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Attorneys for Plaintiffs

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF HAWAI'I

GRAHAM T. CHELIUS, M.D., on behalf of himself and his patients; SOCIETY OF FAMLY PLANNING, on behalf of its members and their patients; CALIFORNIA ACADEMY OF FAMILY PHYSICIANS, on behalf of its members and their patients; and PHARMACISTS PLANNING SERVICES INC., on behalf of its members and their patients,

Plaintiffs,

v.

DON J. WRIGHT, M.D., M.P.H., in his official capacity as ACTING SECRETARY, UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES, and his employees, agents and successors in office; UNITED STATES FOOD AND DRUG ADMINISTRATION; and SCOTT GOTTLIEB, M.D., in his official capacity as COMMISSIONER OF FOOD AND DRUGS, and his employees, agents and successors in office,

Defendants.

CIVIL ACTION

Case No. _____

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. Since 2000, mifepristone has been approved by the United States Food and Drug Administration ("the FDA" or "the Agency") under the brand name Mifeprex® for use, in a regimen with the drug misoprostol, as a medical option for terminating an early pregnancy. Mifeprex remains the only drug approved in the United States for this purpose and is commonly referred to as the "abortion pill." Over the past 17 years, 3 million women in the United States have used Mifeprex to end an early pregnancy. According to the FDA, this medication "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."[1] Within a few days of taking Mifeprex and then misoprostol, the patient will experience a miscarriage. These prescription medications enable a woman to end a pregnancy up to 10 weeks in the privacy and comfort of her home.

2. This case is not about whether Mifeprex should continue to be available only by prescription. Rather, this case is about where a woman must be standing when she receives the pill her health care provider has prescribed for her. The unique and harmful restrictions the FDA imposes on where and how a patient may receive Mifeprex deny women meaningful access to this safe and effective treatment with no medical justification.

[1] U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Research, 020687Orig1s020, Mifeprex Medical Review(s) 12 (Mar. 29, 2016) [hereinafter "2016 Medical Review"], attached hereto as Ex. A.

3. Mifeprex is safe. As the FDA concluded in March 2016, serious adverse events following Mifeprex use are "exceedingly rare," and "the numbers of these adverse events appear to be stable or decreased over time."[2]

4. Indeed, the risks associated with Mifeprex are lower than those of many other common medications, such as Viagra® or anticoagulants (blood thinners). Mifeprex use is also far safer than continuing a pregnancy: the risk of associated fatality is *fourteen times greater* for a woman who carries a pregnancy to term than for a woman who uses Mifeprex.

5. Moreover, because Mifeprex is prescribed and administered as a single pill, there is no risk of a patient developing a dependency (as there is for many widely used prescription drugs).

6. Yet despite the fact that serious adverse events associated with Mifeprex are "exceedingly rare," and despite what the FDA recognizes as the "meaningful therapeutic benefit" that Mifeprex provides to patients seeking to end an early pregnancy using pills rather than a surgical procedure,[3] the FDA subjects Mifeprex to a Risk Evaluation and Mitigation Strategy ("REMS") that burdens health care providers and limits patient access to this medication with no medical benefit.

7. A REMS is a set of requirements beyond the approved prescribing information that the FDA may impose under the federal Food, Drug, and Cosmetic Act ("FDCA") when, and only when, necessary to ensure that a drug's benefits outweigh its risks. 21 U.S.C. § 355-1(a)(1). The most burdensome type of REMS are "Elements to Assure Safe Use" ("ETASU"), which the FDA may impose only when necessary because of the "inherent toxicity or potential

[2] *Id.*, Ex. A, at 47.

[3] Letter from Janet Woodcock, M.D., Director, Ctr. for Drug Evaluation & Research, to Donna Harrison, M.D., *et al.*, Denying Citizen Petition Asking the FDA to Revoke Approval of Mifeprex 4 (Mar. 29, 2016) [hereinafter "Letter Denying Petition to Revoke Mifeprex Approval"], attached hereto as Ex. B.

harmfulness" of a drug. *Id.* § 355-1(f)(1). Specifically, the 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 elements are required." *Id.* § 355-1(f)(1)(A). And, even then, the ETASU must be "*commensurate* with the specific serious risk[s]" listed in the drug label, *id.* § 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 in rural or medically underserved areas," *id.* § 355-1(f)(2)(C) (emphases added).

8. In light of these stringent statutory limitations, of the nearly 1800 prescription drugs and therapeutic biologic active ingredients currently approved by the FDA and marketed in the U.S.,[4] only 73 are subject to a REMS—and just 43 are subject to a REMS *with* ETASU.[5]

9. Nevertheless, in violation of the FDCA, Mifeprex is subject to a REMS with ETASU that significantly restricts how it can be distributed without any corresponding medical benefit.[6]

10. Specifically, the Mifeprex REMS provides that a patient cannot obtain the medication by prescription at a retail pharmacy, as is the normal course. Rather, she must be handed the medication at a clinic, medical office, or hospital under the supervision of a health care provider who has registered with the drug manufacturer, attested to their ability to safely prescribe Mifeprex, and then arranged to order and stock Mifeprex in their health care facility. In addition,

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[4] Elizabeth G. Raymond *et al.*, *Sixteen Years of Overregulation: Time to Unburden Mifeprex*, 376 New Eng. J. Med. 790, 790 (2017).

[5] U.S. Food & Drug Admin., Approved Risk Evaluation and Mitigation Strategies (REMS), https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=RemsData.page (last visited Oct. 1, 2017) [hereinafter "FDA REMS Count"].

[6] Mifeprex Risk Evaluation and Mitigation Strategy (REMS) (2016), *available at* https://www.accessdata.fda.gov/drugsatfda_docs/rems/Mifeprex_2016-03-29_REMS_full.pdf (last visited Oct. 1, 2017) [hereinafter "Current Mifeprex REMS"].

the patient must sign a "Patient Agreement" form confirming that she has received counseling on the risks associated with Mifeprex.

11. Thus, a woman who turns to her trusted local health care provider with an unwanted pregnancy and requests a medication abortion cannot obtain that care unless the clinician has already registered with the drug manufacturer and arranged to stock the drug. This is so even though that same provider can simply write her a prescription for misoprostol, the second drug in the FDA's approved regimen for medication abortion, or virtually any other prescription drug that the clinician deems medically appropriate.

12. For many health care providers across the country, registering with the drug manufacturer and stocking Mifeprex at their office is difficult or impossible. Some cannot obtain approval from their hospital's bureaucracy because of opposition to abortion. Some fear the internal conflict that would arise if colleagues opposed to abortion were asked to be involved in procuring, stocking, or dispensing the abortion pill. Some are deterred by the logistics of being "certified" by a drug manufacturer, entering into a contract with the drug distribution company, and ordering the medication—a process unfamiliar to many clinicians because it is required for such a small number of drugs, and which can be particularly complicated and time-consuming for clinicians at large health care institutions. Others are uncomfortable having their names included on a master list of medication abortion providers in the country, fearful of anti-abortion violence or harassment if the list were ever exposed.

13. The Mifeprex REMS does not improve patient health or safety. Once a woman has been prescribed Mifeprex, there is no medical benefit to requiring that the pill be handed to her at a medical office, clinic, or hospital rather than handed to her at her local pharmacy or via a mail-order pharmacy. Indeed, the Mifeprex REMS does not require that a patient *take* the medication

at the health care facility; as long as the drug is dispensed at an authorized medical setting, she may take the drug with her for later use at home, which some women find desirable if it would be unsafe or inconvenient to experience a miscarriage in the next 24 to 72 hours.

