarriage, or abortion.[4] And FDA has explained that in nearly all of the (very few) cases of fatal infections associated with mifepristone, the "critical risk factor . . . is pregnancy itself."[5]

4. Nevertheless, FDA subjects mifepristone to a Risk Evaluation and Mitigation Strategy ("REMS"), which is a special set of restrictions above and beyond the normal layers of protections that apply to virtually every other prescription drug.

5. Congress permits FDA to impose a REMS *only* when "necessary to ensure that the benefits of a drug outweigh [its] risks," considering certain statutorily mandated factors. 21 U.S.C. §355-1(a)(1). Congress established further safeguards around the imposition of the most burdensome kinds of REMS—Elements To Assure Safe Use ("ETASU")—which FDA may impose only when necessary because of the "inherent toxicity or potential harmfulness" of a drug. *Id.* § 355-1(f)(1). Specifically, FDA may impose ETASU on a drug that "has been shown to be effective" only if it is "associated with a serious adverse drug experience" such that it "can be approved only if, or [approval] would be withdrawn unless, such [ETASU] are required." *Id.* § 355-1(f)(1)(A). Even then, ETASU must be "*commensurate* with the specific serious risk[s]" listed in the drug's labeling, *id.* §

[4] FDA 0398.

[5] FDA 0880–81 & n.69.

355-1(f)(2)(A); "required as part of [a] strategy to *mitigate*" such risks, *id.* § 355-1(f)(1)(A); and not "*unduly burdensome* on patient access to the drug, considering in particular . . . . patients who have difficulty accessing health care (such as patients in rural or medically underserved areas)," *id.* § 355-1(f)(2)(C) (emphases added).

6. FDA imposes a REMS on fewer than 3% of the more than 20,000 drug products it regulates, and 75% of drugs subject to a REMS are opioids[6]—which "are claiming lives at [such] a staggering rate" that they "are reducing life expectancy in the United States."[7]

7. In 2017, Plaintiffs filed this litigation challenging FDA's 2016 final agency action reauthorizing a REMS, including three ETASU, for mifepristone.

8. In 2020, a coalition of medical experts led by the American College of Obstetricians and Gynecologists ("ACOG") challenged one of the mifepristone ETASU in a separate matter: *ACOG v. FDA*, 472 F. Supp. 3d 183 (D. Md. 2020). The plaintiffs in *ACOG* argued that FDA's longstanding requirement that mifepristone be dispensed only in a hospital, clinic, or medical office was medically unnecessary and exposed patients to needless burdens and viral risks during the COVID-19 pandemic. *Id.* The U.S. District Court for the District of Maryland

[6] Joint Stip. of Facts ¶¶ 58–59 (ECF 85).

[7] *Opioid Medications*, U.S. Food & Drug Admin., https://www.fda.gov/drugs/information-drug-class/opioid-medications (last updated Mar. 29, 2021), 2021 REMS 001813–16.

preliminarily enjoined this ETASU over defendants' objection that "based on FDA's scientific judgment, the In-Person Requirements are necessary to assure safe use of mifepristone and thus to protect patients' safety." *Id.* at 228. That injunction remained in place for six months. *FDA v. ACOG*, 141 S. Ct. 578, 578 (2021) (mem.) (granting stay).

9. In April 2021, FDA announced that it would exercise enforcement discretion with respect to the mifepristone in-person dispensing ETASU for the duration of the COVID-19 Public Health Emergency.[8] The Agency conceded that, during the six-month period when the in-person dispensing requirement was enjoined and mifepristone was available through mail-order pharmacies, there was *no* increase in adverse safety events.[9]

10. The next month, in May 2021, Plaintiffs in the instant case moved for summary judgment. Shortly before FDA's brief was due, the Agency notified Plaintiffs that it was undertaking a new review of the mifepristone REMS. On the

[8] U.S. Food & Drug Admin., REMS Review Memorandum (Jan. 3, 2023) [hereinafter "2023 REMS Review"], at 2023 SUPP 001117.

[9] U.S. Food & Drug Admin., REMS Review Memorandum (Dec. 16, 2021) [hereinafter "2021 REMS Review"], at 2021 REMS 001598 ("We further conclude, based our review of the postmarketing safety data from FAERS during the COVID-19 PHE and information submitted by the applicants for the timeframe of January 27, 2020 through September 30, 2021, that there does not appear to be a difference in adverse events between periods during the COVID-19 PHE when the in-person dispensing requirement was being enforced and periods when the in-person dispensing requirement was not being enforced; nor have we identified any new safety concerns with the use of mifepristone for medical termination of early pregnancy.").

condition that FDA would "review any relevant data and evidence submitted by the Plaintiffs," Joint Mot. Stay 2 (ECF 148), the parties jointly moved for a stay.

11. In August and September 2021, Plaintiffs submitted to FDA two letters explaining why the mifepristone REMS is medically unjustified and burdens patients and the health care system. Plaintiffs cited statements opposing the mifepristone REMS by other leading medical associations, including the American Medical Association ("AMA"), ACOG, and the American Academy of Family Physicians ("AAFP").[10] And, among other research, Plaintiffs cited data showing that after Canada eliminated its restrictions on mifepristone in 2017 to allow for normal prescribing, medication abortion remained extremely safe, with a major complication rate of only 0.33%.[11]

12. In addition, Plaintiffs gave examples of other medications that pose risks greater than or comparable to that of mifepristone but are *not* subject to a REMS. For instance, Plaintiffs noted that Jeuveau® is not subject to a REMS, even though it is used for a purely cosmetic purpose—temporarily reducing the appearance of lines between one's eyebrows—and carries an FDA black-box warning for "[s]wallowing and breathing difficulties" that "can be life threatening," with "reports

[10] *See generally* Letter from *Chelius* Plaintiffs to Janet Woodcock, MD (Sept. 29, 2021) [hereinafter "*Chelius* Plaintiffs' Letter"], at 2021 REMS 001159–67; Letter from Soc'y of Family Planning to U.S. Food & Drug Admin. (Aug. 11, 2021), at 2021 REMS 000950–55.

[11] *Chelius* Plaintiffs' Letter, *supra* note 10, at 2021 REMS 001160.

of death."[12]

13. In January 2023, FDA reauthorized the mifepristone REMS.[13] While permanently eliminating in-person dispensing, FDA retained the other two ETASU—including one that the Agency's own scientific review team had recommended removing in 2016 because it is "duplicative" and "does not add to safe use conditions."[14] Moreover, FDA added a *new* ETASU requiring pharmacies to become "certified" before they can dispense mifepristone—notwithstanding that pharmacies had dispensed mifepristone throughout the pandemic with no certification requirement and no increase in adverse events.

14. FDA's REMS Review memoranda reflect that, in reauthorizing the REMS in 2023, the Agency nowhere considered many of the statutory factors Congress requires to inform a decision whether to impose a REMS and ETASU, such as the "background incidence" of adverse events in the population likely to use the drug and whether the drug is a "new molecular entity" posing potentially unknown risks. 21 U.S.C. § 355-1 (a)(1). Accordingly, the Agency never grappled with facts critical to the mifepristone REMS analysis—including FDA's admissions that continuing a pregnancy is many times more dangerous than ending a pregnancy with mifepristone

[12] *Id.* at 2021 REMS 001161.

[13] Risk Evaluation & Mitigation Strategy (REMS) Single Shared System for Mifepristone (2023), 2023 SUPP 001466–70.

[14] FDA 0437, 0674.

and misoprostol;[15] that the risks associated with mifepristone are inherent to pregnancy and have never been shown to be caused by mifepristone rather than by pregnancy itself;[16] and that mifepristone is a very common and well-studied medication with an extremely strong and stable risk profile.[17]

15. FDA also nowhere explained how its ETASU could possibly be "commensurate" with the risks listed in the mifepristone labeling when FDA does not impose similar restrictions on other, riskier drugs. 21 U.S.C. § 355-1(f)(2)(A).

16. And FDA expressly declined to consider, *inter alia*, the positions of leading medical associations that the mifepristone REMS is not supported by science and harms patients and the health care system; and evidence showing that the mifepristone ETASU are "unduly burdensome on patient access to the drug," particularly for "patients in rural or medically underserved areas" who struggle to obtain abortion care. *Id.* § 355-1(f)(2)(C).

17. At bottom, FDA's latest REMS analyses—just like the 2016 REMS decision Plaintiffs originally challenged—assumes without supporting data that the

[15] FDA 0859 & n.6 (FDA relying on study finding that "the risk of childbirth related death was therefore approximately 14 times higher than the rate associated with legal abortion").

[16] FDA 0383–84, 0387, 0398.

[17] *See, e.g.*, 2021 REMS Review, *supra* note 9, at 2021 REMS 001582, 001591; FDA 0535 (after 15 years of mandatory adverse event reporting under the REMS, FDA "has determined that the safety profile of Mifeprex is well-characterized, that no new safety concerns have arisen in recent years, and that the known serious risks occur rarely"); FDA 0574 (major adverse events associated with mifepristone are "exceedingly rare").

restrictions the Agency put in place long ago, when mifepristone was still a novel drug in the United States, remain necessary after millions of uses and mountains of evidence confirming mifepristone's safety and efficacy.

18. The elimination of in-person dispensing—a decision FDA made only *after* a federal court injunction confirmed that the Agency's speculative safety concerns were unfounded—removed one key barrier that had prevented clinicians, including former Plaintiff Dr. Graham Chelius and Plaintiff Dr. Heidi Purcell, from prescribing mifepristone at all, as well as forcing countless patients to travel unnecessarily when they could otherwise safely obtain their prescription through telemedicine and by mail.

19. Nevertheless, the 2023 REMS continues to significantly impede patients' access to mifepristone—including by (1) creating an administrative morass for clinicians seeking to integrate mifepristone into their health care systems, delaying or altogether derailing their efforts to provide this care; (2) posing logistical and technological challenges for patients and providers; (3) deterring qualified clinicians from prescribing mifepristone because they fear anti-abortion violence and harassment if their registration as a mifepristone prescriber were ever exposed; (4) deterring pharmacies from dispensing mifepristone because of the burdens of certification; (5) impeding research and training on mifepristone at academic institutions because of stigma arising from a REMS classification; and (6)

undermining the informed consent process and provider-patient relationship by mandating counseling that is at best duplicative—and often inaccurate, confusing, and distressing.

20. In the wake of the U.S. Supreme Court's decision in *Dobbs v. Jackson Women's Health Org.*, 142 S. Ct. 2228 (2022), abortion access is decimated in much of the country and the United States faces a growing maternal mortality crisis, particularly for people of color. Against that backdrop, there is an ever more urgent need to eliminate FDA's medically unjustified restrictions on mifepristone, which needlessly reduce health care capacity and burden patients in those states where abortion access remains lawful, but is under tremendous strain.

JURISDICTION AND VENUE

21. This Court has subject matter jurisdiction over Plaintiffs' federal claims under Article III of the Constitution and 28 U.S.C. § 1331, as a civil action arising under the laws of the United States; 28 U.S.C. § 1346(a)(2), as a civil action against the federal government; 28 U.S.C. § 1343(a)(4), as a civil action to secure equitable or other relief under any Act of Congress providing for the protection of civil rights; and 5 U.S.C. § 702, as a civil action seeking judicial review of a final agency action.

22. Plaintiffs' action for declaratory and injunctive relief is authorized by 28 U.S.C. §§ 2201, 2202, and 1361, Federal Rules of Civil Procedure 57 and 65, and by the inherent equitable powers of this Court.

23. There exists an actual and justiciable controversy between Plaintiffs and Defendants requiring resolution by this Court. Plaintiffs have no adequate remedy at law.

24. This Court has authority to award costs and attorneys' fees under 28 U.S.C. § 2412.

25. Venue is proper in the District of Hawai‘i pursuant to 28 U.S.C. §§ 1391(b) and (e)(1), and 1402(a)(1), because this is a civil action in which Defendants are an agency, or officers of an agency, of the United States, because a substantial part of the events or omissions giving rise to this action occurred in the District, and because Plaintiff Dr. Heidi Purcell resides in the District.

PARTIES

A. Plaintiffs

26. Plaintiff Heidi Purcell, M.D., FACOG, is a board-certified obstetrician-gynecologist. She works for the Hawaii Health Systems Corporation's ("HHSC") Kaua‘i Region, including at Kauai Veterans Memorial Hospital in Waimea, Kaua‘i, on the western side of the island ("Kauai Veterans"), Samuel Mahelona Memorial Hospital in Kapa‘a, Kaua‘i, on the eastern side of the island, and other outposts of HHSC's Rural Health Clinic. Dr. Purcell is the Medical Director of Obstetrics for the HHSC Kaua‘i Region. She has delivered hundreds of babies over the past three and a half years on an island of approximately 74,000 people, and delivered

thousands more in her career. Dr. Purcell brings this lawsuit solely in her individual capacity and does not speak on behalf of HHSC. Dr. Purcell is a resident of the State of Hawai‘i.

27. The mifepristone REMS undermines Dr. Purcell's relationship with and counseling of her patients who use mifepristone, and jeopardizes her patients' privacy and safety. She sues on her own behalf and on behalf of her patients.

28. Plaintiff Society of Family Planning ("SFP") is a non-profit corporation with staff locations throughout the United States, incorporated in the state of Illinois. SFP is a national member association of clinicians, scholars, and partners united around advancing just and equitable abortion and contraception, informed by science. Membership in SFP is open to individuals who are in good professional standing and have a demonstrated interest in conducting or leveraging family planning research. Since its incorporation in 2005, SFP's membership has grown to over 1,400 members based primarily in the United States. Its members are trained in obstetrics and gynecology, internal medicine, family medicine, pediatrics/adolescent medicine, public health, demography, nursing, epidemiology, and other specialties. SFP works to advance sexual and reproductive health by providing evidence-based insight to improve clinical care in the areas of contraception and abortion. SFP also seeks to cultivate a collaborative and supportive environment to foster scholarly activity and leadership in the areas of reproductive health and family planning.

