IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF VIRGINIA

WHOLE WOMAN'S HEALTH ALLIANCE, *et al.*, Plaintiffs, v. UNITED STATES FOOD AND DRUG ADMINISTRATION, *et al.*, Defendants.	Case No. 3:23-cv-00019-RSB Honorable Robert Ballou

MEMORANDUM OF LAW IN SUPPORT OF PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT

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AAFP	American Academy of Family Physicians
ACOG	American College of Obstetricians and Gynecologists
AMA	American Medical Association
APA	Administrative Procedure Act
APHA	American Public Health Association
ETASU	Elements to assure safe use
FDA	United States Food and Drug Administration, also referred to as "the Agency."
NASEM	National Academies of Sciences, Engineering, and Medicine
REMS	Risk evaluation and mitigation strategy
SFP	Society of Family Planning
SMF	Statement of Material Facts

Introduction

For nearly a decade, the nation's most pre-eminent medical professional societies, medical researchers, and other experts—including the former FDA Commissioner who initially approved mifepristone—have called on FDA to stop overregulating the drug. Over 5.6 million patients in the United States have used mifepristone to terminate their pregnancies since 2000, and FDA itself acknowledges that the drug's safety record is well-established. Nonetheless, FDA clings to anachronistic restrictions on the drug's distribution—the mifepristone REMS—because of the Agency's baseless speculation that the miniscule number of serious complications that occur during medication abortions might increase without them. And FDA's recalcitrance is more than just out of step with the times. It impedes patient access to mifepristone by restricting the number of health care professionals who can prescribe it and pharmacies that can dispense it, thus delaying or obstructing patients' access to time-sensitive abortion care and violating an express statutory mandate *not* to unduly burden that access. *See* 21 U.S.C. § 355-1(f)(2)(C).

This case challenges FDA's 2023 decision to maintain the mifepristone REMS (the "2023 REMS Decision") because it violates the APA in two independent respects: it exceeds FDA's statutory authority and limitations; and it is arbitrary and capricious.

First, FDA did not make the determinations that Congress directed it to make before exercising the authority to impose or maintain a REMS or ETASU. The threshold issue is whether a REMS is "necessary" for a drug's benefits to outweigh its risks; Congress directed FDA to consider six separate factors, spelled out in 21 U.S.C. § 355-1(a)(1), in making that determination. Congress also limited FDA's authority to impose or maintain an ETASU by requiring FDA to first determine that, but for the ETASU, the drug would be so unsafe that it would have to be withdrawn. *See* 21 U.S.C. § 355-1(f)(1). But *FDA did not make either determination* in the 2023 REMS Decision. And even though Congress directed FDA not to unduly burden access for "patients who

have difficulty accessing health care (such as patients in rural or medically underserved areas)," 21 U.S.C. § 355-1(f)(2)(C), FDA categorically refused to look at record evidence on that very subject in the 2023 REMS Decision. *See* Section I, below.

Second, FDA's analysis of the evidence in the administrative record was so flawed as to be arbitrary and capricious. As discussed in Section II.A., below, FDA outright refused to consider crucial evidence when it made the 2023 REMS Decision, including:

- A statistical analysis demonstrating that when Canada deregulated mifepristone by eliminating its REMS-like restrictions in 2017, it saw no decline in safety.
- Statements by AMA, ACOG, AAFP, and other professional medical societies explaining that the linchpin of the mifepristone ETASUs—the requirement that prescribers register with a mifepristone manufacturer by signing a certification that they are qualified to prescribe the drug—is an empty formality because medical professionals are already constrained by ethical, legal and professional codes to prescribe drugs only when they are competent to do so and to obtain their patients' informed consent.
- Qualitative evidence demonstrating that prescriber registration deters nine percent—nearly one in ten—of the country's obstetrician-gynecologists from prescribing mifepristone and that some providers fear registration could expose them to harassment or violence from anti-abortion activists.
- Analyses showing the vast areas of the country that lack adequate access to obstetrical care.

When FDA did proffer purported justifications for the ETASU, they were conclusory, inconsistent and illogical. *See* Section II.B., below. Finally, FDA did not address—indeed, it did not even acknowledge—the argument, made by numerous experts and stakeholders, that mifepristone is regulated far more restrictively than other drugs posing similar or more serious risks to patients, such as aspirin, acetaminophen, and Viagra. *See* Section II.C., below. Each of these grave defects is a telltale sign of an arbitrary and capricious administrative decision.