14. Moreover, having found that "[h]ome administration . . . is efficacious, practical, and safe," the FDA allows a woman to receive the misoprostol (the second drug in the approved regimen, which causes uterine contractions and expulsion of the pregnancy) at a retail pharmacy and take it at home in the timeframe and manner her health care provider instructs.[7] And the FDA authorizes patients to self-administer at home another, less safe, mifepristone product, Korlym®, as treatment for Cushing's syndrome—even though, as the FDA noted, Korlym "is taken in higher doses, in a chronic, daily fashion unlike the single 200 mg dose of Mifeprex . . . [and] the rate of adverse events with Mifeprex is much lower."[8]

15. As for the Mifeprex Patient Agreement requirement, the FDA's own team of expert reviewers uniformly recommended in 2016 that this REMS element be eliminated because it is duplicative of informed consent laws and standards, "does not add to safe use conditions . . . and is a burden for patients."[9] However, they were overruled by then-FDA Commissioner Robert Califf, M.D., and this ETASU was reauthorized in March 2016.[10]

16. Similarly, the requirement that clinicians sign a form stating that they are competent to prescribe Mifeprex provides no additional safety benefit beyond that conferred by the numerous

[7] 2016 Medical Review, *supra* note 1, Ex. A, at 22.

[8] *Id.*, Ex. A, at 10.

[9] U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Research, 020687Orig1s020, Mifeprex Summary Review 25 (Mar. 29, 2016) [hereinafter "2016 Summary Review"], attached hereto as Ex. C.

[10] U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Research, 020687Orig1s020, Mifeprex Risk Assessment and Risk Mitigation Review(s): Letter from Janet Woodcock, M.D., Ctr. for Drug Evaluation & Research, Regarding NDA 020687, Supp 20, 1 (Mar. 28, 2016) [hereinafter "Woodcock Patient Agreement Memo"], attached hereto as Ex. D.

laws and standards already in place to ensure that health care providers practice only within their competency. It is also out of step with how the FDA regulates other, less safe medications. Clinicians are allowed to prescribe countless drugs without first attesting to their competency to make an accurate diagnosis or provide care in the event of a complication. There is no reason why clinicians willing to provide medication abortion care should be trusted any less.

17. In short, this restriction is neither motivated nor supported by science.

18. At the same time, the Mifeprex REMS causes significant harm to patients. When a woman seeks a medication abortion and her clinician cannot provide her with timely care because of the REMS, at best, she will be forced to delay her abortion while she makes an additional, medically unnecessary trip to another health care facility that has the medication on hand. At worst, she will be unable to obtain abortion care at all.

19. A woman whose abortion is delayed by the REMS is exposed to medical risks and psychological burdens that she otherwise would not face, and bears the sometimes prohibitive costs of travel to another health care facility. Making this additional trip—which may necessitate additional child care, additional time off work, and significant transportation expenses—also compromises some women's ability to keep their abortions confidential, with dangerous consequences for women in abusive relationships and young women with abusive parents.

20. Women in the most rural and medically underserved areas of the country—such as the island of Kaua‘i, where Plaintiff Graham Chelius's patients live a flight away from the nearest abortion provider—experience particular harm. Put simply, the Mifeprex REMS makes health care less safe and more costly for rural women.

21. In *Whole Woman's Health v. Hellerstedt*, 136 S. Ct. 2292 (2016), *as revised* (June 27, 2016), the U.S. Supreme Court held that an abortion restriction purportedly designed to protect

patient health and safety must actually do so, and the medical benefit must outweigh the burden on patient access, or else the law is constitutionally invalid. The Mifeprex REMS cannot survive this standard. To the contrary, the REMS *harms* patient health by delaying or preventing women's access to timely medication abortion care and forcing some patients to carry a pregnancy to term against their will.

JURISDICTION AND VENUE

22. 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.

23. 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.

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

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

26. 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 Chelius resides in the District.

PARTIES

A. Plaintiffs

27. Plaintiff Graham T. Chelius, M.D., is a board-certified family medicine physician with a focus in obstetrics. He is the Chief Medical Officer for the Hawaii Health Systems Corporation's Kauaʻi Region, which includes Kauai Veterans Memorial Hospital in Waimea, Kauaʻi, on the western side of the island ("Kauai Veterans") and Samuel Mahelona Memorial Hospital in Kapaʻa, Kauaʻi, on the eastern side of the island. Over the past decade, he has delivered more than 800 babies on an island of just over 65,000 people. Dr. Chelius brings this lawsuit solely in his individual capacity and does not speak on behalf of the Hawaii Health Systems Corporation. Dr. Chelius is a resident of the State of Hawaiʻi.

28. As described *infra*, the Mifeprex REMS prevents Dr. Chelius from providing mifepristone to his patients. He sues on his own behalf and on behalf of his patients.

29. Plaintiff Society of Family Planning ("SFP") is a non-profit corporation located in Philadelphia, Pennsylvania, and incorporated in the state of Pennsylvania. SFP is a national member association of clinician-researchers with expertise in family planning. Membership in SFP is open to qualified individuals who are in good professional standing and have an interest in family planning demonstrated through post-doctoral training, a substantial clinical or laboratory practice, and academic presentations and publications within the field. Since its incorporation in 2005, SFP's membership has grown to nearly 800 fellows based primarily in the United States. Its members are trained in obstetrics and gynecology, internal medicine, family medicine, pediatrics/adolescent medicine, and public health, among other specialties. SFP also has Ph.D. members, including social scientists, epidemiologists, demographers, and nurse-researchers. 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.

30. As described *infra*, SFP has members who are prevented from providing mifepristone to their patients because of the Mifeprex REMS. SFP sues on behalf of its members and its members' patients.

31. The California Academy of Family Physicians ("CAFP") is a non-profit professional association located in San Francisco, California. With more than 9,000 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.

32. As described *infra*, CAFP has members who are prevented from providing mifepristone to their patients because of the Mifeprex REMS. CAFP sues on behalf of its members and its members' patients.

33. Pharmacists Planning Services Inc. ("PPSI") is a non-profit corporation located in San Rafael, California, and incorporated in the state of California. It has hundreds of independent pharmacist and pharmacy members across the country, including in Alaska, Arizona, Arkansas, California, Colorado, Delaware, Florida, Georgia, Hawai'i, Idaho, Illinois, Indiana, Iowa,

Kansas, Kentucky, Louisiana, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Montana, North Carolina, North Dakota, Nebraska, Nevada, New Jersey, New Mexico, New York, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, South Dakota, Tennessee, Texas, Utah, Vermont, Virginia, Washington, West Virginia, and Wisconsin.

34. PPSI is involved in arranging and conducting certified continuing education programs for pharmacists, advocating on behalf of independent pharmacists before the California State Board of Pharmacy and other regulatory bodies, advising its members of developments of interest or concern to health care professionals, promoting public health concerns, and organizing campaigns and programs on health issues for consumers, pharmacists, and other health care professionals.

35. Because the Mifeprex REMS prohibits the sale of Mifeprex at retail pharmacies, PPSI's members—all of whom are pharmacists or pharmacies—are uniformly prevented from stocking and dispensing mifepristone. PPSI sues on behalf of its members and its members' patients.

B. Defendants

36. Defendant Don J. Wright, M.D., M.P.H., 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 Wright maintains an office in Washington, D.C.

37. 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 the FDA the authority to administer the relevant provisions of the FDCA.

38. Defendant Scott Gottlieb, 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 the FDA, including with regard to the imposition or removal of a REMS. Defendant Gottlieb maintains offices in Washington, D.C., and Silver Spring, Maryland.

STATUTORY FRAMEWORK

A. FDA Approval Process for New Drugs

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

40. According to the 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.[11]

[11] U.S. Food & Drug Admin., Development & Approval Process (Drugs), *available at* https://www.fda.gov/drugs/developmentApprovalProcess/default.htm (last visited Sept. 30, 2017).

Second, the FDA performs an "[a]ssessment of benefits and risks from clinical data." The 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."[12] *Third*, the 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)."[13]

41. 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.

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

43. The 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."[14]

[12] *Id.*

[13] *Id.*

[14] *Id.*

44. 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, the 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").

45. 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

46. 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 the 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).

47. 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.*

48. 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).

49. 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).

50. Moreover, the 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 the FDA would not approve, or would withdraw approval for, the drug absent the ETASU. *Id.* § 355-1(f)(1)(A) (emphasis added).

51. Congress imposed several additional requirements to ensure that the 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).

52. 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).

53. 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. Mifeprex Regimen and Safety Record

54. The current FDA-approved regimen for the medical termination of early pregnancy involves two drugs: (1) *mifepristone* (under the brand name Mifeprex), 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. The 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.