29. SFP has members who are prevented from providing mifepristone to their patients because of the REMS. The REMS also impedes some of SFP's members from engaging in research and publication relating to mifepristone; undermines some of SFP's members' relationships with and counseling of their patients; jeopardizes the privacy and safety of some of SFP's members' patients; and prevents some of SFP's members' patients from using telemedicine to obtain mifepristone. SFP sues on behalf of its members and their patients.

30. The California Academy of Family Physicians ("CAFP") is a non-profit professional association located in San Francisco, California. With nearly 11,000 family physician, family medicine resident, and medical student members, CAFP is the largest primary care medical society in California and the largest chapter of the American Academy of Family Physicians. Since 1948, it has engaged in advocacy and education to help family physicians improve their practices and expand access to high-quality and cost-effective patient care in California. To that end, CAFP offers affordable, evidence-based continuing medical education, provides cost-saving practice management resources, and fosters opportunities to promote the family medicine specialty and ensure a strong and healthy primary care pipeline. CAFP brings this lawsuit as an individual chapter and not as a representative of the American Academy of Family Physicians.

31. CAFP has members who are prevented from providing mifepristone to their patients because of the mifepristone REMS. The REMS also impedes some of CAFP's members from engaging in research and publication relating to mifepristone; undermines some of CAFP's members' relationships with and counseling of their patients; jeopardizes the privacy and safety of some of CAFP's members' patients; and prevents some of CAFP's members' patients from using telemedicine to obtain mifepristone. CAFP sues on behalf of its members and their patients.

B. Defendants

32. Defendant Xavier Becerra, J.D., who is being sued in his official capacity only, is the Acting Secretary of the United States Department of Health and Human Services ("HHS") and is responsible for administering and enforcing the FDCA. In particular, the Secretary is responsible for determining, in consultation with the office responsible for reviewing a drug and the office responsible for post-approval safety with respect to a drug, whether a REMS "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 Secretary may also, in consultation with the office responsible for reviewing the drug and the office responsible for post-approval safety with respect to the drug, require that any REMS include such ETASU as are necessary based on the drug's

"inherent toxicity or potential harmfulness." *Id.* § 355-1(f)(1). Defendant Becerra maintains an office in Washington, D.C.

33. Defendant FDA is an agency of the United States Government within HHS with offices in Washington, D.C., and Silver Spring, Maryland. The Secretary of HHS has delegated to FDA the authority to administer the relevant provisions of the FDCA.

34. Defendant Robert M. Califf, M.D., who is being sued in his official capacity only, is the Commissioner of Food and Drugs and is responsible for supervising the activities of FDA, including with regard to the imposition or removal of a REMS. Defendant Califf maintains offices in Washington, D.C., and Silver Spring, Maryland.

STATUTORY FRAMEWORK

A. FDA Approval Process for New Drugs

35. Before a drug can be marketed in the United States, the drug's sponsor must submit a new drug application ("NDA") to FDA. If the NDA demonstrates that the drug is safe and effective, FDA will approve it.

36. According to FDA's website, this approval process incorporates three elements: *First*, "[a]nalysis of the target condition and available treatments," under which the Agency's reviewers

> analyze the condition or illness for which the drug is intended and evaluate the current treatment landscape, which provide the context for weighing the drug's risks and benefits. For example a drug intended to treat patients with a life-threatening disease for which no other therapy exists may be considered to have benefits that outweigh the risks even if those risks would be considered unacceptable for a condition that is not life-threatening.[18]

Second, FDA performs an "[a]ssessment of benefits and risks from clinical data." FDA explains that, "[g]enerally, the agency expects that the drug maker will submit results from two well-designed clinical trials," although "[i]n certain cases . . . convincing evidence from one clinical trial may be enough. Evidence that the drug will benefit the target population should outweigh any risks and uncertainties."[19] *Third*, FDA considers "[s]trategies for managing risks." The Agency notes: "All drugs have risks. Risk management strategies include an FDA-approved drug label, which clearly describes the drug's benefits and risks, and how the risks can be detected and managed. Sometimes, more effort is needed to manage risks. In these cases, a drug maker may need to implement a Risk Management and Mitigation Strategy (REMS)."[20]

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[18] *Development & Approval Process (Drugs)*, U.S. Food & Drug Admin., https://www.fda.gov/drugs/developmentApprovalProcess/default.htm (last updated Aug. 8, 2022).

[19] *Id.*

[20] *Id.*

37. Based on this review, the Agency either: (1) approves the drug; (2) informs the sponsor that the drug is likely to be approved once certain deficiencies in the NDA are resolved; or (3) indicates that approval cannot be obtained without substantial additional data.

38. The Agency follows a similar process in evaluating a *supplemental* NDA, in which a drug sponsor requests approval to make changes to the labeling of a previously approved drug, or to market the drug for a new indication.

39. FDA has authority under Section 506 of the FDCA (codified at 21 U.S.C. § 356) and its "Subpart H" regulations (21 C.F.R. §§ 314.500–560) to expedite approval of a new drug if it is a "promising therap[y] that treat[s] a serious or life-threatening condition and provide[s] therapeutic benefit over available therapies."[21]

40. The Agency can condition approval for an NDA on the adoption of certain safety elements (*i.e.*, ETASU), such as a restricted distribution scheme. Until 2007, FDA's primary authority to impose such elements was derived from the Subpart H regulations. However, this authority was effectively replaced by the REMS statute, described below, which was adopted as part of the Food and Drug Administration Amendments Act of 2007 ("FDA Amendments Act").

[21] *Id.*

41. Section 909 of the FDA Amendments Act states that all drugs licensed before March 2008 that were approved under Subpart H with ETASU would be automatically deemed to have an approved REMS in place. The Agency can, however, impose a REMS for any drug that fits the statutory criteria, not only those drugs originally approved under Subpart H.

B. The REMS Statute

42. The FDA Amendments Act amended the FDCA to add a new section 505-1 (codified at 21 U.S.C. § 355-1) authorizing the Secretary of HHS, in consultation with FDA's Office of New Drugs and the Office of Surveillance and Epidemiology, to impose a REMS if—and only if—"necessary to ensure that the benefits of a drug outweigh [its] risks . . . ." 21 U.S.C. § 355-1(a)(1).

43. To determine whether a REMS is necessary, the Secretary must consider six factors: (1) "[t]he estimated size of the population likely to use the drug involved," (2) "[t]he seriousness of the disease or condition that is to be treated with the drug," (3) "[t]he expected benefit of the drug with respect to such disease or condition," (4) "[t]he expected or actual duration of treatment with the drug," (5) "[t]he seriousness of any known or potential adverse events that may be related to the drug and the background incidence [*i.e.*, frequency] of such events in the population likely to use the drug," and (6) "[w]hether the drug is a new molecular entity." *Id.*

44. A REMS may include any or all of the following: a medication guide and/or patient package insert; a communication plan; and elements to assure safe usage (*i.e.*, ETASU), such as a restricted distribution scheme. *Id.* § 355-1(e)-(f).

45. ETASU are the most restrictive and burdensome type of REMS. The FDCA authorizes the Agency to impose ETASU only where "necessary to assure safe use of the drug, *because of its inherent toxicity or potential harmfulness*," *id.* § 355-1(f)(1) (emphasis added), and only if the drug is "associated with a serious adverse drug experience," *id.* § 355-1(f)(1)(A), which is defined by statute as an adverse event associated with use of the drug that results in death, the immediate risk of death, inpatient hospitalization or prolonging existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, a congenital anomaly or birth defect, or a medical or surgical intervention to prevent these outcomes, *id.* § 355-1(b)(4).

46. Moreover, FDA may impose ETASU only where "required as part of [a] strategy *to mitigate a specific serious risk*"—*i.e.*, a "serious adverse drug experience," *id.* § 355-1(b)(5)—"listed in the labeling of the drug," and the risk must be sufficiently great that FDA would not approve, or would withdraw approval for, the drug absent the ETASU. *Id.* § 355-1(f)(1)(A) (emphasis added).

47. Congress imposed several additional requirements to ensure that FDA appropriately balances such an inherently toxic drug's benefits against its "serious

risks." The ETASU requirements must "be *commensurate* with the specific serious risk[s]" listed in the drug's labeling, and may "not be *unduly burdensome* on patient access to the drug, considering in particular . . . . patients who have difficulty accessing health care (such as patients in rural or medically underserved areas)." *Id.* §§ 355-1(f)(2)(A), (C) (emphases added). In addition, "to the extent practicable, so as to minimize the burden on the health care delivery system," ETASU must "conform with elements to assure safe use for other drugs with similar, serious risks." *Id.* § 355-1(f)(2)(D).

48. A modification or removal of a REMS may be initiated by a "responsible person" (*i.e.*, the drug's sponsor) or by the Secretary of HHS, who may "require a responsible person to submit a proposed modification to the strategy." *Id.* §§ 355-1(g)(4)(A), (B).

49. In addition, the Secretary of HHS must "periodically evaluate, for 1 or more drugs, the [ETASU] to assess whether the elements (i) assure safe use of the drug; (ii) are not unduly burdensome on patient access to the drug; and (iii) to the extent practicable, minimize the burden on the health care delivery system." *Id.* § 355-1(f)(5)(B). Then, "considering such input and evaluations," the Agency must "modify [ETASU] for 1 or more drugs as appropriate." *Id.* § 355-1(f)(5)(C).

FACTUAL ALLEGATIONS

A. Mifepristone Regimen and Safety Record

50. The current FDA-approved regimen for the medical termination of early pregnancy involves two drugs: (1) *mifepristone* (under the brand name Mifeprex or as a generic), which interrupts early pregnancy by blocking the effect of progesterone, a hormone necessary to maintain a pregnancy, and (2) *misoprostol* (under the brand name Cytotec® or as a generic), which causes uterine contractions that expel the pregnancy from the uterus. FDA expressly authorizes misoprostol for use as part of this regimen although misoprostol's own marketing approval is only for the prevention of gastric ulcers.

51. FDA has approved the use of this regimen through 70 days (*i.e.*, 10 weeks) of pregnancy, when the overwhelming majority (more than 80%) of abortions occur.[22]

52. The FDA-approved regimen for mifepristone states that the patient initiates the abortion by taking one 200 mg tablet of mifepristone in a single oral dose on day one, and then 24–48 hours later takes four 200 mcg tablets of misoprostol buccally (*i.e.*, by placing two pills in each cheek pouch—the area between the cheek and the gums—for 30 minutes and then swallowing any remnants with water or another

[22] Katherine Kortsmit et. al., Ctrs. for Disease Control & Prevention, *Abortion Surveillance – United States, 2020*, 71 Morbidity & Mortality Weekly Report 1 (Nov. 25, 2022), https://www.cdc.gov/mmwr/volumes/71/ss/ss7110a1.htm.

liquid). The FDA-approved labeling does not specify where patients should be located when they take either medication. Most people will expel the pregnancy within 2 to 24 hours after taking the misoprostol. The patient is instructed to follow up with their health care provider approximately 7 to 14 days later to confirm that the termination of pregnancy was successful, but the FDA labeling no longer anticipates that this follow-up evaluation will occur in-person.

53. Like all medication labels, the mifepristone labeling warns about potential risks associated with the drug. Its labeling lists as risks "serious and sometimes fatal infections or bleeding."[23]

54. As FDA explained in its Summary Review Memorandum for Mifeprex in March 2016, which evaluated changes to the Mifeprex labeling and REMS, "there have been approximately 2.5 million uses of Mifeprex by U.S. women since the drug's approval in 2000."[24] During that time, FDA noted, medication abortion "has been increasingly used as its efficacy and safety have become well-established by both research and experience, and serious complications have proven to be extremely rare."[25] The Agency further stated that "[t]he safety profile of Mifeprex is well-characterized and its risks well-understood after more than 15 years of

[23] FDA 0383–84.

[24] FDA 0422.

[25] FDA 0539.

marketing. Serious adverse events are rare and the safety profile of Mifeprex has not substantially changed."[26]

55. Mifepristone is also FDA-approved under the brand name Korlym® in 300 mg tablets for *daily use* by patients with endogenous Cushing's syndrome to treat high blood sugar caused by high cortisol levels in the blood. Korlym is available only from a specialty pharmacy, but it is *not* subject to a REMS. A patient's doctor submits a patient enrollment form and prescription for Korlym to a specialty pharmacy, which delivers the drug to the patient's home. The patient is then responsible for taking one to four pills (300 mg to 1200 mg, 1.5 to 6 times the recommended dose for Mifeprex) daily at home according to their prescription. In its 2016 Medical Review of Mifeprex, the Agency observed that "Korlym is taken in higher doses, in a chronic, daily fashion unlike the single 200 mg dose of Mifeprex that is the subject of this supplement; the rate of adverse events with Mifeprex is much lower."[27]

56. Mifepristone is also frequently prescribed with misoprostol as part of a regimen for medical management of early pregnancy loss. SFP, ACOG, and other leading medical associations recommend that clinicians prescribing medications to treat a miscarriage (*i.e.*, to completely evacuate the patient's uterus) utilize the

[26] FDA 0681.

[27] FDA 0537.

combined mifepristone-misoprostol regimen whenever mifepristone is available. But, as ACOG notes in its Practice Bulletin on Early Pregnancy Loss, while "[t]he addition of a dose of mifepristone (200 mg orally) 24 hours before misoprostol administration may significantly improve treatment efficacy . . . the availability of mifepristone is limited by the [FDA]'s Risk Evaluation and Mitigation Strategy restrictions."[28]

B. FDA Approval of Mifeprex and Imposition of the REMS

1. Initial FDA Approval

57. Mifepristone was approved for the medical termination of early pregnancy in France and China in 1988; in the United Kingdom in 1991; in Sweden in 1992; and in numerous other European countries throughout the 1990s.

58. In March 1996, the Population Council, a non-profit organization based in the United States, sponsored an NDA for Mifeprex for use in combination with misoprostol for the medical termination of early pregnancy. In 1999, the Population Council contracted with Danco Laboratories, L.L.C. ("Danco") for the manufacturing and marketing of the medication.