The 2023 REMS Decision plainly violates the APA. This Court should either vacate it or remand it to the FDA with specific instructions to adhere to the statutory directives governing the issuance of REMS and ETASU.

Background

A. The Regulatory Framework

Before introducing a new drug into interstate commerce, its sponsor must apply for FDA approval under 21 U.S.C. § 355. FDA must deny the application if, among other grounds, there is insufficient information on the drug's safety for use under the conditions set out in the drug's label. 21 U.S.C. § 355(d). If FDA later finds that the drug is "not safe" or is "unsafe" for use under those conditions, it must withdraw its approval. 21 U.S.C. § 355(e).

In 2007, Congress authorized FDA to require a REMS when it determined such a strategy "is necessary to ensure that the benefits of the drug outweigh the risks of the drug." Pub. L. 110-85, § 505-1(a)(1), 21 U.S.C. § 355-1(a)(1). Congress directed FDA to consider six factors in making that determination: (i) the estimated size of the population likely to use the drug; (ii) the seriousness of the disease or condition to be treated; (iii) the drug's expected benefit; (iv) the expected or actual duration of treatment; (v) the seriousness of any known or potential adverse events related to the drug and the background incidence of such events in the population likely to use the drug; and (vi) whether the drug is a new molecular entity. 21 U.S.C. § 355-1(a)(1).

Potential elements of a REMS include a non-technical "Medication Guide" for patients, a "Communication Plan" for health care providers, and special packaging. 21 U.S.C. § 355-1(e)(2), (3), (4); *see* 21 C.F.R. § 208.20(a)(1). For drugs with known serious risks "because of [their] inherent toxicity or potential harmfulness," Congress authorized FDA to require an ETASU upon finding that the drug could be approved only if—or would be withdrawn unless—that element was "required . . . to mitigate a specific serious risk listed in the labeling of the drug." 21 U.S.C. § 355-1(f)(1). "Serious risks" include death, hospitalization or significant incapacity. 21 U.S.C. § 355-1(b)(4), (5). The required finding must be made for each ETASU. 21 U.S.C. § 355-1(e).

Congress placed several additional limitations on FDA's ability to impose an ETASU, including that they must be "commensurate with the specific serious risk listed in the labeling of the drug," that they "not be unduly burdensome on patient access to the drug, considering in particular . . . patients in rural or medically underserved areas" and that they "minimize the burden on the health care delivery system" by avoiding both (i) inconsistencies with similar drugs and (ii) incompatibility with existing procedures. 21 U.S.C. § 355-1(f)(2)(A), (C), (D).

Under 21 U.S.C. § 355-1(g)(4)(B), FDA must consider the criteria set out in 21 U.S.C. § 355-1(a) when considering whether to modify or withdraw a REMS and those set out in 21 U.S.C. § 355-1(f) when considering whether to modify or withdraw an ETASU.

B. Statement of Material Facts

1. The mifepristone label and mandated REMS documents

1. As of June 30, 2022, approximately 5.6 million patients had used mifepristone for medication abortion in the United States. 2023 SUPP 1045. Under the FDA-approved protocol, patients take a single, 200 mg mifepristone tablet followed 24 to 48 hours later by four 200 mcg misoprostol tablets. 2023 SUPP 1473; 2023 SUPP 1492.

2. When FDA approved mifepristone in 2000, it found that the drug "provides a meaningful therapeutic benefit to patients over existing treatments," i.e., procedural abortions. FDA 860; FDA 228. FDA also acknowledges that pregnancy itself "can be a serious medical condition in some women" and that the risk of childbirth-related death is "approximately 14 times higher than the rate associated with legal abortion." FDA 859 & n.6 (citing 2021 REMS 695–99).

3. By 2016, FDA recognized that mifepristone "has been increasingly used as its efficacy and safety have become well established by both research and experience and serious complications have proven to be extremely rare." FDA 539. FDA further noted that major adverse

events are "generally far below .1% for any individual adverse event." FDA 574. The current mifepristone label states that cumulatively, fewer than .5% of all patients experience any kind of serious adverse reaction. 2023 SUPP 1496–97; 2023 SUPP 1477–78.

4. The prescribing information on the FDA-approved label enclosed in each mifepristone package highlights two specific risks in a box headed: "WARNING: SERIOUS AND SOMETIMES FATAL INFECTIONS OR BLEEDING." 2023 SUPP 1491; 2023 SUPP 1472. The label characterizes the two risks as "very" rare and notes that they can occur after any pregnancy termination, including through miscarriage and procedural abortion. 2023 SUPP 1491; 2023 SUPP 1472; *see also* FDA 881 (FDA acknowledges that "the critical risk factor in the reported cases of sepsis is pregnancy itself," not mifepristone). Serious infection has "also been reported very rarely following childbirth (vaginal delivery and caesarian section), and in other gynecologic and non-gynecologic conditions." 2023 SUPP 1494; 2023 SUPP 1475.