55. The FDA has approved the use of this regimen through 70 days (*i.e.*, 10 weeks) of pregnancy, when the overwhelming majority (approximately 80%) of abortions occur.[15]

56. Taken alone, misoprostol also acts as an abortifacient—but it is less effective and causes more severe side effects than the Mifeprex/misoprostol regimen. Nevertheless, unlike Mifeprex, misoprostol is not subject to a REMS, and thus patients may obtain it from a pharmacy with a prescription. As a result, some patients receive the two drugs approved for a medication abortion in two different places: the first (Mifeprex) at a clinic, doctor's office, or hospital, as required by the REMS; the second (misoprostol) at a local pharmacy or via a mail-order pharmacy.

57. Under the current FDA-approved regimen, the patient initiates the abortion by taking one 200 mg tablet of Mifeprex in a single oral dose on day one. Then, 24-48 hours later, she 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 liquid). The FDA label does not specify where the patient should be located when she takes either medication. Most women will expel the pregnancy within 2 to 24 hours after taking the misoprostol. The patient is instructed to follow up with her health care provider approximately 7 to 14 days later to confirm that the termination of pregnancy was successful, but the FDA label no longer anticipates that this follow-up evaluation will occur in-person.

58. Like all medication labels, the Mifeprex label warns about potential risks associated with the drug. Its label lists as risks "serious and sometimes fatal infections or bleeding."[16]

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[15] Tara C. Jatlaoui *et. al.*, Ctrs. for Disease Control & Prevention, *Abortion Surveillance – United States, 2013*, 65 Morbidity & Mortality Weekly Report 12, 26, 28 (Nov. 25, 2016), https://www.cdc.gov/mmwr/volumes/65/ss/pdfs/ss6512.pdf.

[16] Mifeprex Label 1, *available at* https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/020687s020lbl.pdf (last visited Oct. 1, 2017) [hereinafter "Mifeprex Label"].

59. As the FDA explained in its Summary Review Memorandum for Mifeprex in March 2016, which evaluated changes to the Mifeprex label and REMS, "[t]here have been approximately 2.5 million uses of Mifeprex by U.S. women since the drug's approval in 2000."[17] During that time, the 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."[18] 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 marketing. Serious adverse events are rare and the safety profile of Mifeprex has not substantially changed."[19]

60. 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."[20]

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[17] 2016 Summary Review, *supra* note 9, Ex. C, at 10.

[18] 2016 Medical Review, *supra* note 1, Ex. A, at 12.

[19] U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Research, 020687Orig1s020, Mifeprex Risk Assessment and Risk Mitigation Review(s): REMS Modification Memorandum 3 (Mar. 29, 2016) [hereinafter "2016 REMS Modification Memorandum"], attached hereto as Ex. E.

[20] 2016 Medical Review, *supra* note 1, Ex. A, at 10.

B. FDA Approval of Mifeprex and Imposition of the REMS

1. Initial FDA Approval

61. 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.

62. 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.

63. There were three historically-controlled clinical trials on the safety and efficacy of the Mifeprex and misoprostol regimen presented to the FDA as part of the 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]."[21] As part of the NDA review, the 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.

[21] Letter Denying Petition to Revoke Mifeprex Approval, *supra* note 3, Ex. B, at 8.

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

65. 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 H (which provides for accelerated approval) and imposed ETASU—a restricted distribution system—as a condition of approval.

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

67. According to a report by the U.S. Government Accountability Office ("GAO"), the 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.[22] The FDA further stated that the restricted distribution scheme was necessary to ensure patient safety, and that approving Mifeprex under Subpart H would allow the FDA to impose comparable restrictions on any future generic mifepristone products.[23]

68. 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 REMS statute), only seven NDAs, including

[22] 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.

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

Mifeprex, were approved subject to ETASU under Subpart H.[24] By comparison, there were 961 NDAs approved in the roughly thirteen years from January 1993 to September 2005.[25]

69. 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

70. 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.

71. In 2011, the 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:

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

73. *Second*, three types of ETASU (A, C, and D).

- ETASU A requires clinicians to self-certify before they may prescribe Mifeprex. Under ETASU A, all health care providers who prescribe Mifeprex must be specially certified. To be certified, the provider completes and faxes to the Mifeprex distributor a one-time Prescriber's Agreement, agreeing that they meet the qualifications and will follow the guidelines outlined in the Prescriber's Agreement. These guidelines

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

[25] 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.

require prescribers to attest that they have the ability to date a pregnancy; have the ability to diagnose an ectopic pregnancy; have 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 have read and understood the prescribing information for Mifeprex. In addition, the prescriber must agree to provide the patient with the Medication Guide and Patient Agreement, give her an opportunity to read and discuss them, obtain her signature, 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 restricts where a patient may receive Mifeprex once it is prescribed. Under ETASU C, Mifeprex may 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 may not be dispensed through retail pharmacies.
- ETASU D places additional requirements on the patient receiving Mifeprex. Under ETASU D, Mifeprex may be dispensed only to a patient who has completed and signed a Patient Agreement form, a copy of which must be placed in her medical record, and who has been provided a copy of the Medication Guide.

74. *Third*, an Implementation System, under which distributors agree 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.

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

3. 2016 Mifeprex Label Change and REMS Assessment

a. Requested Changes to Mifeprex Label and REMS

76. 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 an FDA-approved label—is extremely common and widely accepted in the United States. Thus, shortly after the 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 label (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 the FDA proposing to update the label 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 label).

77. This submission prompted a top-to-bottom review of the Mifeprex label and REMS by the 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.

78. Other signatories requesting that the FDA eliminate the Mifeprex REMS included the American Congress of Obstetricians and Gynecologists ("ACOG"), the leading professional association of physicians specializing in the health care of women, which represents 58,000 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.

79. 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).[26]

80. In the 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]

[26] U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Research, 020687Orig1s020, Cross Discipline Team Leader Review 25 (Mar. 29, 2016) [hereinafter "2016 Team Leader Review"], attached hereto as Ex. F.

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."[27]

81. 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 as well as provider offices. Your letter has been shared with the appropriate FDA staff and will be carefully reviewed.[28]

82. 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

[27] 2016 Medical Review, *supra* note 1, Ex. A, at 23.

[28] Letter from Janet Woodcock, M.D., Ctr. for Drug Evaluation & Research, to Jessica Arons, J.D. (Feb. 25, 2016), attached hereto as Ex. G.

> 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.[29]

83. 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 restricts where Mifeprex may 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."[30] 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

[29] Letter from SFP, *et al.*, to Stephen Ostroff, M.D., Robert M. Califf, M.D., & Janet Woodcock, M.D., 1 (Feb. 4, 2016) [hereinafter "SFP Letter to FDA"], attached hereto as Ex. H.

[30] *Id.*, Ex. H, at 2.

> the doctor significantly increase financial and logistical burdens for these individuals and communities.[31]

84. 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 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."[32]

85. 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.[33]

86. The letter also noted that "[t]he Prescriber's Agreement would be incompatible and unnecessary if there were an expanded distribution system."[34]

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[31] *Id.*, Ex. H, at 2–3.

[32] *Id.*, Ex. H, at 3. According to the FDA, a "boxed" or "black box warning" "appears on a prescription drug's label 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://www.fda.gov/downloads/forconsumers/consumerupdates/ucm107976.pdf.

[33] SFP Letter to FDA, *supra* note 29, Ex. H, at 3.

[34] *Id.*

87. Finally, the letter requested that the Agency remove ETASU D, the Patient Agreement, which is "medically unnecessary and interferes with the clinician-patient relationship."[35]

b. FDA's 2016 Approval of Revised Label

88. The FDA adopted nearly all of Danco's proposed label changes (discussed *supra* at ¶ 76), 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.

89. The FDA also approved two changes regarding where the woman takes the mifepristone and misoprostol. First, the label no longer states that the woman takes the Mifeprex and misoprostol "at [her] provider's office." Rather, although health care providers must still *dispense* the Mifeprex only in certain medical facilities according to the REMS, the new label does not specify where she *takes* the pill; it simply states that the woman takes the Mifeprex in a single oral dose on "Day One," and that she takes four tablets of misoprostol by the buccal route 24-48 hours later.[36] The label 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."[37]

90. In addition, the new label clarifies that Mifeprex can be safely used through 70 days of pregnancy (rather than 49).[38] The Agency concluded in its 2016 Medical Review that, based on

[35] *Id.* at 4.