59. There were three historically-controlled clinical trials on the safety and efficacy of the Mifeprex and misoprostol regimen presented to FDA as part of the

[28] ACOG, Practice Bulletin No. 200: Early Pregnancy Loss (Nov. 2018), 2021 REMS 000578–88.

original NDA application, together involving 4,000 women: two trials conducted in France, which were complete at the time of the application, and one then-ongoing trial in the United States for which summary data on serious adverse events were available. The Agency has explained that "[t]he data from these three clinical trials . . . constitute substantial evidence that Mifeprex is safe and effective for its approved indication in accordance with [the FDCA]."[29] As part of the NDA review, FDA also considered: (1) results from other European trials from the 1980s and 1990s in which mifepristone was studied alone or in combination with misoprostol or similar drugs; (2) a European postmarket safety database of over 620,000 women who used medication to terminate a pregnancy (approximately 415,000 of whom had received a mifepristone/misoprostol regimen); and (3) data on the drug's chemistry and marketing.

60. Four years later, in September 2000, FDA granted final marketing approval for Mifeprex for use in combination with misoprostol for the termination of pregnancy up to 49 days.

61. Despite the strong findings on the safety and efficacy of Mifeprex from clinical trials and European post-market experience, and despite the fact that the approval process was not expedited, the Agency approved Mifeprex under Subpart

[29] FDA 0863.

H (which provides for accelerated approval—though, in fact, this four-year process was not expedited) and imposed ETASU—a restricted distribution system—as a condition of approval.

62. The ETASU imposed at the time of Mifeprex's original approval are substantively identical to the ETASU that FDA renewed in 2011 and again in 2016, described in detail *infra*.

63. According to a report by the U.S. Government Accountability Office ("GAO"), FDA stated that Mifeprex fit within the scope of Subpart H because unwanted pregnancy poses a risk of serious or life-threatening complications, Mifeprex terminates an unwanted pregnancy, and Mifeprex allows patients to avoid the risks incident to a surgical abortion procedure.[30] FDA further stated that the restricted distribution scheme was necessary to ensure patient safety, and that approving Mifeprex under Subpart H would allow FDA to impose comparable restrictions on any future generic mifepristone products.[31]

64. The Agency's decision to subject Mifeprex to an ETASU under Subpart H was highly unusual. In the fifteen years from 1992 (the year the Subpart H regulations were promulgated) to February 2007 (just before the creation of the

[30] U.S. Gov't Accountability Office, *Food and Drug Administration: Approval and Oversight of the Drug Mifeprex*, GAO-08-751, 22 (Aug. 2008), *available at* http://www.gao.gov/new.items/d08751.pdf.

[31] *Id.* at n.41.

REMS statute), only seven NDAs, including Mifeprex, were approved subject to ETASU under Subpart H.[32] By comparison, there were 961 NDAs approved in the roughly thirteen years from January 1993 to September 2005.[33]

65. Though noting its objections, the Population Council agreed to the restrictions in September 2000, and Danco began distribution of Mifeprex in November 2000. The Population Council subsequently transferred ownership of the NDA to Danco.

2. 2008 and 2011 Imposition of the Mifeprex REMS

66. In a rule released in March 2008 pursuant to the FDA Amendments Act, the Agency identified Mifeprex as one of the drugs deemed to have an approved REMS in effect because it already had ETASU in place under Subpart H. Mifeprex continued to be distributed subject to the same restrictions under which it was originally approved.

67. In 2011, FDA issued a new REMS for Mifeprex incorporating the same restrictions under which the drug was approved eleven years earlier. Specifically, the Mifeprex REMS approved in 2011 required three elements:

68. *First*, a Medication Guide to be dispensed with each Mifeprex prescription.

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[32] *Id.* at n.6, 27.

[33] U.S. Gov't Accountability Office, *New Drug Development: Science, Business, Regulatory, and Intellectual Property Issues Cited as Hampering Drug Development Efforts*, GAO-07-49, 20 (Nov. 2006), *available at* http://www.gao.gov/new.items/d0749.pdf.

69. *Second*, the 2011 REMS included three types of ETASU (A, C, and D):

- ETASU A required clinicians to self-certify before they could prescribe Mifeprex. To be certified, the provider completed and faxed to the Mifeprex distributor a one-time Prescriber's Agreement, agreeing that they met the qualifications and would follow the guidelines outlined in the Prescriber's Agreement. These guidelines required prescribers to attest that they had the ability to date a pregnancy; had the ability to diagnose an ectopic pregnancy; had made plans for the patient to receive surgical abortion care in cases of incomplete abortion or severe bleeding, and to ensure the patient has access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary; and had read and understood the prescribing information for Mifeprex. In addition, the prescriber agreed to provide the patient with the Medication Guide and Patient Agreement, give her an opportunity to read and discuss them, obtain her signature on the Patient Agreement, and then sign it as well; notify the manufacturer of any cases of incomplete abortion, hospitalization, transfusion, or other serious event; and record the unique serial number on each package of Mifeprex in each patient's record.
- ETASU C restricted where a patient could receive Mifeprex once prescribed. Under ETASU C, Mifeprex could be dispensed only in certain

health care settings, specifically clinics, medical offices, and hospitals, by or under the supervision of a prescriber specially certified under ETASU A. Mifeprex could not be dispensed through retail pharmacies.

- ETASU D placed additional requirements on the patient receiving Mifeprex. Under ETASU D, Mifeprex could be dispensed only to a patient who had completed and signed a Patient Agreement form, a copy of which was required to be placed in her medical record, and who had been provided a copy of the Medication Guide.

70. *Third*, an Implementation System, under which distributors agreed to ship the drug only to site locations identified by specially certified prescribers in signed Prescriber's Agreements; maintain secure and confidential records of shipments; and follow all distribution guidelines, including for storage, tracking, proof of delivery, and controlled returns.

71. *Fourth*, as is typical for any REMS, the sponsor was required to submit a REMS "assessment" to FDA one year from the date of the initial approval of the REMS and every three years thereafter.

3. 2016 Mifeprex Labeling Changes and REMS Assessment

a. Requested Changes to Mifeprex Label and REMS

72. Off-label use of drugs—*i.e.*, in accordance with prevailing clinical evidence, using a medication for a different indication or in a different regimen than that listed

on the FDA-approved labeling—is extremely common and widely accepted in the United States. Thus, shortly after FDA approved Mifeprex in 2000, abortion providers started prescribing the evidence-based protocol (using 200 mg of mifepristone) rather than the regimen listed on the labeling (using 600 mg of mifepristone). However, after several states banned off-label use of mifepristone—forcing patients to use an outdated regimen that was less safe and less effective than prevailing practice—in May 2015, Danco submitted a supplemental NDA to FDA proposing to update the labeling to reflect evidence-based practice across the country. In July 2015, Danco also submitted its statutorily required REMS assessment, proposing minor modifications to the REMS (primarily to ensure that the language used in the prescriber and patient agreement forms reflected the proposed changes to the labeling).

73. This submission prompted a top-to-bottom review of the Mifeprex labeling and REMS by FDA in 2015-2016. As part of that review, the Agency stated that it considered three letters submitted by more than 40 medical experts, researchers, advocacy groups, and professional associations—including Plaintiff SFP—who asked, *inter alia*, that the REMS be eliminated.

74. Other signatories requesting that FDA eliminate the Mifeprex REMS included ACOG, the leading professional association of physicians specializing in the health care of women, which represents more than 60,000 physicians and

partners in women's health; the American Public Health Association ("APHA"), the nation's leading public health organization; the Director of Stanford University School of Medicine's Division of Family Planning Services and Research; the Chair of the Department of Obstetrics and Gynecology at the University of New Mexico School of Medicine; and the Senior Research Demographer in the Office of Population Research at Princeton University.

75. The Agency's March 2016 Cross Discipline Team Leader Review Memorandum for Mifeprex ("2016 Team Leader Review"), in a section entitled "Advocacy Group Communications," noted:

> The Agency received three letters from representatives from academia and various professional organizations, including [ACOG], [APHA], the National Abortion Federation (NAF), Ibis Reproductive Health and Gynuity [Health Projects]. In general, these advocates requested FDA to revise labeling in a manner that would reflect current clinical practice, including the new dose regimen submitted by the Sponsor, and proposing to extend the gestational age through 70 days. Other requests were that the labeling not require that the drug-taking location for both Mifeprex and misoprostol be restricted to the clinic, and that labeling not specify that an in-person follow-up visit is required. *The advocates also requested that any licensed healthcare provider should be able to prescribe Mifeprex and that the REMS be modified or eliminated, to remove the Patient Agreement and eliminate the prescriber certification, while allowing Mifeprex to be dispensed through retail pharmacies*. (emphasis added).[34]

[34] FDA 0465.

76. In FDA's 2016 Medical Review, in a section entitled "Methods," the Agency further noted: "Articles were also cited in three letters sent to [Center for Drug Evaluation and Research] Center Director Janet Woodcock, MD from 1) ACOG, 2) a group of academic professionals and women's health non-profit organizations, and 3) thirty professional and academic organizations, all of which requested changes to the Mifeprex labeling and REMS."[35]

77. Director Woodcock also directly acknowledged receipt of the letter submitted by thirty professional and academic organizations, including Plaintiff SFP. In a February 25, 2016, letter addressed to the individual serving as the liaison for those groups, she wrote:

> Thank you for your letter dated February 4, 2016, to [then-Acting FDA Commissioner] Dr. Ostroff, Dr. Califf, and me with recommendations to lift the Risk Evaluation and Mitigation Strategy (REMS) for Mifeprex (mifepristone), and to extend the indicated use of Mifeprex through a gestational age of 70 days. Dr. Ostroff has asked me to respond on behalf of the FDA because the Center for Drug Evaluation and Research is responsible for regulating all drugs, including mifepristone. Please share this response with your cosigners. In your letter, you strongly encouraged FDA to revise the mifepristone label and eliminate the REMS restrictions, especially the Elements to Assure Safe Use [ETASU] . . . . You also recommended not restricting the location where the patient should take these drugs . . . . Moreover, you proposed that any licensed health care provider should be able to prescribe mifepristone, and that it be available through pharmacies

[35] FDA 0550.

> as well as provider offices. Your letter has been shared with the appropriate FDA staff and will be carefully reviewed.[36]

78. The letter submitted by Plaintiff SFP argued, *inter alia*:

> In the 15 years since mifepristone's approval, multiple clinical trials, dozens of studies, and extensive experience across the globe have confirmed the FDA's finding that mifepristone is a safe and reliable method of abortion. Studies have shown that mifepristone in combination with misoprostol is up to 99% effective for first trimester abortion and that serious complications are rare. The steady increase in use of medication abortion – now 23% of U.S. abortions – shows that many women prefer this option, and that it has the ability to improve access to abortion, even in states with restrictive laws . . . . However, many who could benefit from mifepristone still do not have access to it due to multiple types of restrictions, including those required by the FDA . . . . As policy, advocacy, social science, research, and academic organizations, we ask the FDA to consider the substantial evidence presented in the [letter previously submitted by academic professionals and women's health non-profit organizations], alongside the burdens that the REMS and the label's 49-day gestational age indication place on patient access, which we describe here. The FDA held a public meeting in October 2015 to discuss improving patient access to drugs under REMS, evidencing the Agency's own awareness of patient burden caused specifically by restrictions imposed under REMS. We applaud these efforts and urge the FDA to use its regulatory authority to remove the medically unnecessary barriers to mifepristone.[37]

[36] FDA 1265.

[37] FDA 1254.

79. SFP's letter also explained in detail why the Mifeprex REMS with ETASU harms patient access to Mifeprex. In particular, SFP's letter stated that ETASU C, which restricted where Mifeprex could be dispensed, "significantly curtails mifepristone's potential to expand patient access to abortion care" because it "[is] a burden to providers and, therefore, deter[s] some health care providers from offering medication abortion."[38] They explained:

> When fewer providers are willing to stock mifepristone in their offices because of the REMS and ETASU, fewer patients can access medication abortion. In some cases this requirement may also force the patient to make an unnecessary visit to a clinic, medical office, or hospital to pick up the medication, rather than being able to pick up an order called into a pharmacy. This requirement is especially significant in underserved and rural areas where access to a health care provider is already difficult, and for those with low incomes for whom taking off work or getting to a provider multiple times in short order is impossible due to cost or family needs . . . . [T]he majority of people who seek abortion care are already in difficult financial situations, and are disproportionately people of color. Costly and unnecessary visits to the doctor significantly increase financial and logistical burdens for these individuals and communities.[39]

80. SFP's letter explained why ETASU A, the Prescriber's Agreement, "is unnecessary for the safe dispensation of mifepristone," noting, *inter alia*, that "health care professionals are already subject to many laws, policies, and ordinary

[38] FDA 1255.

[39] FDA 1255–56.

standards of practice that ensure they can accurately and safely understand and prescribe medications. Provider certification is not required for health care professionals to dispense other drugs, including drugs that carry black box, or boxed, warnings about their medical risks."[40]

81. SFP and the other signatories further argued that the Prescriber's Agreement

> forces providers to identify themselves as abortion providers to a centralized entity (Danco Laboratories) inspected and regulated by the FDA, which could discourage some from offering medication abortion care to their patients. In 2014, more than half of U.S. health care facilities that provide abortions (52%) experienced threats and other types of targeted intimidation, and one in five experienced severe violence, such as blockades, invasions, bombings, arsons, chemical attacks, physical violence, stalking, gunfire, bomb threats, arson threats, or death threats. Robert Dear's November 27, 2015, standoff at a Planned Parenthood health center in Colorado, which resulted in three deaths, provides one recent and chilling example of anti-abortion violence. Given such escalating harassment and violence against known abortion providers, clinicians may be understandably reluctant to add their names to a centralized database of mifepristone providers.[41]

[40] FDA 1256. According to FDA, a "boxed" or "black box warning" "appears on a prescription drug's labeling and is designed to call attention to serious or life-threatening risks." U.S. Food & Drug Admin., Consumer Health Information, *A Guide to Drug Safety Terms at FDA* 2 (Nov. 2012), *available at* https://perma.cc/6JEZ-TSYQ.

[41] FDA 1256.