5. An FDA-approved Medication Guide is also part of the label. 2023 SUPP 1505–09; 2023 SUPP 1486–89. The non-technical Medication Guide advises that "rarely, serious and potentially life-threatening bleeding, infections, or other problems can occur following a miscarriage, surgical abortion, medical abortion, or childbirth," and that patients should "contact [their] healthcare provider promptly" or "go to the nearest hospital emergency room" if they experience certain symptoms. 2023 SUPP 1505; 2023 SUPP 1486.

6. On January 3, 2023, FDA approved a modified mifepristone REMS with the stated goal of "mitigat[ing] the risk of serious complications associated with mifepristone." 2023 SUPP 1466. In the name of accomplishing this goal, the REMS mandates three ETASUs: a "Prescriber Certification ETASU," requiring prescribers to register with a mifepristone manufacturer using a "Prescriber Agreement Form;" a "Patient Agreement ETASU," requiring patients and their

providers to sign a "Patient Agreement Form"; and a "Pharmacy Certification ETASU," requiring pharmacies to register with a mifepristone manufacturer using a "Pharmacy Agreement Form." 2023 SUPP 1466–70.

7. The Prescriber Agreement Form requires prescribers to certify that they can: assess the gestational age of a pregnancy accurately; diagnose ectopic pregnancies; and provide surgical intervention in cases of incomplete abortion or severe bleeding, or otherwise assure patient access to medical facilities equipped to provide blood transfusions and resuscitation. 2023 SUPP 1516; 2023 SUPP 1514. Prescribers must also certify that they have read and understand the prescribing information on the mifepristone label and that they will adhere to other REMS requirements when prescribing the drug. 2023 SUPP 1516; 2023 SUPP 1514.

8. FDA's periodic reviews of compliance with the mifepristone REMS program have never assessed whether certified prescribers meet the qualifications set out in the Prescriber Agreement Form. 2021 REMS 1509–32; FDA 331–41; FDA 361–70.

9. In the Patient Agreement Form, each patient must acknowledge, among other things, that she "ha[s] decided to take mifepristone and misoprostol to end [her] pregnancy," has been advised of the risks of heavy bleeding and infection, and has been instructed where to go if she experiences such adverse events. 2023 SUPP 1510.

10. The Medication Guide addresses all risks discussed in the Patient Agreement Form. FDA 616; *compare* 2023 SUPP 1505–09 and 2023 SUPP 1486–89 *with* 2023 SUPP 1510.

11. The Pharmacy Agreement Form requires pharmacies to certify, among other things, that they will verify that each prescriber is certified, deliver mifepristone within four calendar days of receiving the prescription and, if delivery will be later, confirm with the prescriber that it is still appropriate to dispense the drug to the patient. 2023 SUPP 1513. The form also requires

pharmacies to track and verify each mifepristone shipment, to maintain copious records (of all Prescriber Agreement Forms, dispensing and shipping records, and their own processes and procedures), and to comply with audits by the mifepristone manufacturers. *Id.*

2. FDA's 2011 approval of mifepristone REMS with ETASU

12. On September 28, 2000, FDA approved a new drug application for mifepristone for medication abortion. FDA 3. At the time, the statute authorizing FDA to impose a REMS had not been enacted. FDA imposed "restrictions as per [21] CFR 314.520 on the distribution and use of mifepristone" in order "to assure safe use of this product." FDA 32.

13. When Congress authorized FDA to issue REMS in 2007, it included an interim provision for drugs, like mifepristone, that previously had been approved by FDA with restrictions under 21 C.F.R. § 314.520. Those drugs initially were "deemed" to have an approved REMS in place on the law's effective date, and their sponsors then had 180 days to submit a proposed REMS that would be subject to FDA review as if the proposed strategy had been included in the original new drug application. Pub. L. 110-85, § 909; 21 U.S.C. § 331, Statutory Notes and Related Subsidiaries, Effective Date of 2007 Amendment.