[36] Mifeprex Label, *supra* note 16, at 3.

[37] *Id.*

[38] *Id.* at 1.

the scientific evidence, "[m]edical termination of pregnancies through 70 days gestation is safe and effective and should be approved."[39]

c. FDA's 2016 Reauthorization of the REMS

91. As part of its review of the proposed label 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."[40] This assessment was conducted by a multidisciplinary reviewing team and elevated to the Commissioner of the FDA, a political appointee, who gave specific feedback on proposed changes to the Mifeprex REMS.

92. 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 here 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 about current clinical practice."[41]

93. 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.[42]

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[39] 2016 Medical Review, *supra* note 1, Ex. A, at 21.

[40] U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Research, 020687Orig1s020, Supplement Approval Letter for Mifeprex 2 (Mar. 29, 2016) [hereinafter "2016 Supplement Approval Letter"], attached hereto as Ex. I.

[41] U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Research, 020687Orig1s020, Mifeprex Risk Assessment and Risk Mitigation Review(s): REMS Modification Review 5 (Mar. 29, 2016), attached hereto as Ex. J.

[42] U.S. Food & Drug Admin., Mifeprex (mifepristone) Information, *available at* https://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111323.htm (last visited Sept. 30, 2017).

94. 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 flow.

95. 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 with respect to deaths.[43] The stated goal of the current 2016 Mifeprex REMS program is "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 health care settings under the supervision of a certified prescriber, and (c) Informing patients about the risk of serious complications associated with Mifprex."[44]

96. 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."[45] Agency reviewers observed that "[i]t is standard of care for

[43] 2016 REMS Modification Memorandum, *supra* note 19, Ex. E, at 2 (listing changes), 4 (discussing retention of ETASU D); *see also* U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Research, 020687Orig1s020, Mifeprex Risk Assessment and Risk Mitigation Review(s): Addendum to REMS Modification Review 5 (Mar. 29, 2016), attached hereto as Ex. K (discussing modifications to the reporting requirement).

[44] Current Mifeprex REMS, *supra* note 6, at 1.

[45] Woodcock Patient Agreement Memo, *supra* note 10, Ex. D, at 1.

patients undergoing pregnancy termination to undergo extensive counseling and informed consent,"[46] and noted that the "FDA has removed REMS requirements in other programs based on the integration of the REMS safe use condition into clinical practice."[47] 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*."[48]

97. 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 the FDA] . . . requested that the Patient Agreement Form be retained as an element of the REMS."[49] Therefore, Director Woodcock "asked [Agency staff] to include a Patient Agreement Form in the REMS for Mifeprex," which they did.[50]

98. 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 (E.D.N.Y. 2013) (finding that FDA did not have authority to mandate point-of-sale restrictions on

[46] 2016 Summary Review, *supra* note 9, Ex. C, at 25.

[47] 2016 Team Leader Review, *supra* note 26, Ex. F, at 25.

[48] 2016 Summary Review, *supra* note 9, Ex. C, at 25 (emphasis added).

[49] Woodock Patient Agreement Memo, *supra* note 10, Ex. D, at 1.

[50] *Id.*, Ex. D.

levonorgestrel-based emergency contraception given the scientific data demonstrating that adolescents could safely use Plan B).

C. The Mifeprex 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 Mifeprex Outweigh Its Risks

99. 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 the FDA's decision to reauthorize the Mifeprex REMS in 2016:

100. **"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."[51] Between September 2000 and March 2016, when the Agency reauthorized the REMS, 2.5 million United States women chose Mifeprex for use to end an early pregnancy.

101. Many more women could potentially benefit from Mifeprex. 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." [52]

[51] 2016 Medical Review, *supra* note 1, Ex. A, at 12.

[52] SFP Letter to FDA, *supra* note 29, Ex. H, at 1.

102. Because Mifeprex has already been safely used by millions of U.S. women, and increasing access to this medication would help many more, this factor weighs against a REMS.

103. **"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 unintended pregnancy is a serious condition. On the same day that it updated the Mifeprex label and reauthorized the REMS (March 29, 2016), the Agency also finally denied a citizen petition filed fourteen years earlier asking the Agency to withdraw the initial (September 2000) approval for Mifeprex. In its denial of that citizen petition, the 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.[53]

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

[53] Letter Denying Petition to Revoke Mifeprex Approval, *supra* note 3, Ex. B, at 4-5 (citations omitted).

105. **"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 Mifeprex approval, the 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."[54] 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.[55]

106. In addition, some women prefer medication abortion because it feels more natural, and allows them to pass the pregnancy in the privacy and comfort of their home. Indeed, in its 2016 Medical Review, the Agency noted that "[t]he studies [supporting the Mifeprex label 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."[56] In short, Mifeprex allows a woman to have an abortion in a private, comfortable, and safe location, on her own terms.

107. While misoprostol also has abortifacient properties acting alone, it is safer and more effective in early pregnancy when used in the FDA-approved regimen with Mifeprex.

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[54] *Id.*, Ex. B, at 5 (citations omitted).

[55] *Id.*, Ex. B.

[56] 2016 Medical Review, *supra* note 1, Ex. A, at 62 (emphasis added).

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

109. **"The expected or actual duration of treatment with the drug,"** 21 U.S.C. § 355-1(a)(1): Mifeprex 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; 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,[57] and the agency trusts patients to use it accordingly.

110. Because Mifeprex 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.

111. **"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 the FDA's own admission, major adverse events associated with Mifeprex are "exceedingly rare, generally far below 0.1% for any individual adverse event."[58] 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-

[57] Korlym Label, *available at* https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/202107s000lbl.pdf (last visited Sept. 30, 2017).

[58] 2016 Medical Review, *supra* note 1, Ex. A, at 47.

characterized, that no new safety concerns have arisen in recent years, and that the known serious risks occur rarely."[59] 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 Mifeprex "is pregnancy itself," because similar infections "have been identified both in pregnant women who have undergone medical abortion and those who have not[.]"[60] The FDA's 2016 Medical Review also expressly concludes that "[m]edical abortion in adolescents appears to be at least as safe, if not safer, as in adult women."[61]

112. Because numerous studies and over 15 years of clinical data in the United States confirm that Mifeprex is safe—and that serious adverse events are rare, decreasing, and never shown to have been caused by Mifeprex—this factor weighs against a REMS.

113. **"Whether the drug is a new molecular entity,"** 21 U.S.C. § 355-1(a)(1): Mifeprex is not a new molecular entity. Mifepristone had already been approved in the United States for nearly 16 years when the FDA reauthorized the REMS in March 2016.

114. Because Mifeprex is a well-known compound, this factor weighs against a REMS.

115. Finally, because none of these factors supports maintaining the Mifeprex REMS, the implementation system and timetable for assessments from the drug manufacturer also are unnecessary. Indeed, as the FDA's 2016 Medical Review acknowledges, even without a REMS, "the [drug manufacturer] will still be required by law, as is every NDA holder, to report serious,

[59] *Id.*, Ex. A, at 8.

[60] Letter Denying Petition to Revoke Mifeprex Approval, *supra* note 3, Ex. B, at 26 n.69.

[61] 2016 Medical Review, *supra* note 1, Ex. A, at 76.

unexpected adverse events as 15-day safety reports, and to submit non-expedited individual case safety reports, and periodic adverse drug experience reports."[62]

2. The Mifeprex ETASU Are Not "Commensurate With" and Do Not Mitigate the "Specific Serious Risk[s]" Listed on the Mifeprex Label

116. In violation of the FDCA, the Mifeprex ETASU are not "commensurate with the specific serious risk[s]" listed on Mifeprex's label, 21 U.S.C. § 355-1(f)(2)(A), which are "[s]erious and sometimes fatal infections or bleeding."[63] To the contrary, the ETASU are disproportionate to, have no nexus with, and will not mitigate, the risks listed on the Mifeprex label. In short, there is no relationship between where a woman is standing when she receives the Mifeprex pill and any potential risk of infection or bleeding.