82. The letter also noted that "[t]he Prescriber's Agreement would be incompatible and unnecessary if there were an expanded distribution system."[42]

83. Finally, the letter requested that the Agency remove ETASU D, the Patient Agreement, which is "medically unnecessary and interferes with the clinician-patient relationship."[43]

b. FDA's 2016 Approval of Revised Label

84. FDA adopted nearly all of Danco's proposed labeling changes (discussed *supra* at ¶ 72), including reducing the recommended dosage of mifepristone from three 200 mg tablets to one 200 mg tablet and removing the reference to the patient's follow-up assessment—to assure completion of the abortion seven to fourteen days after taking the mifepristone—as an in-person examination.

85. FDA also approved two changes regarding where the patient takes the mifepristone and misoprostol. First, the labeling no longer stated that the patient takes the mifepristone and misoprostol "at [their] provider's office." Rather, although health care providers were still required to *dispense* the Mifeprex only in certain medical facilities according to the REMS, the updated labeling no longer specified where they *take* the pill; it simply stated that the patient takes the mifepristone in a single oral dose on "Day One," and then takes four tablets of

[42] *Id.*

[43] FDA 1257.

misoprostol by the buccal route 24-48 hours later.[44] The labeling advises the health care provider to "discuss with the patient an appropriate location for her to be when she takes the misoprostol, taking into account that expulsion [*i.e.*, the miscarriage] could begin within 2 hours of administration."[45]

86. In addition, the labeling clarified that mifepristone can be safely used through 70 days of pregnancy (rather than 49).[46] The Agency concluded in its 2016 Medical Review that, based on the scientific evidence, "[m]edical termination of pregnancies through 70 days gestation is safe and effective and should be approved."[47]

c. FDA's 2016 Reauthorization of the REMS

87. As part of its review of the proposed labeling changes, the Agency undertook to "assess[] the current REMS program to determine whether each Mifeprex REMS element remains necessary to ensure that the drug's benefits outweigh the risks."[48] This assessment was conducted by a multidisciplinary reviewing team and elevated to the Commissioner of FDA, a political appointee—Defendant Robert Califf, who

[44] FDA 0385.

[45] *Id.*

[46] FDA 0383, 0384, 0391, 0399.

[47] FDA 0548.

[48] FDA 0375.

would later also helm FDA at the time of the 2023 REMS updates—who gave specific feedback on proposed changes to the Mifeprex REMS.

88. FDA reviewers met on January 15, 2016, "to discuss proposed revisions to the REMS," and the Agency's review process was documented in detail in at least seven internal memoranda (attached to Plaintiffs' original complaint as Exhibits A, C-F, J-K). In evaluating each element of the REMS, the Agency considered, *inter alia*, "safety data gathered over the past 16 years since approval, and information regarding current clinical practice."[49]

89. Following this comprehensive review, the Agency "determined that a REMS continues to be necessary to ensure the safe use of Mifeprex," and reauthorized the REMS program, including all of the ETASU, with only minor modifications.[50]

90. The reauthorization of the REMS in March 2016 constituted a final agency action. It marked the consummation of the Agency's decision-making process and was a decision from which legal consequences flowed.

91. The Agency made the following modifications to the REMS: (1) revisions to the language in the Prescriber's Agreement form; (2) removal of the Medication Guide as a REMS element; (3) updating of the REMS goals to reflect these changes; and (4) removal of the additional adverse event reporting requirements, other than

[49] FDA 0702.

[50] FDA 0849.

with respect to deaths.[51] The stated goal of the 2016 Mifeprex REMS program was "to mitigate the risk of serious complications associated with Mifeprex by: (a) Requiring health care providers who prescribe Mifeprex to be certified in the Mifeprex REMS Program[,] (b) Ensuring that Mifeprex is only dispensed in certain healthcare settings by or under the supervision of a certified prescriber[,] [and] (c) Informing patients about the risk of serious complications associated with Mifprex."[52]

92. The Agency's multidisciplinary team of reviewers had also recommended eliminating ETASU D, the Patient Agreement form, because they concluded that it was no longer necessary. As Director Woodcock explained in a March 28, 2016, internal memorandum, Agency staff "found that the information contained in the Patient Agreement Form [required by the REMS] is generally duplicative of information in the Medication Guide and of information and counseling provided to patients under standard informed consent practices for medical care and under professional practice guidelines."[53] Agency reviewers observed that "[i]t is standard of care for patients undergoing pregnancy termination to undergo extensive counseling and informed consent,"[54] and noted that "FDA has removed REMS

[51] FDA 0680–81; *see also* FDA 0688.

[52] FDA 0404.

[53] FDA 0674.

[54] FDA 0437.

requirements in other programs based on the integration of the REMS safe use condition into clinical practice."[55] The Agency's 2016 Summary Review "concur[red] with the clinical review team that the Patient Agreement Form, which requires a patient's signature, *does not add to safe use conditions for the patient for this REMS and is a burden for patients*."[56]

93. However, "[a]fter being briefed on the planned changes to the NDA that the Center [for Drug Evaluation and Research] was considering, the Commissioner [of FDA] . . . requested that the Patient Agreement Form be retained as an element of the REMS."[57] Therefore, Director Woodcock "asked [Agency staff] to include a Patient Agreement Form in the REMS for Mifeprex," which they did.[58]

94. It is extremely rare that the FDA Commissioner, a political appointee, would weigh in on a REMS assessment. This unusual interference is consistent with the Agency's conduct denying the application to make Plan B® (commonly known as "the morning after pill"), which is used to prevent pregnancy, available over-the-counter with no age restrictions—where the U.S. District Court for the Eastern District of New York found "overwhelming evidence of political pressure underlying the agency's actions." *Tummino v. Hamburg*, 936 F. Supp. 2d 162, 166

[55] FDA 0465.

[56] FDA 0437.

[57] FDA 0674.

[58] *Id*.

(E.D.N.Y. 2013) (finding that FDA did not have authority to mandate point-of-sale restrictions on levonorgestrel-based emergency contraception given the scientific data demonstrating that adolescents could safely use Plan B).

d. Events Post-Dating Plaintiffs' Filing

95. In October 2017, Plaintiffs filed the instant matter.

96. In 2019, FDA approved a generic version of mifepristone with substantively identical labeling, and established a single, shared system REMS encompassing both Mifeprex and the generic version that is substantively identical to the REMS approved for Mifeprex in 2016. The single, shared system REMS is known as the Mifepristone REMS Program.[59]

97. In March 2020, in response to the COVID-19 pandemic, Defendants FDA and HHS took extraordinary measures to promote the use of telemedicine and reduce the need for in-person health care visits, in order to mitigate viral exposure risks. For instance, FDA issued guidance declaring its intention not to enforce REMS requirements for in-person laboratory testing for the duration of the public health emergency, and the Secretary of HHS activated an emergency exception allowing

[59] 2023 REMS Review, *supra* note 8, at 2023 SUPP 001117.

health care providers to prescribe controlled substances, including opioids, via telemedicine without first conducting an in-person examination.[60]

98. Leading medical associations and health care providers asked FDA to likewise exercise enforcement guidance with respect to the in-person dispensing ETASU for mifepristone.[61] But FDA left that restriction in place, offering no explanation for its constructive denial—and continuing its singular treatment of mifepristone.

99. In May 2020, ACOG led a coalition of plaintiffs in a challenge to the mifepristone in-person dispensing ETASU in the U.S. District Court for the District of Maryland, resulting in a preliminary injunction that blocked enforcement of this requirement for the six months the injunction was in place, and for the first time enabled mifepristone patients to obtain their medication from a mail-order pharmacy. *ACOG v. FDA*, 472 F. Supp. 3d 183 (D. Md. 2020), *stayed*, 141 S. Ct. 578 (2021) (mem.).

[60] U.S. Food & Drug Admin., Policy for Certain REMS Requirements During the COVID-19 Public Health Emergency: Guidance for Industry and Health Care Professionals (Mar. 2020), 2021 REMS 000012–19; *COVID-19 Information Page, Telemedicine*, U.S. Drug Enf't Admin., https://www.deadiversion.usdoj.gov/coronavirus.html#TELE (last visited Mar. 30, 2023).

[61] *See, e.g.*, Letter from Maureen G. Phipps, MD, MPH, FACOG, Judette Louis, MD, MPH, and Matt J. Granato, LLM, MBA, to Stephen M. Hahn, MD (Apr. 20, 2020), 2021 ED 000001–03.

100. On April 12, 2021, FDA announced that it intended to exercise enforcement discretion for the remainder of the COVID-19 Public Health Emergency with respect to the mifepristone in-person dispensing requirement.[62]

101. On April 16, 2021, Plaintiffs moved for summary judgment in the instant matter. Shortly thereafter, FDA informed Plaintiffs that it was comprehensively reviewing the mifepristone REMS. On the condition that FDA would also "review any relevant data and evidence submitted by the Plaintiffs," Joint Mot. Stay 2 (ECF 148), the parties jointly moved for a stay, which this Court granted on May 7, 2021. As FDA explains in its Frequently Asked Questions for mifepristone, this litigation was the catalyst for its REMS Review: "The agency's comprehensive review of the Mifepristone REMS Program, which led to the agency's December 16, 2021, decision that a modification is required, was related to the litigation in *Chelius v. Becerra*."[63]

[62] 2023 REMS Review, *supra* note 8, at 2023 SUPP 001117.

[63] *Questions and Answers on Mifepristone for Medical Termination of Pregnancy Through Ten Weeks Gestation*, U.S. Food & Drug Admin. (last updated Jan. 4, 2023), https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/questions-and-answers-mifepristone-medical-termination-pregnancy-through-ten-weeks-gestation (answer to question 29, under "Litigation and Other Legal Issues"; *accord id.* (answer to question 35, under "The January 2023 REMS Modification").

102. In May 2021, FDA approved a supplemental new drug application seeking to modify the Patient Agreement Form for mifepristone to reflect gender-neutral language.[64]

103. In August and September 2021, Plaintiffs submitted to FDA two letters containing evidence demonstrating that the mifepristone REMS is medically unnecessary and burdensome on patients (especially patients who face difficulties accessing health care) and on the health care delivery system itself. For instance, Plaintiffs' letters included:

- Statements opposing the mifepristone REMS by other leading medical associations, including the American Medical Association ("AMA"), ACOG, and the American Academy of Family Physicians ("AAFP").[65]

- Specific examples of other medications posing risks greater than or comparable to that of mifepristone that are *not* subject to a REMS.[66]

- A study abstract showing that after Canada eliminated its restrictions on mifepristone in 2017 to allow normal prescribing, medication abortion remained extremely safe, with a major complication rate of 0.33%.[67]

- Sworn testimony from seven physicians in different states detailing how the mifepristone REMS prevented or substantially delayed them and other doctors they know from prescribing mifepristone, impeding patients' access. For instance, Dr. Joey Banks cited specific examples of physicians who have told her that the reason they do not provide mifepristone is because they are

[64] 2023 REMS Review, *supra* note 8, at 2023 SUPP 001114.

[65] *Chelius* Plaintiffs' Letter, *supra* note 10, at 2021 REMS 001159.

[66] *Id.* at 2021 REMS 001161.

[67] *Id.* at 2021 REMS 001160.

"worried" about being placed "on a list of abortion providers."[68] Dr. Charisse Loder explained how it took years to make mifepristone available at the University of Michigan's Women's Clinic, including because of "concerns that the University would face legal liability if clinicians who were not acting pursuant to a REMS prescriber agreement prescribed this drug," which a special taskforce spent "many meetings" discussing.[69] Dr. Jane Roe discussed how the patient agreement "actively *undermines* my informed consent process by forcing me to discuss with my patients information that is inconsistent with my clinical approach and increasingly out-of-step with the research on Mifeprex as science moves forward," for instance by requiring patients to attest that they are having an abortion even if they are in fact using the medication to treat a miscarriage.[70]

- An analysis from a leading national expert in poverty and women's welfare regarding how the REMS reduces patients' access to mifepristone, particularly for patients with lower incomes and patients living in rural and medically underserved areas.

104. Other leading medical professional associations, such as ACOG, also submitted their own letters opposing the REMS. For instance, in a letter submitted on October 6, 2021, ACOG noted that "[t]he REMS and ETASU requirements for mifepristone are inconsistent with those for other medications with similar safety profiles, and create barriers to access without demonstrated improvements to patient safety or outcomes."[71]

[68] *Id.* at 2021 REMS 001962–63.

[69] *Id.* at 2021 REMS 001988–91.

[70] *Id.* at 2021 REMS 002006–07.

[71] Letter from Maureen G. Phipps, MD, MPH, FACOG, to Janet Woodcock, MD (Oct. 6, 2021), 2021 REMS 002051–52.

105. FDA's 2021 REMS Review memorandum states that the agency's review encompassed a search of published literature through July 26, 2021, as well as "safety information collected during the COVID-19 public health emergency (PHE); the one-year REMS assessment report of the Mifepristone REMS Program; adverse event data; and information provided by advocacy groups, individuals and the Applicants [*i.e.*, Danco and GenBioPro, which manufactures the generic]." FDA's "review also included an examination of literature references provided by plaintiffs in the *Chelius v. Becerra* litigation discussed below."[72]

106. In fact, FDA expressly omitted from its analysis much of the data and evidence provided by the *Chelius* Plaintiffs. FDA refused to consider, *inter alia*, "[i]nformation from survey studies or qualitative studies that evaluated perspectives on and/or satisfaction with medical abortion procedures from patients, pharmacists, clinic staff, or providers, *even if the study assessed REMS ETASUs*," "[o]pinions, commentaries, or policy/advocacy statements," and "[d]ata on the logistics of accessing abortion care in general, such as time to appointment or the distance traveled to obtain care."[73] FDA refused to consider this information even though it is relevant to whether a REMS is "necessary" for mifepristone; whether the mifepristone ETASU are "commensurate with the specific serious risk[s]" listed in

[72] 2021 REMS Review, *supra* note 9, at 2021 REMS 001570.