14. Mifepristone's sponsor, Danco Laboratories ("Danco"), timely submitted a proposed REMS to FDA on September 16, 2008, FDA 232, and FDA conducted a "deemed REMS REVIEW" of the proposal. FDA 231–57. In June, 2011, FDA approved a mifepristone REMS calling for a Medication Guide to be given to patients with each mifepristone tablet, as well as three ETASU: a Prescriber Certification ETASU; a requirement that mifepristone be dispensed only in clinics, medical offices and hospitals (the "In-Person Dispensing ETASU"); and a Patient Agreement ETASU. FDA 233; FDA 235; FDA 258–60; FDA 1281–84.

15. On October 4, 2012, the Director of FDA's Center for Drug Evaluation and Research ("CDER") asked FDA staff to reevaluate the mifepristone REMS and ETASU. FDA 345. One year later, FDA concluded in a "Final Risk Evaluation and Mitigation Strategy (REMS) Review" that it would retain them. FDA 342–60. In this review, FDA acknowledged that "[t]here have been no new safety concerns identified with Mifeprex[1] since [certain labeling changes made in 2004 and 2005] and the serious complications being reported now are consistent with labeling." FDA 354. FDA also recognized that the "rare[]" complications "sometimes" seen with mifepristone were "consistent with what one can expect with spontaneous abortion and surgical abortions," and that they could be managed with timely treatment. FDA 354.

3. FDA's 2016 revision of the mifepristone REMS with ETASU

16. On May 28, 2015, Danco submitted a supplemental new drug application to FDA that sought to expand the use of mifepristone through a later gestational age, to revise the labeled dose and dosing regimen, and to modify the REMS by, among other things, allowing state-licensed prescribers who were not physicians to prescribe the drug. FDA 374; FDA 414.

17. FDA approved Danco's supplemental new drug application in a supplement approval letter dated March 29, 2016. FDA 374–81. FDA's analysis of the application confirms that mifepristone is very safe. FDA 412–39; FDA 527–634. Serious complications or risks, including deaths, hospitalization, serious infection, or transfusion, were described as "rare," "extremely rare" or "exceedingly rare." FDA 422; FDA 423; FDA 429; FDA535; FDA 539; FDA 578; FDA 583; FDA 705. The rates of serious adverse events reported in published studies using the new dose and dosing regimen were "generally far below 1%." FDA 583; FDA 578–84.

[1] "Mifeprex" is the brand name for mifepristone tablets sold by Danco. This memorandum uses the term "mifepristone" for both the brand-name and generic versions of the drug, which are subject to the same REMS and ETASU, and "Mifeprex" only when quoting from a document that uses the term.

18. The 2016 Mifepristone Review resulted in several changes to the REMS, including expressly permitting state-licensed prescribers who were not physicians to prescribe the drug. FDA 436–37. All three ETASU, however, remained in place. FDA 437–38.

19. While FDA was reviewing Danco's application, prominent medical professional societies and other experts submitted three letters asking FDA to eliminate the REMS, especially the ETASU. FDA 1245–53; FDA 1254–62; FDA 1263–64. These letters were submitted on behalf of (i) ACOG, which represents 58,000 physicians and other women's health care providers, FDA 1263–64; (ii) SFP and 29 other policy, social science, advocacy and research organizations, FDA 1254–62; and (iii) APHA, and fifteen other organizations and individuals that research or provide abortion, FDA 1245–53.

20. The medical professional societies explained that the qualifications required by the Prescriber Certification ETASU were unnecessary because "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." FDA 1256; *see* 2019 CP 793 (AMA Principles of Medical Ethics require physicians "to use sound medical judgment on patients' behalf") (cited by FDA at 2019 CP 664 n.118).

21. The medical professional societies also explained that no specialized medical expertise is needed to prescribe mifepristone:

> "Although many clinicians use history and/or clinical examination to assess the duration and location of a pregnancy, any provider who is not comfortable with these approaches can order an ultrasound. Similarly, any provider can appropriately plan to provide care for emergencies by referring patients to an emergency room if needed. No licensed healthcare professional would be unable to read or understand the prescribing information. A standard clinical license should be sufficient to assure that a provider meets these qualifications; an exceptional certification for mifepristone is unnecessary." FDA 1247.
>
> "[C]linicians with routine professional training can provide [mifepristone] appropriately." FDA 1257.

> "A standard clinical license should be sufficient to ensure that a practitioner meets qualifications for prescribing mifepristone. . . ." FDA 1264.