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

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

118. The Agency concedes that serious adverse events associated with Mifeprex are "exceedingly rare."[64] 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

[62] *Id.*, Ex. A, at 8.

[63] Mifeprex Label, *supra* note 16, at 1.

[64] 2016 Medical Review, *supra* note 1, Ex. A. at 47.

pregnancy will likely remain acceptably low. The numbers of each of these adverse events appears to have remained steady over time, with a possible decrease in severe infections."[65]

119. In the 15 years of U.S. post-marketing data available to the FDA when it reauthorized the REMS, there were only 17 reported associated deaths out of 2.5 million uses—an associated fatality rate of 0.00068%.[66] Since then, there have been only two additional associated deaths out of more than half a million additional uses.[67] 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 4 times the Mifeprex-associated mortality rate.[68]

120. Five of the reported deaths in women who had taken Mifeprex involved events clearly unrelated to the medication, such as narcotic overdose or suspected homicide. And the FDA acknowledges that "[t]here is no information that use of Mifeprex and misoprostol caused" the "very small number" of deaths from infection.[69] Rather, as explained *supra*, 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.[70]

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[65] *Id.*, Ex. A, at 84.

[66] *Id.*, Ex. A, at 82-83.

[67] Raymond *et al.*, *supra* note 4, at 791.

[68] 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).

[69] Mifeprex Medication Guide 1, *available at* https://www.fda.gov/downloads/Drugs/DrugSafety/UCM088643.pdf (last visited Oct. 1, 2017).

[70] Letter Denying Petition to Revoke Mifeprex Approval, *supra* note 3, Ex. B, at 26 n.69.

121. Indeed, a woman is at least fourteen times more likely to die if she carries a pregnancy to term than if she uses Mifeprex to end a pregnancy.[71] Moreover, the two risks listed on the Mifeprex label are also 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"). As the Mifeprex Medication Guide acknowledges: "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 abortion, or *childbirth*." (emphasis added).[72]

b. The ETASU Do Not "Mitigate" the Risks Listed on the Label

122. 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

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

124. Those unanimous conclusions were amended only after then-FDA 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

[71] 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).

[72] Mifeprex Medication Guide 1, *supra* note 69, at 1.

provide additional assurance that the patient is aware of the nature of the procedure, its risks, and the need for appropriate follow-up care."[73]

125. Commissioner Califf made this request notwithstanding that medication abortion does not involve any "procedure," only pills, and notwithstanding that the 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."[74]

ii. ETASU C: Restricted Distribution

126. ETASU C provides that Mifeprex may be dispensed only in certain health care facilities and not in retail pharmacies. Although in 2016 the FDA "assessed the current REMS program to determine whether each Mifeprex REMS element remains necessary to ensure that the drug's benefits outweigh the risks[,]"[75] the Agency's only documented rationale for this ETASU is that it "ensures that Mifeprex can only be dispensed by or under the direct supervision of a certified prescriber."[76]

127. This explanation is medically unjustified for several reasons.

128. *First*, although ETASU C requires that Mifeprex be *dispensed* only in a clinic, medical office, or hospital, it does not require that the patient *take* the Mifeprex only in a clinic, medical office, or hospital. A provider may give her the Mifeprex to take at home, just as they may give her the misoprostol to take at home, or give her a prescription to obtain the misoprostol at a pharmacy and then take at home. Where a woman takes the Mifeprex is a function of the

[73] Woodcock Patient Agreement Memo, *supra* note 10, Ex. D, at 1.

[74] 2016 Summary Review, *supra* note 9, Ex. C, at 25.

[75] 2016 Supplement Approval Letter, *supra* note 40, Ex. I, at 2.

[76] 2016 REMS Modification Memorandum, *supra* note 19, Ex. E, at 3.

exigencies of her life: she knows when and where she wants to be when she passes the pregnancy; from that decision, she works backward to decide when and where to take first the Mifeprex and then the misoprostol.

129. The FDA's 2016 Medical Review notes that "[t]he studies, 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."[77] The memorandum describes another study as including "safety" among the benefits of home administration of Mifeprex and misoprostol.[78]

130. There is *no* safety benefit to requiring that a woman be handed a single pill at a clinic, medical office, or hospital to be swallowed at home, rather than be handed a single pill at a retail pharmacy to be swallowed at home.

131. *Second*, the pharmacologic effects of Mifeprex do not begin until hours after ingestion, and as the label explains, "most women will expel the pregnancy within 2 to 24 hours of taking *misoprostol*"[79]—i.e., 26 to 72 hours after taking the Mifeprex. Thus, regardless of where the woman takes the Mifeprex or misoprostol, she will almost never be under the direct supervision of her prescriber by the time the bleeding (a necessary part of the miscarriage) begins.

132. In short, banning pharmacists from dispensing Mifeprex once it has been prescribed to a patient has no bearing on whether, hours later, a woman will have the "exceedingly rare" experience of one of the risks listed on the label.

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[77] 2016 Medical Review, *supra* note 1, Ex. A, at 62.

[78] *Id.*, Ex. A.

[79] Mifeprex Label, *supra* note 16, at 3.

iii. ETASU A: Special Certification for Prescribers

133. To become certified to prescribe Mifeprex, 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.

134. The Agency's only documented rationale for maintaining ETASU A is that it "ensures that Mifeprex can only be dispensed by or under the direct supervision of a certified prescriber"[80] (the same as ETASU C).

135. This explanation is medically unjustified for several reasons.

136. *First*, numerous other mechanisms, including 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.

137. *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.

[80] 2016 REMS Modification Memorandum, *supra* note 19, Ex. E, at 3.

138. *Third*, fulfilling these criteria requires no specialized medical expertise. 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.

139. Similarly, any provider can arrange for emergency care by referring patients to an emergency room in the rare event that such care is needed.

140. *Fourth*, as discussed *infra*, the REMS forces some patients to travel outside their communities for abortion care. A patient who receives Mifeprex from a REMS-certified provider outside 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 Mifeprex prescriber thus has no bearing on the care the patient would receive in the unusual event of a complication.

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

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

142. 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 Mifeprex are not subject to comparable restrictions.

143. Today, according to the FDA's REMS database, only 73 of the nearly 1800 prescription drugs and therapeutic biologic active ingredients approved by the FDA and marketed in the United States are subject to a REMS.[81]

144. Only 43 of those, including Mifeprex, are subject to a REMS *with* ETASU.[82] Thus, in effect, the Agency has classified Mifeprex—alongside drugs such as OxyContin® and other opioids—as one of the 43 drugs with the most "inherent toxicity or potential harmfulness" available in the United States. And even within the group of 43 drugs that are subject to a REMS with ETASU, only a handful, including Mifeprex, are subject to the stringent restriction that the drug be dispensed only in certain health care settings and not in a pharmacy by prescription.

145. Moreover, many drugs that have higher safety risks than Mifeprex are permitted to be marketed without restrictions comparable to the Mifeprex REMS.

146. For instance, Viagra is associated with death in up to 0.0026% of users, roughly 4 times the Mifeprex-associated mortality rate.[83] Yet, according to the FDA's REMS database, Viagra does not have a REMS.

147. Similarly, many anticoagulant products, commonly known as "blood thinners," are associated with "serious and fatal bleeding," and, like Mifeprex, carry warnings of that risk on their FDA-approved labels.[84] But unlike Mifeprex, anticoagulants are a frequent cause of

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[81] FDA REMS Count, *supra* note 5; Raymond *et al.*, *supra* note 4, at 791.

[82] FDA REMS Count, *supra* note 5.

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

[84] *See, e.g.*, Coumadin® label, *available at* https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/009218s107lbl.pdf (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).

emergency room visits for documented hemorrhage.[85] Yet anticoagulants are available by prescription at a pharmacy, whereas Mifeprex is not.

148. Perhaps most telling is that, despite the prescription opioid abuse crisis—which is estimated to result in more than 22,000 overdose deaths in the United States each year (about 62 people per day)[86]—opioid products are permitted to be dispensed at pharmacies. But Mifeprex is not.