[73] *Id.* at 2021 REMS 001571–72 (emphasis added).

the drug's labeling, and/or "unduly burdensome on patient access to the drug, considering in particular . . . . patients who have difficulty accessing health care (such as patients in rural or medically underserved areas)"; and whether the ETASU "conform with elements to assure safe use for other drugs with similar, serious risks" "so as to minimize the burden on the health care delivery system." *Id.* §§ 355-1(a)(1), (f)(2)(A), (C), (D).

107. On December 16, 2021, FDA completed its review of the Mifepristone REMS Program and determined that it would: retain the REMS Program; retain the prescriber certification ETASU; retain the patient agreement ETASU; remove the in-person dispensing ETASU; and add a new pharmacy certification ETASU. FDA sent REMS Modification Notification letters to the two drug application holders notifying them that the REMS Program must be retained with these modifications.

108. In June 2022, the drug application holders submitted supplemental new drug applications consistent with FDA's REMS Modification Notification letters. Over the following months, the application holders held several meetings with FDA, responded to information requests by the Agency, and submitted several amendments to their supplemental applications.

109. On January 3, 2023, FDA completed a subsequent review memorandum ("2023 REMS Review") and released an updated REMS for mifepristone. This constituted a final agency action. It marked the consummation of

the Agency's decision-making process and was a decision from which legal consequences flowed.

C. The Mifepristone REMS Confers No Benefit on Patients and Does Not Satisfy the Statutory Requirements for a REMS with ETASU

1. A REMS is Not Necessary to Ensure That the Benefits of Mifepristone Outweigh Its Risks

110. The FDCA allows the Agency to impose a REMS only when "necessary to ensure that the benefits of the drug outweigh the risks of the drug[.]" 21 U.S.C. § 355-1(a)(1). None of the six factors the Secretary is statutorily required to consider in making this determination supports FDA's decision to reauthorize the Mifepristone REMS Program in 2023:

111. **"The estimated size of the population likely to use the drug involved,"** 21 U.S.C. § 355-1(a)(1): Since Mifeprex's approval in 2000 for use in the United States, medication abortion has, the agency noted, "been increasingly used as its efficacy and safety have become well-established by both research and experience, and serious complications have proven to be extremely rare."[74] Between September 2000 and 2022, mifepristone had been used 5.6 million times in the United States.

[74] FDA 0539.

112. Statutory guidance released by FDA in April 2019 states that, in applying this REMS factor, FDA "considers, among other things, the extent to which that population includes patients expected to use the drug for unapproved uses and the risks associated with those uses."[75] But unlike opioids, which comprised approximately 75% of REMS drugs as of 2019,[76] patients use mifepristone only for its labeled indication—ending a pregnancy—or for other evidence-based reproductive health care like miscarriage care.

113. Many more people could potentially benefit from mifepristone. Indeed, the Guttmacher Institute has found that one in four women in the United States will have an abortion during her lifetime, and as SFP observed in its letter to the Agency, "[t]he steady increase in use of medication abortion . . . shows that many women prefer this option, and that it has the ability to improve access to abortion, even in states with restrictive laws."[77]

114. Because mifepristone has already been safely used by millions of U.S. patients for its approved indication or for another safe, evidence-based regimen

[75] U.S. Food & Drug Admin., REMS: FDA's Application of Statutory Factors in Determining When a REMS Is Necessary Guidance for Industry 9 (Apr. 2019), *available at* https://www.fda.gov/media/100307/download [hereinafter "FDA Statutory Factor Guidance"].

[76] Joint Stip. of Facts ¶ 59.

[77] FDA 1254.

endorsed by leading medical authorities like SFP and ACOG, and because increasing access to this medication would help many more, this factor weighs against a REMS.

115. **"The seriousness of the disease or condition that is to be treated with the drug,"** 21 U.S.C. § 355-1(a)(1): The Agency acknowledges that pregnancy is a serious condition. In a 2016 denial of a citizen petition seeking to withdraw FDA approval for mifepristone, FDA explained:

> Pregnancy can be a serious medical condition in some women. Pregnancy is the only condition associated with preeclampsia and eclampsia and causes an increased risk of thromboembolic complications, including deep vein thrombophlebitis and pulmonary embolus. Additionally, there is a significant risk of a major surgical procedure and anesthesia if a pregnancy is continued; for 2013 (the most recent data available), the Centers for Disease Control and Prevention reported an overall 32.7 percent rate of cesarean sections in the United States. Other medical concerns associated with pregnancy include the following: disseminated intravascular coagulopathy (a rare but serious complication); amniotic fluid embolism; life-threatening hemorrhage associated with placenta previa, placenta accreta, placental abruption, labor and delivery, or surgical delivery; postpartum depression; and exacerbation or more difficult management of preexisting medical conditions (e.g., diabetes, lupus, cardiac disease, hypertension). In addition, approximately 50 percent of all pregnancies in the United States each year are unintended. According to the Institute of Medicine, women experiencing an unintended pregnancy may experience depression, anxiety, or other conditions.[78]

[78] FDA 0859.

116. Because mifepristone treats a serious condition, and thus offers a substantial potential benefit, this factor weighs against a REMS.

117. **"The expected benefit of the drug with respect to such disease or condition,"** 21 U.S.C. § 355-1(a)(1): In denying the citizen petition asking the Agency to withdraw the mifepristone approval, FDA—on the same day that it reauthorized the REMS—further explained: "[M]edical abortion through the use of Mifeprex provides a meaningful therapeutic benefit to some patients over surgical abortion."[79] For instance, in one of the clinical studies conducted in the U.S. shortly before Mifeprex's approval,

> medical termination of pregnancy avoided an invasive surgical procedure and anesthesia in 92 percent of the [study participants]. Complications of general or local anesthesia, or of intravenous sedation ("twilight" anesthesia), can include a severe allergic reaction, a sudden drop in blood pressure with cardiorespiratory arrest, death, and a longer recovery time following the procedure. Medical (non-surgical) termination of pregnancy provides an alternative to surgical abortion; it is up to the patient and her provider to decide whether a medical or surgical abortion is preferable and safer in her particular situation.[80]

118. In addition, some people prefer medication abortion because it feels more natural, and allows them to pass the pregnancy in the privacy and comfort of

[79] FDA 0860.

[80] *Id.*

their home. Indeed, in its 2016 Medical Review, the Agency noted that "[t]he studies [supporting the Mifeprex labeling changes], *including those of home use of mifepristone* and misoprostol, show increased convenience, autonomy and privacy for the woman, a smaller impact on their lifestyles, and no increased burden on the healthcare system."[81] In short, mifepristone allows patients to have an abortion in a private, comfortable, and safe location, on their own terms.

119. While misoprostol also has abortifacient properties acting alone, the combined regimen of mifepristone and misoprostol is the preferred regimen for medication abortion care and the most common regimen for medication abortion care in the United States; and is associated with fewer side effects than the misoprostol-only treatment.

120. Because the benefits that mifepristone offers to patients seeking to end an unwanted pregnancy without surgical intervention are significant and well-established, this factor weighs against a REMS.

121. **"The expected or actual duration of treatment with the drug,"** 21 U.S.C. § 355-1(a)(1): mifepristone is a single 200 mg tablet that is only prescribed for a single use. Korlym, by contrast, is an identical product prescribed for chronic, daily use in dosages ranging from 300 to 1200 mg. Korlym is not subject to a REMS;

[81] FDA 0589.

it is delivered to the patient's home, and the patient is expected to take up to four pills daily per physician instruction. The label includes a boxed warning that Korlym may have abortifacient effects and that patients should not use it if they are pregnant,[82] and the Agency trusts patients to use it accordingly.

122. Because mifepristone is prescribed as a single tablet and poses virtually no risk of misuse, whereas an identical drug that is prescribed in higher doses for daily home administration is not subject to a REMS, this factor weighs against a REMS.

123. **"The seriousness of any known or potential adverse events that may be related to the drug and the background incidence [*i.e.*, frequency] of such events in the population likely to use the drug,"** 21 U.S.C. § 355-1(a)(1): By FDA's own admission, major adverse events associated with mifepristone are "exceedingly rare, generally far below 0.1% for any individual adverse event."[83] Accordingly, the Agency concluded in March 2016 that it was appropriate to *remove* the requirement that Danco report any hospitalizations, blood transfusions, or other serious events relating to Mifeprex other than death, as the "FDA has received such reports for 15 years, and it has determined that the safety profile of Mifeprex is well-

[82] FDA 0269.

[83] FDA 0574.

characterized, that no new safety concerns have arisen in recent years, and that the known serious risks occur rarely."[84]

124. Similarly, in December 2021, FDA confirmed that "[o]ur review of [mifepristone's] postmarketing data indicates there have not been any new safety concerns with the use of mifepristone for medical termination of pregnancy through 70 days gestation, including during the time when in-person dispensing was not enforced."[85]

125. Mifepristone's FDA-approved labeling explains that "[n]o causal relationship between the use of [mifepristone] and [serious or fatal infections or bleeding] has been established."[86] To the contrary, the FDA-approved Mifepristone Medication Guide acknowledges that the risks listed in the labeling are not inherent to mifepristone, but rather are risks associated with emptying a pregnant uterus by any means: "Although cramping and bleeding are an expected part of ending a pregnancy, rarely, serious and potentially life-threatening bleeding, infections, or other problems can occur following a *miscarriage*, *surgical abortion*, medical

[84] FDA 0535.

[85] Letter from Patrizia Cavazzoni, MD, to Donna J. Harrison, MD & Quentin L. Van Meter, MD, FCP, Re: Docket No. FDA-2019-P-1534 [hereinafter "2021 AAPLOG Pet. Denial"], at 2019 CP 000654; *accord* 2021 REMS Review, *supra* note 9, at 2021 REMS 001582.

[86] FDA 0384; *accord* FDA 0387, 0398.

abortion, or *childbirth*." (emphasis added).[87] In other words, there is a relatively *high* background incidence of such adverse events among pregnant people generally.[88]

126. Moreover, the Agency acknowledges that "data from the medical literature and findings by the [U.S. Centers for Disease Control and Prevention ("CDC")] suggest that the critical risk factor" in nearly all of the few cases of fatal infections associated with mifepristone "is pregnancy itself," because similar infections "have been identified both in pregnant women who have undergone medical abortion and those who have not[.]"[89]

127. FDA's 2016 Medical Review also expressly concluded that "[m]edical abortion in adolescents appears to be at least as safe, if not safer, as in adult women."[90]

128. Because numerous studies and over two decades of clinical data in the United States confirm that mifepristone is safe—and that serious adverse events are rare, decreasing, and never shown to have been caused by mifepristone—this factor weighs against a REMS.

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[87] FDA 0383; *accord* FDA 0398.

[88] FDA 0398 ("[R]arely, serious and potentially life-threatening bleeding, infections, or other problems can occur *following a miscarriage, surgical abortion, medical abortion, or childbirth*." (emphasis added)); *accord* 2021 AAPLOG Pet. Denial, *supra* note 85, at 2019 CP 000664.

[89] FDA 0880–81 & n.69.

[90] FDA 0603.

129. **"Whether the drug is a new molecular entity,"** 21 U.S.C. § 355-1(a)(1): Mifepristone is not a new molecular entity. Mifepristone has been marketed in the United States since 2000, with no new safety concerns since 2005.[91] "Available information about" mifepristone is far from "limited," and there is no "uncertainty about risks associated with the use of the drug that might emerge in the post-approval setting."[92] Because mifepristone is a well-known compound, this factor weighs against a REMS.

130. Finally, because none of these factors supports maintaining the Mifepristone REMS Program, the implementation system and timetable for assessments from the drug manufacturer also are unnecessary. Indeed, as FDA's 2016 Medical Review acknowledged, even without a REMS, "the [drug manufacturer] will still be required by law, as is every NDA holder, to report serious, unexpected adverse events as 15-day safety reports, and to submit non-expedited individual case safety reports, and periodic adverse drug experience reports."[93]

[91] FDA 0354.

[92] FDA Statutory Factor Guidance, *supra* note 75, at 8.

[93] FDA 0535.

2. The Mifepristone ETASU Are Not "Commensurate With" and Do Not Mitigate the "Specific Serious Risk[s]" Listed in the Labeling.

131. In violation of the FDCA, the mifepristone ETASU are not "commensurate with the specific serious risk[s]" listed in the labeling, 21 U.S.C. § 355-1(f)(2)(A), which are "[s]erious and sometimes fatal infections or bleeding."[94] To the contrary, the ETASU are disproportionate to, have no nexus with, and will not mitigate, the risks listed in the labeling.

132. Moreover, drugs whose risks are similar to or greater than those of mifepristone are not subject to comparable restrictions.

a. The Mifeprex ETASU Are Disproportionate Because Serious Adverse Events Are "Exceedingly Rare"

133. The Agency concedes that serious adverse events associated with Mifeprex are "exceedingly rare."[95] In its 2016 Medical Review, the Agency concluded: "Given that there have been over 2.5 million uses of Mifeprex by US women since its marketing in 2000, including the use of the [revised] dosing regimen and extended gestational age at many clinic/office sites, the numbers of hospitalizations, severe infections, blood loss requiring transfusion and ectopic pregnancy will likely remain acceptably low. The numbers of each of these adverse

[94] FDA 0383.

[95] FDA 0574.

events appears to have remained steady over time, with a possible decrease in severe infections."[96]

134. Similarly, as detailed *supra* ¶ 124, FDA found in 2021 that serious adverse events remained very low even when the in-person dispensing ETASU was eliminated, notwithstanding FDA's insistence from 2000 until April 2021 that this requirement was essential for safe use.

135. In the nearly 22 years of U.S. post-marketing data available to FDA when it reauthorized the REMS in 2023, there were only 28 reported associated deaths out of 5.6 million uses—an associated fatality rate of 0.0005%.[97] By contrast, the fatality rate associated with phosphodiesterase type 5 inhibitors for the treatment of erectile dysfunction (*e.g.*, Viagra), which are not subject to a REMS, is estimated at 0.0026% of users, roughly 5 times the mifepristone-associated mortality rate.[98]

136. At least 9 of the reported deaths in women who had taken mifepristone involved events clearly unrelated to the medication: narcotic overdose or suspected homicide.[99] And FDA acknowledges that "[t]here is no information that use of Mifeprex and misoprostol caused" the "very small number" of deaths from

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[96] FDA 0611.