22. The medical professional societies noted that the Prescriber Certification ETASU was inconsistent with FDA's treatment of other drugs:

> "Provider certification for mifepristone is also inconsistent with the requirement for prescribing other drugs that require careful patient screening to ensure safety. For example, clinicians are not required to certify their ability to diagnose heart disease before prescribing powerful cardiovascular drugs, to diagnose infections before prescribing antibiotics, or to assess schizophrenia before prescribing antipsychotics. Evaluating a patient for each of these conditions is much more complicated than assessing the duration or location of a pregnancy." FDA 1247.

> "Provider certification is not required for health care professionals to dispense other drugs, including drugs that carry black box, or boxed, warning about their medical risks. Accutane, for example, has a boxed warning that describes the potential risks of the drug, but Accutane prescribers are not required to submit a certification form in order to prescribe it." FDA 1256.

23. The medical professional societies told FDA that some providers were deterred from offering mifepristone to their patients because of the Prescriber Certification ETASU:

> "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."*Id.*

> "Given the history of harassment and violence against abortion providers in this country and the demonstrated difficulty in maintaining confidentiality in the current environment, some clinicians are understandably reluctant to allow their names to be included in a list of abortion providers." FDA 1247.

24. The medical professional societies also faulted the Patient Agreement ETASU as potentially confusing to patients if a practitioner prescribed mifepristone in a way that departed from the labeled use. FDA 1247; FDA 1257.

25. Two FDA teams considered revising the mifepristone REMS as part of the review of Danco's application. FDA 527–634; FDA 679–83. Their recommendations are set out in a "REMS Modification Review," which concluded that the Prescriber Certification ETASU should

remain in place. FDA 698–709. FDA did not mention the professional medical societies' opposition in concluding that "the qualifications of a health care provider who prescribes Mifeprex have not changed and continue to be necessary to ensure the benefits outweigh the risks." FDA 706.

26. The FDA staff who reviewed the Patient Agreement ETASU all agreed that it should be removed. FDA 535; FDA 437; FDA 447; FDA 464–65; FDA 470; FDA 615–16; FDA 680–81; FDA 704–05. The Clinical Review team stated:

> The safety profile of Mifeprex is well-characterized over 15 years of experience, with known risks occurring rarely; the safety profile has not changed over the period of surveillance.
>
> Established clinical practice includes patient counseling and documentation of Informed Consent, and, more specifically with Mifeprex, includes counseling [on] all options for termination of pregnancy, access to pain management and emergency services if needed. The National Abortion Federation (NAF) provides clinical practice guidelines and evidence shows that practitioners are providing appropriate patient counseling and education; a survey published in 2009 demonstrated that 99% of facilities surveyed provided pre-abortion counseling with patient education. This indicates that the Patient Agreement form is duplicative and no longer necessary to ensure that the benefits of the drug outweigh the risks.
>
> Medical abortion with Mifeprex is provided by a small group of organizations and their associated providers. Their documents and guidelines cover the safety information that is duplicated in the Patient Agreement.
>
> [. . .]
>
> Labeling mitigates risk: The Medication Guide, which will remain a part of labeling, contains the same risk information covered under the Patient Agreement.

FDA 615–16. *See* FDA 437 (concluding that the Patient Agreement Form "does not add to safe use conditions" and "is a burden for patients").

27. The REMS Review team concurred in the recommendation, as did CDER's director and other FDA supervisors. FDA 680–81; FDA 447; FDA 464–65; FDA 470; FDA 437; FDA 704–05. Reviewers noted that previously, FDA had "removed REMS requirements in other programs based on the integration of the REMS safe use condition into clinical practice." FDA 465.

28. When presented with this recommendation, the newly-appointed FDA Commissioner rejected it, asserting that "continuing the REMS requirement for a signed Patient Agreement would not interfere with access and would provide additional assurance that the patient is aware of the nature of the procedure, its risks, and the need for appropriate follow-up care." FDA retained the Patient Agreement ETASU. FDA 674; FDA 438; FDA 682; FDA 685. The record does not reflect a factual basis for the Commissioner's decision. FDA 674.

4. Medical experts' critiques of the mifepristone REMS with ETASU

29. In the following years, more experts concluded that the mifepristone REMS and ETASU were medically unnecessary and urged FDA to withdraw them. 2021 ED 126–348; 2021 REMS 166–67; 2021 REMS 139; 2021 REMS 163–64; 2021 ED 11–13; 2021 REMS 1168–71; 2019 CP 370–74; 2021 REMS 565.