149. In sum, the Mifeprex REMS with ETASU is a medically unjustified restriction on abortion, as evidenced both by the drug's own record and by how the FDA regulates other drugs with a safety profile comparable to or weaker than that of Mifeprex.

150. These restrictions simply are not motivated by science.

D. The Impact of the Mifeprex REMS on Plaintiffs and Plaintiffs' Patients

151. In addition to lacking any medical benefit, the Mifeprex REMS also significantly burdens patient access to abortion.

152. The harms the REMS causes are particularly acute for women who live in rural or medically underserved areas, have low income, are experiencing domestic abuse, and/or are young. Any or all of these factors, together with the REMS, can make it especially difficult for a woman to access abortion care.

153. Because of the Mifeprex REMS, many health care providers across the country—including Dr. Chelius and members of SFP and CAFP—cannot prescribe Mifeprex to a patient

[85] 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).

[86] U.S. Ctrs. for Disease Control & Prevention, Opioid Data Analysis (Feb. 9, 2017), *available at* https://www.cdc.gov/drugoverdose/data/analysis.html.

seeking medication abortion care, no matter how urgent the patient's need or the obstacles she would face in attempting to obtain timely care elsewhere.

154. In a recent, nationally representative survey of ACOG Fellows (who are currently practicing board-certified OB-GYNs), only 14% of the more than 1,100 respondents reported providing medication abortion care during the previous year, and those who had provided abortion care were disproportionately located in urban areas. Of the 86% of respondents who had *not* provided medication abortion care within the past 12 months, nearly one in five said that they *would* start providing such care if they could write a prescription for Mifeprex—*i.e.*, if not for the REMS.[87]

155. There are multiple reasons why health care providers may be unable to stock Mifeprex at their clinic, office, or hospital, often stemming from ideological or political opposition to abortion within their health care facility.

156. Indeed, because of the Mifeprex REMS, even a single individual with influence over a health care facility's approval or procurement process for stocking a new drug can significantly delay, or altogether derail, a clinician's ability to prescribe Mifeprex in accordance with a patient's needs and with the provider's medical judgment. The Mifeprex REMS thus interferes with and undermines the clinician-patient relationship.

157. In addition, some health care providers, aware of the long history and ongoing threat of violence and harassment against abortion providers, are fearful of having their names included among a list of abortion providers maintained by Danco and the distribution company with

[87] Daniel Grossman *et al., Abortion Provision Among a National Sample of Obstetrician–Gynecologists*, 96 Contraception 273 (2017).

which it partners. Although Danco and the distribution company take significant measures to protect provider confidentiality, this concern remains an understandable deterrent to some.

158. Finally, because it typically takes several weeks for a health care provider to get certified by Danco, set up an account with the distribution company, and receive the first delivery of Mifeprex, even those health care providers who are willing to register with Danco as an abortion provider, *and* who have permission or authority to stock Mifeprex in their clinics, offices, or hospitals, will not be able to provide timely medication abortion care unless they have started this process long before a patient presents for care.

159. To set up an account with the drug distribution company, the prescriber must certify that a resolution (to become a Mifeprex dispenser) was adopted "by written consent or at a special meeting of the (circle applicable) board of directors/shareholders/managers/members/partners of said Company duly called, convened, and held in accordance with its governing documents . . ." Registrants must also provide a hard copy of their U.S. Drug Enforcement Agency license and state medical license.

160. These complicated and time-consuming logistics are not necessary for nearly any other prescription drug, and would not be necessary for Mifeprex if not for the REMS. Instead, a clinician who has diagnosed and dated an intrauterine pregnancy and obtained a patient's informed consent for medication abortion care could simply write a prescription for *both* Mifeprex and misoprostol, which the patient could then fill at a local or mail-order pharmacy.

1. Plaintiff Graham Chelius, M.D.

a. Access to Abortion Care in Hawai‘i

161. Numerous factors—including where a woman lives, whether she has reliable housing, how much money she earns, how old she is, whether she has children, and whether she is experiencing domestic abuse—affect her ability to access an abortion.

162. Kaua‘i, the second most western of the eight main islands in Hawai‘i, is one of the most remote regions in the United States. The entire island, together with the islands of Ni‘ihau, Lehua, and Ka‘ula (together, Kaua‘i County), is federally designated as a "medically underserved area" by the Health Resources and Services Administration within HHS because of a shortage of professional health care services.

163. According to the United States Census Bureau's Supplemental Poverty Measure 2015 report, the State of Hawai‘i has the ninth highest poverty rate in the nation when the state's cost of living is taken into account, with one in six people living in poverty.[88] Because of their low household income, the majority of public school students in Kaua‘i receive free or reduced-priced meals.[89]

164. Hawai‘i is also the state with the highest homelessness rate in the United States,[90] and Kaua‘i's homelessness rate is even higher—at 57.2 homeless per 10,000 people.[91]

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[88] U.S. Census Bureau, The Supplemental Poverty Measure: 2015, at 9, *available at* https://www.census.gov/content/dam/Census/library/publications/2016/demo/p60-258.pdf.

[89] David McCracken, *Over Half of Students Receive School Lunches Free or Reduced Price*, The Garden Island, March 14, 2017, *available a*t http://thegardenisland.com/news/local/over-half-of-students-receive-school-lunches-free-or-reduced/article_18a6fb7d-41a0-5f8f-a8fe-c719dd546032.html.

[90] National Alliance to End Homelessness, The State of Homelessness in America 2016, at 15, *available at* http://endhomelessness.org/wp-content/uploads/2016/10/2016-soh.pdf.

[91] Assuming a population estimate for the Kaua‘i County of 72,029 people per the Census Bureau's latest estimates. *See* Bridging the Gap & Partners in Care, State of Hawaii Homeless Point-in-Time Count January 22, 2017, at 24,

165. According to the CDC's National Intimate Partner and Sexual Violence Survey published in 2017, in their lifetime, 1 in 3 women in Hawai'i have experienced sexual violence, and 2 in 5 are victims of psychological aggression by an intimate partner.[92] The State of Hawai'i Attorney General reported that in 2016 Kaua'i had an index crime rate for rape of 62.7 per 100,000 people, which is almost 50% higher than the average state rate of 42.1 per 100,000 people.[93] Additionally, in 2016, the Kaua'i Police Department reported that, based on arrest data, domestic violence is the second most prevalent crime in Kaua'i.[94]

166. According to the United States Census Bureau's latest data, roughly 1 in 5 households in Kaua'i are non-English speaking.[95]

167. Hawai'i has the second-highest unintended pregnancy rate in the nation. In 2010, the last year for which data are publicly available, 56% of all pregnancies in the state were unintended, at a rate of 61 per 1,000 women ages 15-44.[96] Only one state, Delaware, has a higher unintended pregnancy rate; Hawai'i is tied with New York for second.[97]

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available at http://www.partnersincareoahu.org/sites/default/files/2017%20Statewide%20PIT%20Report%20-%20Full%20Report%20-%20FINAL.pdf.

[92] Centers for Disease Control and Prevention, The National Intimate Partner and Sexual Violence Survey 2010-12 State Report, at 33, 128, and 149, *available at* https://www.cdc.gov/violenceprevention/pdf/NISVS-StateReportBook.pdf.

[93] Attorney General State of Hawai'i, 2016 A Review of Uniform Crime Reports, at v, *available a*t https://ag.hawaii.gov/cpja/files/2017/08/Crime-in-Hawaii-2016.pdf.

[94] Michelle Iracheta, *Domestic Violence Leads in Arrests*, The Garden Isle, January 31, 2016, *available at* http://thegardenisland.com/news/local/domestic-violence-leads-in-arrests/article_3b3e2007-0b3d-5e69-a177-34547d075879.html.

[95] U.S. Census Bureau, Selected Social Characteristics in the United States, *available at* https://factfinder.census.gov/faces/nav/jsf/pages/index.xhtml.

[96] Guttmacher Institute, State Facts About Unintended Pregnancy: Hawaii (Aug. 2017), *available at* https://www.guttmacher.org/fact-sheet/state-facts-about-unintended-pregnancy-hawaii.