[97] FDA 0609–10.

[98] Gregory Lowe & Raymond A. Costabile, *10-Year Analysis of Adverse Event Reports to the Food and Drug Administration for Phosphodiesterase Type-5 Inhibitors*, 9 J. Sex. Med. 265, 268-69 (2012).

[99] Mifepristone U.S. Post-Marketing Adverse Events, *supra* note 3, at 2023 SUPP 001052.

infection.[100] Rather, as explained *supra* ¶¶ 125–26, CDC findings and the medical literature suggest that pregnancy itself, not Mifeprex usage, was the "critical risk factor" in nearly all of the (very few) cases of fatal infection.[101]

137. Indeed, as FDA acknowledges, a woman is at least 14 times more likely to die if she carries a pregnancy to term than if she uses mifepristone to end a pregnancy.[102] Moreover, the two risks listed in the mifepristone labeling are associated with many common obstetrical and gynecological procedures, such as vaginal delivery, surgical or medical miscarriage management, or insertion of an intrauterine long-acting reversible contraceptive ("IUD").

b. The ETASU Do Not "Mitigate" the Risks Listed in the Mifepristone Labeling

138. An essential flaw in the Mifeprex REMS is that there is no nexus between the risks listed on the Mifeprex label and the ETASU—they do not serve to "mitigate" any such risks, as required by 21 U.S.C. § 355-1(f)(1)(A). Specifically:

i. ETASU D: Patient Agreement

139. Every one of the FDA experts who participated in the Agency's formal March 2016 review for Mifeprex concluded that the Patient Agreement provides no

[100] FDA 0261.

[101] FDA 0880– 81 n.69.

[102] FDA 0859 & n.6 (citing Elizabeth G. Raymond & David E. Grimes, *The Comparative Safety of Legal Induced Abortion and Childbirth in the United States*, 119 Obstetrics & Gynecology 215, 215 (2012), 2021 REMS 000695–99).

medical benefit.

140. Those unanimous conclusions were amended only after defendant Commissioner Robert Califf requested that this ETASU be maintained nonetheless. The sole rationale for the Commissioner's unusual intervention is documented in a memorandum from Director Woodcock, in which she states that "the Commissioner concluded that continuing the REMS requirement for a signed Patient Agreement form would not interfere with access and would provide additional assurance that the patient is aware of the nature of the procedure, its risks, and the need for appropriate follow-up care."[103]

141. Commissioner Califf made this request notwithstanding that medication abortion does not involve any "procedure," only pills, and notwithstanding that FDA's 2016 Summary Review "concur[red] with the clinical review team that the Patient Agreement Form, which requires a patient's signature," is duplicative of existing informed consent laws and standards, "does not add to safe use conditions for the patient for this REMS[,] and is a burden for patients."[104]

142. In its 2021 review, FDA "agree[d] that informed consent in medicine is an established practice" as a general matter,[105] and specifically found that a survey

[103] FDA 0674.

[104] FDA 0437, 0674.

[105] 2021 REMS Review, *supra* note 9, at 2021 REMS 001577.

of abortion providers in the United States and Canada in 2017 "did reveal strong adherence to evidence-based guidelines."[106]

143. Nevertheless, FDA noted that "removal of the in-person dispensing requirement could significantly increase the number of [mifepristone] providers to a larger group of practitioners,"[107] and reasoned that the Patient Agreement ETASU will ensure that "each provider, including new providers, informs each patient of the appropriate use of mifepristone, risks associated with treatment, and what to do if the patient experiences symptoms that may require emergency care."[108]

144. FDA offered no explanation at all for why a special counseling form is necessary to ensure adequate counseling by new prescribers with respect to the use, risks, and follow-up care for mifepristone—a medication with a well-established risk profile, which has been available in the United States for nearly a quarter of a century—when FDA approves *entirely new drugs* all the time without a patient agreement form, even though *every* prescriber will be unfamiliar with that novel medication.

145. Moreover, mifepristone already has a special "medication guide" as part of its labeling that discusses mifepristone's use, risks, and follow-up care. The

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[106] *Id.*

[107] *Id.* at 2021 REMS 001578; *accord id.* at 2021 REMS 001597; 2023 REMS Review, *supra* note 8, at 2023 SUPP 001122–23.

[108] 2021 REMS Review, *supra* note 9, at 2021 REMS 001578.

2016 FDA review team specifically found the patient agreement form "duplicative" of the mifepristone medication guide, which "contains the same risk information covered under the Patient Agreement form,"[109] using patient-friendly language.[110] Yet FDA nowhere addressed this duplication in its 2021 or 2023 reviews.

ii. ETASU A: Special Certification for Prescribers

146. To become certified to prescribe mifepristone, health care providers must submit a form attesting that they (1) can assess the duration of pregnancy accurately; (2) can diagnose ectopic pregnancies; (3) can provide surgical intervention in cases of incomplete abortion or severe bleeding, or have made plans to provide such care through others, and to assure patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary; and (4) have read and understood the prescribing information.

147. In 2016, the Agency's only documented rationale for maintaining ETASU A was that it "ensures that Mifeprex can only be dispensed by or under the direct supervision of a certified prescriber"[111]—a pure tautology.

148. In 2023, FDA reauthorized this ETASU because its "review of the literature did not identify any studies comparing providers who met these

[109] Joint Stip. of Facts ¶ 57.

[110] *Id.* ¶ 41.

[111] FDA 0681.

qualifications with providers who did not. In the absence of such studies, there is no evidence to contradict our previous finding that prescribers' ability to accurately date pregnancies, diagnose ectopic pregnancies, and provide surgical intervention or arrange for such care through others if needed, is necessary to mitigate the serious risks associated with the use of mifepristone in a regimen with misoprostol."[112]

149. But FDA's rationale is premised on two wholly unsupported, purely speculative premises: (1) that clinicians providing pregnancy-related care would not already possess these fundamental abilities; and/or (2) that, in the absence of this ETASU, clinicians would prescribe mifepristone despite lacking appropriate qualifications.

150. FDA's explanation is medically unjustified for several reasons.

151. *First*, numerous other mechanisms, including licensing requirements, ethical and professional obligations, and malpractice liability, exist to ensure that health care providers practice only to the extent of their training and abilities. An attestation of competency provides no greater assurance that a health care provider will not provide care outside of their scope of practice than do these existing legal requirements and ethical norms.

[112] 2023 REMS Review, *supra* note 8, at 2023 SUPP 001373; *accord, e.g.*, 2021 REMS Review, *supra* note 9, at 2021 REMS 001596; *accord* 2021 AAPLOG Pet. Denial, *supra* note 85, at 2019 CP 000651.

152. *Second*, there are countless other drugs that require careful patient screening to ensure safe use, yet are not subject to ETASU. Indeed, clinicians are not required to make a comparable attestation of their qualifications before prescribing Korlym—which is the *exact same product* as Mifeprex (mifepristone), in higher doses.

153. *Third*, fulfilling these criteria requires no specialized medical expertise. FDA has conceded that any provider who is not comfortable using patient medical history or a clinical examination to assess the duration and location of a pregnancy can obtain that information by ordering an ultrasound.

154. Similarly, any provider can arrange for emergency care by referring patients to an emergency room in the rare event that such care is needed. Indeed, as FDA acknowledged in a citizen petition denial issued on the *very same day* the Agency completed its December 2021 REMS Review concluding that the Prescriber ETASU must be retained: "It is common practice for healthcare providers to provide emergency care coverage for other healthcare providers' patients."[113]

155. *Fourth*, as discussed *infra*, due to a number of factors, including the REMS, many patients are forced to travel outside their communities for abortion care. A patient who receives mifepristone from a REMS-certified provider outside

[113] 2021 AAPLOG Pet. Denial, *supra* note 85, at 2019 CP 000640.

her community and then initiates her medication abortion once she is back home generally will not (and should not) travel to seek in-person follow-up care from her REMS-certified prescriber; instead, she will receive any such follow-up care in her own community. The certification of the mifepristone prescriber thus has no bearing on the care the patient would receive in the unusual event of a complication.

156. *Finally*, reading and understanding the prescribing information for mifepristone is well within the scope of practice for any licensed prescriber.

iii. ETASU B: Pharmacy Certification

157. In order to dispense mifepristone, a pharmacy must become REMS-certified, which means agreeing to take on significant costs and burdens far beyond what is required for virtually every other prescription drug. These requirements include (but are not limited to) verifying that mifepristone prescriptions are written only by REMS-certified prescribers and storing prescriber certification information in a manner that is both dynamic and confidential; tracking shipments of mifepristone by mail; engaging in two-way communications with the mifepristone prescriber regarding the timing of the medication's delivery; "reporting any patient deaths" (with no further clarification as to what this reporting entails); and being regularly audited for REMS compliance.

158. FDA concedes that the Pharmacy Certification ETASU is burdensome and will deter pharmacies from dispensing mifepristone: the Agency

"acknowledge[d] that the provision in the REMS related to pharmacies' verification of prescriber enrollment will likely limit the types of pharmacies that will choose to certify in the REMS."[114] And FDA did not even account for any of the other burdens imposed by this ETASU beyond verifying prescriber certification, and their inevitable deterrence effect on pharmacy participation.

159. FDA justified adding this new ETASU based principally on its interaction with the prescriber certification requirement. FDA explained that "[w]ithout pharmacy certification, a pharmacy might dispense product that was not prescribed by a certified prescriber."[115] The purpose of this ETASU is to "incorporate[] pharmacies into the REMS, ensure[] that pharmacies are aware of and agree to follow applicable REMS requirements, and ensure[] that mifepristone is only dispensed pursuant to prescriptions that are written by certified prescribers."[116]

160. FDA nowhere addressed the fact that pharmacies had already been dispensing mifepristone for more than a year—from July 2020 until January 2021, and from April 2021 until December 2021—with *no* certification requirement and no increase in adverse events. Indeed, by January 3, 2023—when FDA completed its 2023 REMS Review, reauthorized the REMS, and for the first time imposed the

[114] 2023 REMS Review, *supra* note 8, at 2023 SUPP 001125.

[115] *Id.* at 2023 SUPP 001124.

[116] *Id.*

Pharmacy Certification ETASU—pharmacies had been safely dispensing mifepristone without certification for well over two years.

c. Drugs That Pose Similar or Greater Risks Than Mifepristone Are Not Subject to Comparable Restrictions

161. The FDCA requires that, "to the extent practicable," ETASU "conform with elements to assure safe use for other drugs with similar, serious risks[.]" 21 U.S.C. § 355-1(f)(2)(D). But most other drugs that pose similar or greater risks than mifepristone are not subject to comparable restrictions.

162. As of November 2019, fewer than 3% of FDA-approved prescription drug products were subject to a REMS, 75% of which were opioids.

163. Many drugs that have higher safety risks than mifepristone are permitted to be marketed without restrictions comparable to the Mifeprex REMS.

164. For instance, Viagra is associated with death in up to 0.0026% of users, roughly 5 times the mifepristone-associated mortality rate.[117] And acetaminophen (Tylenol) toxicity is the most common cause of liver transplantation in the United States, and responsible for 56,000 emergency department visits, 2,600 hospitalizations, and 500 deaths per year in this country. Yet, neither Viagra nor Tylenol has a REMS.[118]

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[117] Lowe & Costabile, *supra* note 98, at 268-69.

[118] Suneil Agrawal & Babak Khazaeni, Acetaminophen Toxicity, Nat'l Library of Med. (Aug. 1, 2022), *available at*

165. Similarly, as the *Chelius* Plaintiffs highlighted in their letter to FDA—and FDA nowhere addressed—many anticoagulant products, commonly known as "blood thinners," are associated with "serious and fatal bleeding," and, like mifepristone, carry warnings of that risk on their FDA-approved labels.[119] But unlike mifepristone, anticoagulants are a frequent cause of emergency room visits for documented hemorrhage.[120] Yet anticoagulants are available by prescription without a REMS, whereas Mifeprex is not.

166. The *Chelius* Plaintiffs also highlighted in their letter to FDA that Jeuveau® is indicated for a purely cosmetic purpose among a healthy population—the "temporary improvement in the appearance of moderate to severe glabellar lines" (i.e., lines between one's eyebrows). It carries a black-box warning for "[s]wallowing and breathing difficulties" that "can be life threatening" if this botulinum toxin product spreads beyond the area of injection, and the labeling notes

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https://www.ncbi.nlm.nih.gov/books/NBK441917/#:~:text=It%20is%20responsible%20for%2056%2C000,is%20contained%20in%20combined%20products.

[119] *See, e.g.*, Coumadin® label, 2021 REMS 001885–1920 (containing boxed warning for, *inter alia*, "major or fatal bleeding"); Pradaxa® label, *available at* https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/022512s027lbl.pdf (warning of "serious and fatal bleeding"); Xarelto® label, *available at* https://www.xareltohcp.com/shared/product/xarelto/prescribing-information.pdf (same).

[120] Nadine Shehab, *et. al.*, *US Emergency Department Visits for Outpatient Adverse Drug Events*, 2013-2014, 316 J. Am. Med. Ass'n 2115-25 (2016) (17.6% of emergency room visits based on adverse drug events in 2013-2014 were related to anticoagulants, and of those, roughly 80% involved documented hemorrhage).

"there have been reports of death."[121] Yet FDA nowhere explained in its 2021 or 2023 REMS reviews why a REMS is necessary for mifepristone but not for Jeuveau.

167. In sum, the Mifepristone REMS and its ETASU are medically unjustified restrictions on abortion, as evidenced both by the drug's own record and by how FDA regulates other drugs with a safety profile comparable to or weaker than that of mifepristone.

168. These restrictions simply are not motivated by science.

D. The Impact of the Mifepristone REMS on Plaintiffs, Plaintiffs' Members, and Plaintiffs' Members' Patients

1. Harms Caused by the 2023 REMS

169. FDA's 2023 REMS reauthorization extends many of the same kinds of burdens on patients and the health care delivery system that FDA's unique restrictions on mifepristone have imposed from the beginning.