[97] Guttmacher Institute, Unintended Pregnancy in the United States (Sept. 2016), *available at* https://www.guttmacher.org/fact-sheet/unintended-pregnancy-united-states.

168. According to the Guttmacher Institute, there has been a 12% decline in the number of abortion providers across Hawai‘i since 2011, and a 33% decline in the number of abortion *clinics*; as of 2014, there were only four abortion clinics in the state.[98] The majority of abortion providers in Hawai‘i are private doctors who provide care only to established patients.

169. There are no abortion providers on Kaua‘i. The nearest island with an abortion provider is on O‘ahu, which Dr. Chelius's patients can reach only by plane.

b. Dr. Chelius's Practice

170. Kauai Veterans, where Dr. Chelius works, is located in Waimea, a small town of fewer than 2,000 people on the western side of Kaua‘i. Kauai Veterans employs approximately 275 people, many of whom—like Dr. Chelius—live nearby in the Waimea area. Most members of the community have a family member, friend, or neighbor employed at the hospital.

171. Dr. Chelius practices family medicine with a focus on obstetrics at Kauai Veterans and its associated clinics, West Kauai Clinics. Since joining Kauai Veterans in January 2009, he has delivered more than 800 babies on the island.

172. In addition, Dr. Chelius serves as the Chief Medical Officer ("CMO") for the Hawaii Health Systems Corporation's Kaua‘i Region, which includes both Kauai Veterans and a second hospital on the eastern side of the island. As CMO, Dr. Chelius is primarily responsible for managing the relationship between Hawaii Health Systems Corporation and the physicians who serve the Kaua‘i region, including participating in contract negotiations, overseeing physician staffing assignments, and responding to any complaints brought against physicians (whether by

[98] Guttmacher Institute, State Facts About Abortion: Hawaii (July 2017), *available at* https://www.guttmacher.org/fact-sheet/state-facts-about-abortion-hawaii.

patients or staff). His position requires that he be involved in resolving most of the conflicts that arise among the small clinical team at Kauai Veterans.

173. Dr. Chelius is aware that some of his colleagues are opposed to abortion, and that they would be upset, angry, and/or uncomfortable if asked to be involved either in an abortion procedure or in the process of procuring, stocking, and dispensing Mifeprex, as required by the REMS. In addition to clinical staff, this process would likely involve staff who are responsible for hospital contracts; staff who work in the hospital pharmacy; and staff who dispense medications at West Kauai Clinics.

174. Because Dr. Chelius believes that any such request would create internal conflict, he does not provide any abortion care at Kauai Veterans or West Kauai Clinics. Instead, Dr. Chelius typically refers patients to O‘ahu for care.

175. If not for the REMS, Dr. Chelius would be willing and able to write a prescription for Mifeprex for a patient seeking abortion care through ten weeks of pregnancy—without involving any of his colleagues—which the patient could then fill at one of the pharmacies on Kaua‘i or via mail-order pharmacy.

c. The Harms Dr. Chelius’s Patients Experience Because of the Mifeprex REMS

176. Traveling to O‘ahu is a severe burden for Dr. Chelius’s patients, particularly those with low incomes. Patients must arrange (1) transportation to the Lihue Airport on the south-eastern coast of Kaua‘i, (2) a flight to O‘ahu, (3) transportation from the airport in O‘ahu to an abortion clinic, (4) transportation back to the airport in O‘ahu from the abortion clinic, (5) a return flight to Kaua‘i, and (6) transportation from the airport in Kaua‘i to the patient’s home. Thus, the cost of transportation alone can easily exceed $300.

177. In addition, a patient with children must also arrange for child care, which may add costs. A working patient must arrange to miss at least one day of work—which, for many low-income workers who do not have paid time off, means a day of lost wages.

178. For poor and low-income women who receive health insurance through Hawai‘i’s Medicaid program (“Med-Quest”), the costs of the abortion procedure and travel to obtain it are covered. However, to receive that benefit, Dr. Chelius must submit a referral and other paperwork directly to Med-Quest, which then works with the patient to arrange the travel. This process can be especially time-consuming and complicated for patients who are homeless, who do not own a reliable cell phone, for whom English is not a first language, or who do not have reliable cell phone service because of the rural area in which they live.

179. Because of the logistics involved in this process, Dr. Chelius’s Med-Quest (*i.e.*, low-income) patients typically are delayed by two to three weeks before they can leave the island to receive abortion care.

180. While abortion is extremely safe, the risks increase as pregnancy advances.

181. The cost of an abortion also increases as pregnancy advances.

182. In addition, some of Dr. Chelius’s patients are delayed past the point in pregnancy at which they can obtain a medication abortion. Instead, their only options are a surgical procedure, which in many cases involves anesthesia, or carrying the pregnancy to term.

183. Medication abortion is medically indicated for certain women (*e.g.*, women with uterine anomalies), and strongly preferred by others (*e.g.*, sexual assault survivors for whom the insertion of instruments into the vagina may cause emotional and psychological trauma, or minors who have never had a pelvic exam).

184. It is especially difficult for a patient to keep her abortion decision confidential from employers, neighbors, friends, or relatives when she must fly to another island to effectuate that decision. Women in abusive relationships, whose safety may be jeopardized if their partner is aware of their pregnancy and/or abortion, are at particular risk.

185. In addition, traveling to another island can be psychologically and emotionally taxing for some of Dr. Chelius's patients, particularly young women, women struggling with substance abuse, women for whom English is not a first language, and women who are homeless.

186. The time, costs, logistics, and emotional strain involved in traveling to O'ahu for care are insurmountable for some of Dr. Chelius's patients. Because of the REMS, some women on Kaua'i have been forced to carry a pregnancy to term against their will.

187. For the moment, a study of the efficacy and safety of medication abortion care delivered by mail is providing some temporary and imperfect relief to certain of Dr. Chelius's patients.

188. Patients participating in the study, which is not subject to the REMS, mail, fax, or email blood test and ultrasound results to a physician at the University of Hawai'i, who then meets with the patient by videoconference, obtains her informed consent, and mails her the medications. This study has allowed abortion access without flying to O'ahu for certain of Dr. Chelius's patients who have a device on which they can have a private medical conversation by videoconference at a set appointment time; a private location with reliable cell phone service in which to do so; and an address where the package can be securely and confidentially mailed. For others of Dr. Chelius's patients—including those who are homeless, live in extremely remote areas, and/or need to keep their abortion decision confidential—this study offers no relief. Moreover, the study is temporary.

189. In sum, because of the Mifeprex REMS, Dr. Chelius's patients suffer significant physical, financial, and emotional harm.

2. Plaintiff Society of Family Planning

a. The Challenges SFP Members Face Because of the REMS

190. SFP members include many of the leading national experts in family planning, including abortion care.

191. Yet some of SFP's members are delayed in, or prevented from, prescribing Mifeprex to their patients because of the REMS.

192. Many SFP members work at hospitals or clinics associated with hospitals. At these facilities, as in most clinical settings, the decision to write a prescription is usually determined solely by the patient and her health care provider(s), and effectuated within the privacy of the office or examination room.

193. By contrast, in most hospitals and associated clinics, multiple layers of approval are required before a drug can be added to the hospital or clinic formulary. This often includes an individual or committee at the department level (*e.g.*, the chair of the hospital's OB-GYN department); a pharmacy committee at the clinic or hospital level; and, in some cases, a pharmacy committee at the health care system level (when there is more than one hospital or clinic within the health care system). Often, these committees meet only on a periodic basis—for instance, once per quarter. Additional hospital staff, including those responsible for contract development, purchasing, and warehousing, may also be involved in the decision to procure and stock a drug.

194. This already lengthy process may be subject to additional complications when the drug in question is controversial—as is often the case with the abortion pill.

195. Because of the stigma surrounding abortion, some institutions where SFP members work have imposed additional, unique procedural hurdles to adding Mifeprex to the formulary, such as a requirement that the SFP member compile and present data on the safety of Mifeprex to the pharmacy committee.

196. Thus, in order to provide Mifeprex to their patients, some SFP members must first gain approval from dozens of people at a variety of levels within their institutions. This process is usually time-consuming, complicated, and requires SFP members to spend significant personal capital that they might otherwise put towards championing other patient health issues or advancing their careers.

197. In some cases, SFP members simply cannot get Mifeprex approved at their facility.

198. In addition, because the REMS may necessitate the involvement of additional hospital staff (such as medical assistants or hospital pharmacists) in the process of stocking or dispensing this medication, some hospitals require special staff training before allowing clinicians to start prescribing Mifeprex. For instance, a hospital may require a "values clarification training," through which health care professionals assess their own attitudes towards abortion in order to provide objective, respectful care. While this may be a beneficial service, because of the time necessary to develop and implement this training for all relevant staff, some SFP members are further delayed in their ability to prescribe Mifeprex to their patients.

199. Because of the REMS, some SFP members have been delayed by months or years in prescribing Mifeprex to their patients.

200. Because of the REMS, some SFP members have been delayed by months or years in incorporating Mifeprex into a hospital residency program, and are thus also delayed in (or prevented altogether) from training residents in the use of Mifeprex.

201. Because of the REMS, some SFP members are prevented from providing Mifeprex to their patients.

b. The Harms SFP's Members' Patients Experience Because of the Mifeprex REMS

202. SFP members prevented from prescribing Mifeprex because of the REMS often attempt to refer their patients elsewhere for care. For many patients, making a second trip to a second health care provider in order to obtain time-sensitive abortion care is a heavy burden because of the time and costs involved (for transportation, child care, and missed work), and because of the confidentiality risks. For women in rural or medically underserved areas, low-income women, young women, and women experiencing domestic violence, these harms are especially severe.

203. Because of the REMS, SFP members are also forced to refer long-time patients who seek to use Mifeprex—patients for whom they may have been providing obstetrical, gynecological, and/or primary care for years—to a different health care provider for abortion, even though they are qualified to provide such care themselves. This interferes with the clinician-patient relationship and can pose an additional psychological barrier to care for some patients, particularly young patients.

204. The need to make a second trip to a second health care provider delays some patients in accessing abortion care, and prevents some patients from accessing abortion care altogether.

205. Because it is challenging for some patients to travel to a different health care provider, and because of the time-sensitive nature of abortion care, some of SFP's members' patients use a method of abortion that is not as safe and effective as Mifeprex (such as using misoprostol only) or that is not their or their health care provider's preferred method (such as a surgical procedure),

or are altogether prevented from accessing abortion care and instead carry a pregnancy to term against their will.

3. Plaintiff California Academy of Family Physicians

a. The Challenges CAFP's Members Face Because of the REMS

206. CAFP members are family physicians located throughout the state of California, including in rural and medically underserved areas.

207. CAFP members face many of the same barriers to prescribing Mifeprex as Dr. Chelius and the members of SFP, including opposition among colleagues to procuring, stocking, or dispensing Mifeprex at the health care facilities where CAFP members work, and complicated, multi-layer approval processes for stocking a medication at a hospital, clinic, or medical office.

208. These barriers caused by the REMS significantly delay some CAFP members in prescribing Mifeprex to patients presenting with an unwanted pregnancy.

209. In some cases, because of the REMS, CAFP members are prevented altogether from prescribing Mifeprex to their patients.

210. In addition, some of CAFP's members provide home-based care to patients who are unable to safely or comfortably travel, or who have a strong preference for privacy. Because of the REMS, CAFP members are prevented from dispensing Mifeprex to their patients at home, as they do with other medications.

211. A patient seeking abortion care may prefer to have her physician deliver her Mifeprex to her home if she is experiencing a pregnancy-related illness (such as the severe nausea and vomiting of hyperemesis gravidarum); if she does not want to walk through a gauntlet of protesters outside an abortion clinic; or if she needs to keep her abortion decision private and fears that traveling to an abortion clinic will compromise her confidentiality.

212. However, because of the REMS, CAFP members are prohibited from delivering Mifeprex directly to their patients' homes, even if that is a delivery model they regularly use for other types of care, and even if the patient is too ill to travel to the physician's office or clinic or otherwise would strongly prefer such home-based care.

b. The Harms CAFP's Members' Patients Experience Because of the Mifeprex REMS

213. CAFP's members' patients face similar burdens as SFP's members' patients because of the Mifeprex REMS.

214. Some are forced to make a second trip to a second health care provider for abortion care and bear the costs and emotional burdens associated with that travel.

215. Some are delayed in accessing abortion care, which increases the associated risks.

216. Some are prevented from receiving abortion care through their preferred method, and/or receive abortion care (using misoprostol alone) that is less safe and effective than the FDA-approved Mifeprex/misoprostol regimen.

217. Some are prevented from accessing abortion care altogether and instead carry a pregnancy to term against their will.

218. In addition, some are prevented from having abortion care delivered to them at home by their physician, notwithstanding their medical and/or emotional reasons for preferring to receive such care in the privacy of their home.

4. <u>Plaintiff Pharmacists Planning Services Inc.</u>

219. PPSI members include independent pharmacies and pharmacists across the state of California and in nearly all 50 states. Many PPSI members have been providing pharmacy care in their communities for years or decades and have trusted relationships with their patients.

220. Some PPSI members currently dispense misoprostol to patients for use as part of the FDA-approved two-drug regimen to terminate an early pregnancy.

221. However, because of the REMS, PPSI members are uniformly prohibited from stocking and dispensing Mifeprex.

222. The Mifeprex REMS prevents PPSI members from providing a service that is wholly within their scope of practice: dispensing prescription medication, and providing patients with information about any risks associated with the medication or its interaction with other drugs the patient is taking (in addition to the informed consent process performed by the prescriber).

223. If not for the Mifeprex REMS, some PPSI members would stock and dispense Mifeprex to patients who present with a prescription.

224. Because of the REMS, PPSI members are unable to serve their patients who need Mifeprex, which causes them to lose business.

225. Because of the REMS, some of PPSI's members' patients are delayed in accessing medication abortion care, or prevented from obtaining a medication abortion altogether.

CLAIMS FOR RELIEF

COUNT I

(Substantive Due Process – Patients' Right to Privacy)

226. The allegations of paragraphs 1 through 225 are incorporated as though fully set forth herein.

227. The Mifeprex REMS violates Plaintiff Dr. Chelius's patients' and the other Plaintiffs' members' patients' right to liberty and privacy as guaranteed by the due process clause of the Fifth Amendment to the U.S. Constitution by imposing significant burdens on abortion access

that are not justified by the law's purported benefits, thereby imposing an undue burden on a woman's right to abortion.

COUNT II

(Equal Protection)

228. The allegations of paragraphs 1 through 225 are incorporated as though fully set forth herein.

229. The Mifeprex REMS 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 III

(Administrative Procedure Act: Contrary to Constitutional Right)

230. The allegations of paragraphs 1 through 225 are incorporated as though fully set forth herein.

231. The FDA's 2016 reauthorization of the Mifeprex 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.

232. The FDA's 2016 reauthorization of the Mifeprex 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 IV

(Administrative Procedure Act: In Excess of Statutory Authority)

233. The allegations of paragraphs 1 through 225 are incorporated as though fully set forth herein.

234. The FDA's 2016 reauthorization of the Mifeprex 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.

235. The FDA's 2016 reauthorization of the Mifeprex 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 V

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

236. The allegations of paragraphs 1 through 225 are incorporated as though fully set forth herein.

237. The FDA's 2016 reauthorization of the Mifeprex 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.

238. The FDA's 2016 reauthorization of the Mifeprex 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).

239. The FDA's 2016 reauthorization of the Mifeprex 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).

240. The FDA's 2016 reauthorization of the Mifeprex 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 Mifeprex 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 Mifeprex REMS violate the Fifth Amendment of the United States Constitution:
    a. ETASU A (Special Certification for Prescribers); and/or
    b. ETASU C (Dispensed Only in Certain Health Care Settings); 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 Mifeprex 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 Mifeprex REMS violate the Administrative Procedure Act:
    a. ETASU A (Special Certification for Prescribers); and/or
    b. ETASU C (Dispensed Only in Certain Health Care Settings); 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; and/or
6) Remand to the FDA with instructions to remove the Mifeprex REMS; 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, October 3, 2017.

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†*pro hac vice forthcoming*

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