170. ***First***, by continuing to classify mifepristone as among the tiny fraction of drugs for which REMS restrictions are necessary—on par with dangerous opioids causing "staggering" numbers of deaths each year—FDA's REMS reauthorization sends a false message about mifepristone's safety that complicates, delays, and derails efforts by health care providers to prescribe, research, and/or provide trainings on mifepristone.

[121] Jeuveau Prescribing Information, 2021 REMS 001817–30 .

171. For instance, clinicians seeking to begin prescribing mifepristone at their hospital or clinic have been required by health system leadership and/or decision-making committees to put together special presentations on mifepristone safety that are not required for other drugs with safety records comparable to mifepristone before the health care provider is permitted to prescribe it and/or the health system pharmacy is permitted to stock it. Such bureaucratic hurdles delay—and in some cases entirely prevent—health care providers in providing mifepristone to their patients, and would not arise if mifepristone were not subject to a REMS.

172. As another example, clinicians in doctoral programs have been unable to complete research and training projects relating to mifepristone because of institutional concerns and stigma expressly relating to mifepristone's classification as a REMS drug—e.g., requiring a doctoral student to seek Institutional Review Board ("IRB") approval for a project that would not otherwise necessitate IRB approval, because it involves "a REMS drug."

173. ***Second,*** FDA's REMS reauthorization still means that a clinician seeking to prescribe mifepristone often must involve many other colleagues in their health system—such as administrators, nurses, and information technology staff—in the provision of mifepristone, which can delay or altogether derail their ability to provide this medication to their patients.

174. For instance, because FDA requires mifepristone prescribers to be specially certified, health systems may need to develop special systems to track and update clinicians' certifications. Because FDA requires mifepristone patients to sign a special counseling form, health care facilities that use electronic medical records must come up with a system for storing the signed Patient Agreement form in the patient's medical record, and health care facilities that wish to utilize telemedicine for mifepristone must implement HIPAA-compliant technology to allow for patients to remotely sign the Patient Agreement.

175. These and other logistical and technological burdens imposed by the REMS—layered on top of the broader deterrent effect of the REMS classification—frequently prevent patients from obtaining a mifepristone prescription from their primary health care provider.

176. ***Third***, by maintaining the Prescriber Certification ETASU, FDA continues to substantially reduce the pool of qualified health care providers willing to prescribe mifepristone because many clinicians are fearful that they will face anti-abortion violence and harassment if their registration as a mifepristone prescriber were ever exposed. FDA's own actions underscore the severity of this concern: the Agency redacted from the administrative record in this matter the names and offices of every one of its employees who has done any work relating to mifepristone. FDA explained that it feared that, "[i]n light of the violence and harassment surrounding

the provision of abortion," releasing this information—*even subject to a protective order designed to ensure the confidentiality of that information*—"could expose those employees to threats, intimidation, harassment and/or violence."[122]

177. These fears are heightened now due to the growing criminalization and penalization of abortion care in many states across the country following *Dobbs v. Jackson Women's Health Org.*, with a particularly chilling effect on clinicians who hold medical licenses in multiple states, or medical residents who intend to eventually practice in a state with severe abortion restrictions. For instance, in recent years, several states have enacted laws allowing "bounty-hunter" vigilantes to drag into court anyone whom they suspect to have aided in the performance of an unlawful abortion, with no opportunity for the person sued to recover their litigation costs and fees even if they ultimately prevail. *See, e.g.*, Tex. Health & Safety Code § 171.208; Idaho Code Ann. § 18-8807.

178. ***Fourth***, the Patient Agreement ETASU *undermines* informed consent by requiring patients to review and sign a form containing fossilized science that may be inconsistent with their individual clinical circumstances. For example, the Patient Agreement states that the patient will take the misoprostol "24 to 48 hours" after taking the mifepristone. But some clinicians instruct patients to use an

[122] Joint Stip. of Facts. ¶ 47.

evidence-based protocol in which the misoprostol is taken simultaneously with mifepristone, or at another timeframe shorter than 24 hours, consistent with high-quality research and the patients' individual circumstances.[123] At best, the Patient Agreement duplicates counseling that mifepristone prescribers would already do, consistent with professional and ethical standards. More often, it complicates and confuses the counseling—particularly for patients with limited English proficiency who need translation services.

179. The Patient Agreement is often particularly confusing and distressing for patients using mifepristone for miscarriage care, who must attest that they are taking the medication "to end [their] pregnancy," even when this is false. Clinicians unwilling to require their patients undergoing miscarriages to sign a form containing knowingly false information about their medical condition and decision—or who work at a health care facility whose administration is concerned about the confusion or liability resulting from such a requirement—are unable to prescribe mifepristone to their patients experiencing early pregnancy loss at all.

180. ***Fifth***, by compelling patients using mifepristone to sign and take with them a form stating that they have had an abortion, FDA's REMS Reauthorization jeopardizes patients' privacy—because of the risk that the form will inadvertently

[123] *See, e.g.*, Nat'l Abortion Fed., 2020 Clinical Policy Guidelines for Abortion Care (2020), 2021 REMS 000805.

be found by others with whom the patient might not otherwise disclose their pregnancy and/or abortion decision. Relatedly, by requiring that patients sign and take with them a form in which they attest that they have had an abortion, this ETASU increases the risk that patients will face anti-abortion violence and harassment (even if they actually used the mifepristone for miscarriage treatment).

181. ***Sixth***, the Pharmacy Certification ETASU imposes significant costs and burdens that deter pharmacies—especially smaller community pharmacies—from dispensing mifepristone, reducing patients' access to this medication. In order to comply with this ETASU, pharmacies seeking to dispense mifepristone must have the infrastructure and human and financial resources to, *inter alia*, develop a system to confidentially maintain prescriber certifications; verify that any prescription sent in for mifepristone comes from a certified prescriber; if the prescription does not come from a certified prescriber, either contact the prescriber to try to verify their certification or inform the patient that the prescription cannot be filled (in either case, delaying the patient's access); and train staff and prepare for special audits of their mifepristone REMS compliance procedures.

182. The Pharmacy Certification ETASU also necessitates that pharmacies commit to fill mifepristone prescriptions by mail using a carrier service that will ensure the medication is delivered within four calendar days, and if it appears the shipment may take more than four calendar days to arrive—e.g., due to a shipment

delay or incomplete patient address—attempt to contact the prescriber to confirm "the appropriateness of dispensing mifepristone for patients who will receive the drug more than 4 calendar days after the date the pharmacy receives the prescription," and then maintain records documenting the prescriber's decision. By requiring that all shipments arrive within four calendar days except with documented confirmation from the prescriber, the Pharmacy Certification ETASU necessitates that pharmacies use more expensive carrier services—and then either absorb those costs themselves (a further deterrent to become certified) or else pass those costs on to patients. This ETASU strips patients of the autonomy to choose a less expensive shipping option even if they know that, given the length of their pregnancy, receiving the medication in slightly more than 4 days would still be perfectly fine.

183. While some larger pharmacy chains or national mail-order pharmacies may be able to bear the financial and logistical burdens of the REMS requirements, mail-order delivery is not an appropriate option for many patients, such as those who are homeless or housing insecure or those living with an abusive partner or parent from whom they must keep their abortion decision private.

184. ***Seventh***, by prohibiting all but certified pharmacies to dispense mifepristone, FDA's REMS Reauthorization makes it practically impossible for many health care providers to know where to send the patient's prescription for fulfillment, particularly if the patient does not live in the prescriber's immediate area.

There is no system to enable prescribers to know which pharmacies are certified. Without a REMS, clinicians can generally send in a prescription to the patient's preferred pharmacy, which will fill the medication if they have it in stock; request the medication from their pharmaceutical vendor; or else transfer the prescription to another pharmacy able to fill it. But the Pharmacy Certification ETASU replaces this common and common-sense process with confusion and delay, and will necessitate that busy health care providers call around to multiple pharmacies or try to do research online in order to determine where to send the patient's prescription.

185. For the reasons described *supra* and others, the 2023 Mifepristone REMS Program unduly burdens patients' access to a safe and effective medication, compounding the profound abortion access issues that already exist in the United States—including in states where abortion remains legal after *Dobbs*. The REMS thus specifically harms "patients who [already] have difficulty accessing health care." 21 U.S.C. §355-1(f)(2)(C)(ii).

186. As the *Chelius* Plaintiffs highlighted in their 2021 submission to FDA, and FDA expressly ignored (*see supra* ¶¶ 103–06):

> A nationally representative sample of 8,000 abortion patients found that patients traveled, on average, 68 miles round-trip to receive an abortion. In a majority of states, at least 20% of reproductive-age women live more than 100 miles round-trip from the nearest abortion clinic. And while rural areas are particularly lacking, patients in urban areas also struggle. A 2018 study found that 27 major

> cities have no publicly advertised abortion provider within 100 miles.[124]

187. Like all restrictions on abortion, the burdens of the Mifepristone REMS Program are not borne equally. As the *Chelius* Plaintiffs explained, restrictions that necessitate that patients travel farther in order to find a mifepristone provider can make it "incredibly difficult and in some cases impossible" for patients with unwanted pregnancies to access any abortion care at all.[125]

188. The REMS burdens are particularly harmful "[g]iven the mifepristone patient population."[126] As Plaintiffs explained:

> [I]n 2014 (the most recent year for which such data are available), 75 percent of abortion patients had incomes at or below the U.S. Official Poverty Measure. Sixty percent of abortion patients identify as people of color, including 53 percent of patients who identify as Black or Hispanic. And 60 percent of abortion patients have at least one child.[127]

By further reducing where abortion care is available in this country, the *Chelius* Plaintiffs told FDA, the REMS "imposes costs and burdens relating to transportation, childcare, and lost wages for missed work that many in this patient population simply cannot afford. Indeed, a robust body of research, spanning

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[124] *Chelius* Plaintiffs' Letter, *supra* note 10, at 2021 REMS 001163; *accord id.* at 2021 REMS 002011–44.

[125] *Id.* at 2021 REMS 001163.

[126] *Id*.

[127] *Id.* at 2021 REMS 001163–64.

multiple states and decades, confirms that forcing patients to travel even slightly farther (e.g., 10 miles) delays or blocks patients from accessing desired abortions."[128]

189. In addition to reducing the number of mifepristone prescribers, the 2023 REMS poses specific burdens for, *inter alia*, low-income populations (in which people of color are disproportionately represented because of structural racism), homeless populations (which disproportionately include LGBT people), people with limited English proficiency, and people living in abusive households. For example, people with housing insecurity who do not have a reliable mailing address must find and travel to a health center that stocks and dispenses mifepristone onsite when the burdens of the Pharmacy Certification ETASU prevent local retail pharmacies from stocking mifepristone. FDA failed to consider these and many other ways in which the mifepristone ETASU disproportionately harm patients that already face difficulties accessing healthcare.

2. Illustrative Harms to Plaintiffs and Plaintiffs' Members

190. Dr. Purcell is now able to prescribe mifepristone through a mail-order pharmacy, but she and her patients continue to experience harm as a result of the REMS. In particular, the REMS jeopardizes the privacy of Dr. Purcell's patients

[128] *Id.* at 2021 REMS 001164.

who need medication abortion care. Kauai Veterans, where Dr. Purcell works, is located in Waimea, a small town of fewer than 2,000 people on the western side of Kauaʻi. Kauai Veterans employs nearly 500 people across the island, with the majority working at its Waimea hospital and clinic site; many employees, including Dr. Purcell, live in or near Waimea. Most members of the community have a family member, friend, or neighbor employed at the hospital; Dr. Purcell frequently encounters current and former patients in the community in her day-to-day life. Dr. Purcell previously provided a medication abortion to a patient who shortly thereafter became a member of hospital staff. Generally, patient records are maintained through an electronic medical system, but the system does not have the capacity to store the Patient Agreement form—a unique form generated outside of the hospital system (*i.e.*, by FDA) that needs to be scanned in from a hard copy. In order to comply with the requirement in the Prescriber Agreement form that prescribers "ensure that the signed Patient Agreement Form is placed in the patient's medical record," Dr. Purcell had to involve administrative staff in creating a hard copy file for her patient, thus potentially revealing the patient's private medical decision to her future colleagues. In addition to causing direct harm to this patient and jeopardizing Dr. Purcell's relationship with someone who is both a patient and now also a colleague, Dr. Purcell is concerned about potential HIPAA implications of the Patient Agreement ETASU when similar situations occur in the future. In the insular

community in which Dr. Purcell lives and works, there is a strong likelihood that similar privacy issues will arise again as a result of the REMS. Indeed, the same scenario involving the provision of medication abortion care to a Kauai Veterans employee, and related patient privacy concerns, previously occurred for former plaintiff Dr. Graham Chelius.

191. SFP and CAFP each has members experiencing harm(s) traceable to the REMS, including many or all of the harms detailed *supra*. For instance, as of March 30, 2023:

192. Sarah McNeil, MD, is a member of both SFP and CAFP and a family medicine doctor. Among other work, Dr. McNeil provides primary care, including mifepristone for abortion and miscarriage, within a large county health system in northern California primarily serving a low-income patient population disproportionately comprising people of color. While there are more than 20 primary care offices located throughout the county—often hours apart from each other by car or bus—mifepristone is typically only prescribed at a single site within the county health system, and the REMS is impeding Dr. McNeil and her colleagues from expanding the provision of mifepristone to outlying clinics. She and her colleagues have already spent tens of hours over multiple years trying to navigate the administrative barriers imposed by the REMS, and developing technology to increase awareness of the REMS among clinicians across the health system and

streamline their ability to make mifepristone available for abortion and miscarriage care. These efforts have yielded only limited success, and Dr. McNeil's work to surmount the REMS barriers is ongoing.

193. For instance, as a direct result of the Prescriber Certification ETASU, Dr. McNeil's health system requires that would-be mifepristone prescribers go through the added hurdle of obtaining internal privileges for mifepristone through their Medical Staff Office. To become credentialed, a clinician must submit an application that is then reviewed by the credentialing committee through a formal process occurring only once per month—delaying a clinician's ability to integrate mifepristone into their practice. Dr. McNeil's health system does not require OB-GYN or Family Medicine doctors to obtain privileging before prescribing *any* other medication—only mifepristone.

194. As another example, the REMS creates an array of challenges for Dr. McNeil and her colleagues with respect to mifepristone dispensing. After countless meetings and emails with the numerous colleagues that must be involved in REMS compliance, Dr. McNeil's health system recently developed a process for its inpatient pharmacy to maintain records of whether a clinician is certified to prescribe mifepristone, and to dynamically update the system's electronic health records to reflect that information—a substantial and ongoing investment of human labor.

195. Even with this system in place, the Prescriber Certification ETASU is likely to still cause confusion and delays in patient care. Dr. McNeil's system has determined that, if a clinician unaware of the REMS requirements submits a mifepristone prescription to the health system's inpatient pharmacy without already being REMS-certified, someone at the inpatient pharmacy—which is also responsible for, *e.g.*, filling time-sensitive prescriptions for the hospital's intensive care unit—will have to send a copy of the certification form to that prescriber, who must then print, sign, and fax it back to the inpatient pharmacy before the prescriber can be considered temporarily privileged for mifepristone and the medication can be dispensed. Alternatively, if a clinician working at one of the few clinics in the county health system that stock mifepristone onsite writes a prescription for a patient without having already been REMS-certified, the nurse responsible for dispensing medications would have to notify the prescriber that certification is required before it can be dispensed; the clinician would then have to coordinate with the inpatient pharmacy to complete their certification and fax it to the pharmacy; and the pharmacy would then have to get in touch with the nurse to give the green-light to dispense the mifepristone. Meanwhile, the patient either must wait at the clinic for this entire process to be completed in order to obtain their prescription, or else leave the clinic—for instance, because of work or family responsibilities—and then make

another trip back at a later time to obtain the pill, with all of the burdens and costs of transportation, child care, and time off work that entails.

196. Dr. McNeil shares her story in her individual capacity and as an SFP and CAFP member, and not as a representative of any other institution.

197. Julie Jenkins, DNP, APRN, WHNP-BC, is a member of SFP and a nurse practitioner specializing in women's health who also holds a Doctor of Nursing Practice degree. The Doctor of Nursing Practice degree culminates in a final project intended to provide the doctoral candidate with an opportunity to publish and to gain other meaningful experience that will help position them for the academic job market. Dr. Jenkins intended to focus her project on developing and implementing a training on mifepristone for advanced practice registered nurses, the methodology and results of which she would then publish. However, Dr. Jenkins faced repeated REMS-related hurdles in attempting to implement this straightforward project. For instance, while IRB approval would normally not be required for a project of this nature, Dr. Jenkins was advised by leadership at her academic institution to seek IRB approval—expressly because of mifepristone's REMS classification. Despite months of efforts to try to overcome these barriers, Dr. Jenkins was unable to complete the project at all, forfeiting an important professional opportunity. Indeed, Dr. Jenkins later had to explain in a job interview for an

academic position why she did not complete a project during her doctoral program, and ultimately did not get that job.

198. Dr. Jenkins shares her story in her individual capacity and as an SFP member, and not as a representative of any other institution.

199. Angela Chen, MD, is a member of SFP and an OB-GYN practicing in a large university medical center in Los Angeles. Dr. Chen is a certified prescriber in the mifepristone REMS Program who prescribes mifepristone to patients seeking medication abortion and miscarriage care. But the Prescriber Certification ETASU poses significant burdens for Dr. Chen and her colleagues. Dr. Chen has colleagues within her institution and at the institution's satellite clinics who, although trained to provide medication abortion and miscarriage care with mifepristone, do not prescribe mifepristone because of the Prescriber Certification ETASU. These colleagues have informed Dr. Chen that they are not comfortable becoming certified prescribers because of concerns about security and stigma if they were ever publicly identified as an abortion provider. Instead, they refer their patients who need mifepristone for medication abortion or miscarriage care to Dr. Chen and other certified prescribers in her practice. Similarly, OB-GYNs, family medicine physicians, internal medicine doctors, pediatricians, and other clinicians who practice in private settings and in community health centers in the Los Angeles area regularly refer patients to Dr. Chen and her colleagues for medication abortion and

miscarriage care using mifepristone because they are unwilling or unable to become REMS-certified. These referrals occur nearly every week. Because of the frequency with which the referrals occur, and the time-sensitive medical care involved, these referrals impose burdens and logistical challenges for the certified prescribers as well as other institutional staff who have to work to try to squeeze these patients into already packed schedules.

200. The Patient Agreement ETASU also burdens Dr. Chen and her patients. Dr. Chen's institution uses an electronic medical record and e-signature system that could not accommodate the Patient Agreement form required under the REMS. As a result, they had to set up an entirely new system, separate from their existing system, to obtain e-signatures from the patients prescribed mifepristone. The Patient Agreement ETASU has also imposed emotional harm on some of Dr. Chen's patients seeking care for miscarriage, because they are forced to sign a form that says they have decided to take mifepristone to end their pregnancy when they are, in reality, suffering the loss of a wanted pregnancy.

201. Dr. Chen shares her story in her individual capacity and as an SFP member, and not as a representative of any other institution.

202. Zeynep Uzumcu, MD, is a member of CAFP and a family medicine doctor specializing in obstetrics care. Among other work, she provides primary care at a safety net community health center serving a low-income population,

disproportionately comprising people of color, in the northern central valley of California. In that capacity, Dr. Uzumcu regularly has patients present who are experiencing early pregnancy loss, and who request medication to complete the miscarriage. But Dr. Uzumcu is unable to provide her patients with the combined mifepristone-misoprostol regimen for early pregnancy loss because of the REMS. For years, she and her colleagues have been attempting to make mifepristone available at their health center, but the clinic administration is deeply concerned about having to require miscarriage patients to sign a form stating that they are having an abortion. As a result, Dr. Uzumcu either offers patients the misoprostol-only regimen for miscarriage—while informing them that it is less effective than the combined regimen and thus they are more likely to require an additional in-office procedure if it fails—or else must refer them elsewhere for care. Both options have significant downsides: Dr. Uzumcu's patients in the midst of a miscarriage who opt to be referred elsewhere must make an extra visit to a health center, and typically cannot obtain an appointment (even with Dr. Uzumcu's help) for three to seven days. On the other hand, if patients opt for the misoprostol-only regimen and then have the treatment regimen fail, they generally must seek an in-office dilation and curettage procedure that they were hoping to avoid. Moreover, because Dr. Uzumcu's health center does not offer that service, such patients have to travel to another facility for the procedure, often with a multi-week delay before they can

obtain an appointment. If not for the REMS, Dr. Uzumcu would be able to provide her patients with the preferred treatment regimen for medical management of miscarriage.

203. Dr. Uzumcu shares her story in her individual capacity and as a CAFP member, and not as a representative of any other institution.

204. Panna Lossy, MD, is a member of CAFP and a family medicine doctor; she also currently serves as the North Bay Chapter President for CAFP and as an alternate delegate to the CAFP board of directors. Dr. Lossy previously ran an early pregnancy options clinic within a full-spectrum primary care practice in California, where she was a certified mifepristone prescriber. She has retired from that role, but is still regularly contacted by doctors who want to integrate mifepristone into their practices and seek Dr. Lossy's help understanding and navigating the REMS barriers—including numerous such requests for help in the two months since FDA's 2023 REMS reauthorization. Doctors frequently seek out Dr. Lossy, for instance, to discuss their fears about being on an abortion provider "list," or to strategize about how they can try to reduce the burdens of REMS compliance on other departments within their health care system. Unfortunately, while Dr. Lossy can tell these colleagues that there are measures in place to try to ensure the confidentiality of mifepristone prescriber certifications, it is impossible for her to reassure them that they would not face anti-abortion violence or harassment if their certification as a

mifepristone prescriber were to be leaked—especially now, post *Dobbs*. Ultimately, even with Dr. Lossy's help, the REMS often delays or deters clinicians with whom she consults from becoming certified mifepristone prescribers.

205. While Dr. Lossy is motivated to provide this support because of her commitment to expanding safe and equitable access to reproductive health care, these conversations require time that she would otherwise spend on paid work or time with her family. Dr. Lossy does not have comparable conversations with respect to any other drug or health care service, and if FDA regulated mifepristone like other equally safe prescription drugs, these REMS-related burdens on Dr. Lossy would be eliminated.

206. Dr. Lossy shares her story in an individual capacity and as a member of CAFP and SFP, not on behalf of any other institution.

207. Additionally, SFP and CAFP each must divert resources from other organizational priorities to try to mitigate the burdens of the mifepristone REMS. As of March 30, 2023:

208. For instance, separate and apart from this litigation, SFP regularly participates in meetings and consults with members regarding the impact of the REMS and how to mitigate the burdens of those restrictions, and is in the process of developing guidance about seeking IRB approval for studies relating to abortion and contraception that may include a component about navigating the mifepristone

REMS. These efforts require staff time and resources that SFP would otherwise spend on other clinical and policy matters relating to abortion and contraception.

209. Similarly, separate and apart from this litigation, CAFP regularly participates in meetings and consults with members regarding the impact of the mifepristone REMS and how to mitigate the burdens of those restrictions. CAFP has also engaged in specific efforts to educate its members about compliance with the REMS, for instance through a webinar. These efforts require staff time and resources that CAFP would otherwise spend on advocacy, clinical education, professional development, and other efforts to support its family physician members.

CLAIMS FOR RELIEF

COUNT I

(Equal Protection)

210. The allegations of paragraphs 1 through 209 are incorporated as though fully set forth herein.

211. The Mifepristone REMS Program violates Plaintiffs', Plaintiffs' members', and Plaintiffs' members' patients' right to equal protection of the laws under the Fifth Amendment to the United States Constitution by treating Plaintiffs, Plaintiffs' members, and Plaintiffs' members' patients differently from other similarly situated parties without a sufficient state interest.

COUNT II

(Administrative Procedure Act: Contrary to Constitutional Right)

212. The allegations of paragraphs 1 through 209 are incorporated as though fully set forth herein.

213. FDA's 2023 reauthorization of the mifepristone REMS and other agency action and inaction described herein constituted final agency action for which Plaintiffs have no other adequate remedy within the meaning of 5 U.S.C. § 704.

214. FDA's 2023 reauthorization of the mifepristone REMS and other agency action and inaction described herein is contrary to Plaintiffs', Plaintiffs' members', and Plaintiffs' members' patients' constitutional rights, including their rights under the Fifth Amendment to the U.S. Constitution, in violation of 5 U.S.C. § 706(2)(B).

COUNT III

(Administrative Procedure Act: In Excess of Statutory Authority)

215. The allegations of paragraphs 1 through 209 are incorporated as though fully set forth herein.

216. FDA's 2023 reauthorization of the mifepristone REMS and other agency action and inaction described herein constituted final agency action for

which Plaintiffs have no other adequate remedy within the meaning of 5 U.S.C. § 704.

217. FDA's 2023 reauthorization of the mifepristone REMS and other agency action and inaction described herein is in excess of the Agency's statutory authority under the FDCA in violation of 5 U.S.C. § 706(2)(C).

COUNT IV

**(Administrative Procedure Act:
Arbitrary, Capricious, Abuse of Discretion, and Contrary to Law)**

218. The allegations of paragraphs 1 through 209 are incorporated as though fully set forth herein.

219. FDA's 2023 reauthorization of the mifepristone REMS and other agency action and inaction described herein constituted final agency action for which Plaintiffs have no other adequate remedy within the meaning of 5 U.S.C. § 704.

220. FDA's 2023 reauthorization of the mifepristone REMS was not based on any reasoned decision or rational basis, and therefore was arbitrary, capricious, an abuse of discretion and otherwise not in accordance with law in violation of 5 U.S.C. § 706(2)(A).

221. FDA's 2023 reauthorization of the mifepristone REMS treated similarly situated entities differently without adequate justification, and therefore

was arbitrary, capricious, an abuse of discretion and otherwise not in accordance with law in violation of 5 U.S.C. § 706(2)(A).

222. FDA's 2023 reauthorization of the mifepristone REMS violated the Agency's governing statute and therefore is not in accordance with law in violation of 5 U.S.C. § 706(2)(A).

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully request that the Court enter judgment in their favor and:

1) Declare, pursuant to 28 U.S.C. § 2201, that the mifepristone REMS in its entirety, as set forth above, violates the Fifth Amendment of the United States Constitution; and/or
2) Declare, pursuant to 28 U.S.C. § 2201, that certain components of the mifepristone REMS violate the Fifth Amendment of the United States Constitution:
    a. ETASU A (Prescriber Certification); and/or
    b. ETASU B (Pharmacy Certification); and/or
    c. ETASU D (Patient Agreement Form); and/or
    d. Implementation System; and/or
    e. Timetable for Assessments; and/or

3) Declare, pursuant to 28 U.S.C. § 2201, that the mifepristone REMS in its entirety, as set forth above, violates the Administrative Procedure Act; and/or

4) Declare, pursuant to 28 U.S.C. § 2201, that certain components of the mifepristone REMS violate the Administrative Procedure Act:

    a. ETASU A (Prescriber Certification); and/or

    b. ETASU B (Pharmacy Certification); and/or

    c. ETASU D (Patient Agreement Form); and/or

    d. Implementation System; and/or

    e. Timetable for Assessments; and

5) Enter an injunction prohibiting Defendants, their employees, agents, and successors in office, from requiring a REMS for Mifeprex (mifepristone), NDA 020687, mifepristone (ANDA 091178), or any future ANDA associated with these applications; and/or

6) Remand to FDA with instructions to remove the Mifepristone REMS Program while maintaining the approvals of Mifeprex (mifepristone), NDA 020687, and mifepristone (ANDA 091178); and

7) Award to Plaintiffs costs, expenses, and attorneys' fees pursuant to 28 U.S.C. § 2412; and

8) Award such other, further, and different relief as the Court deems just and proper.

DATED: Honolulu, Hawai‘i, August 2, 2024.

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