30. In 2018, NASEM published "The Safety and Quality of Abortion Care in the United States" (the "NASEM Report"). 2021 ED 126–348. This peer-reviewed report "represents the position of the National Academies" and examines the extensive research into the use of mifepristone for medication abortion in the United States. 2021 ED 130; *see, e.g.*, 2021 ED 191–98; ED 219; ED 240. It states that "[t]he risks of medication abortion are similar in magnitude to the risks of taking commonly prescribed and over-the-counter medications such as antibiotics and NSAIDs," such as ibuprofen and aspirin, and that "[p]rescribing medication abortion is no different from prescribing other medications." 2021 ED 240; 2021 ED 219. The NASEM Report suggested FDA should reconsider the mifepristone REMS "given its increasing use and the extensive body of research demonstrating its safety and effectiveness." 2021 ED 146.

31. In July 2018, Jane E. Henney, the former FDA Commissioner who had approved mifepristone in September 2000, explained in the New England Journal of Medicine why FDA

initially had restricted mifepristone's distribution. 2021 REMS 166–67. The drug application was based on two French studies and presented "limited clinical trial data from the United States," raising questions about "whether the rate and severity of adverse events would be similar or greater with mifepristone than with surgical abortions in the United States." 2021 REMS 166; *see* FDA 0223 (describing clinical trials). But after reading the NASEM Report's "comprehensive review" of the safety of medication abortion in the United States, she now considered the REMS and ETASU "overly prescriptive" and urged FDA to "reevaluate" them. 2021 REMS 167.

32. At its 2018 annual meeting, the AMA adopted a resolution supporting efforts to urge the FDA to lift the mifepristone REMS. 2021 REMS 139.

33. In June, 2018, ACOG issued a formal position statement urging "the removal of the REMS and ETASU for Mifeprex," noting that they "are outdated and substantially limit access to this safe, effective medication." 2021 ED 11–13.

34. At its 2018 annual meeting, AAFP resolved to advocate against the mifepristone REMS after finding that it was "not based on scientific evidence and causes significant barriers to accessing abortion care," contributing to "delays in care, thereby increasing second trimester and surgical abortion, both of which have increased complication rates." 2021 REMS 1168–71.

35. The New England Journal of Medicine published an article by leading medical researchers, titled "Sixteen Years of Overregulation: Time to Unburden Mifeprex." 2019 CP 370–74. This article characterized the self-certification required by the Prescriber Certification ETASU as an "empty formality":

> The provider certification criteria can technically be met by any health care professional with the ability to read an ultrasound report and familiarity with emergency services, and thus the certification process itself—which is a self-certification without any validation component—is, in essence, an empty formality. Serious complications of mifepristone treatment are uncommon and are very

> familiar to clinicians who provide care to women of reproductive age; those risks should be manageable through routine labeling and standard clinical counseling.

2019 CP 373. The article further noted that "other countries that have not instituted regulations similar to the REMS have not encountered substantial safety problems." 2019 CP 372.

36. On October 3, 2017, SFP and the California Academy of Family Physicians challenged the mifepristone REMS in federal district court. *Chelius v. Becerra*, No. 17-00493 JAO-RT, 2023 WL 5041616 at *1 (D. Haw. Aug. 8, 2023).

5. FDA's approval of the 2023 mifepristone REMS with ETASU

37. On April 11, 2019, FDA approved an application by GenBioPro to distribute a generic version of mifepristone and a single, shared-system REMS applicable to both generic and brand-name mifepristone. 2021 REMS 1567.

38. On July 13, 2020, a federal district court ordered FDA to suspend enforcement of the In-Person Dispensing ETASU due to the risks of in-person healthcare during the COVID-19 public health emergency. *Id.* Six months later, on January 12, 2021, the United States Supreme Court stayed that injunction. *Id.*

39. Several studies of the data generated during the six months that the injunction was in effect did not show any "increases in serious safety concerns" resulting from suspension of the In-Person Dispensing ETASU. 2021 ED 510–11. FDA itself found no connection between the adverse events reported during this period and any deviation from the REMS. 2021 ED 511. Accordingly, on April 12, 2021, FDA suspended enforcement of the In-Person Dispensing ETASU for the balance of the COVID-19 public health emergency. 2021 ED 510–11; 2021 ED 512–14; 2021 ED 515–17.

40. While the In-Person Dispensing ETASU was suspended, mail-order pharmacies could dispense mifepristone under the supervision of a certified prescriber; the pharmacies were

not themselves certified and they were not required to ensure that mifepristone would be delivered within four calendar days. 2021 ED 510–11.

41. On May 7, 2021, FDA announced that it had reached agreement with SFP and the other *Chelius* plaintiffs to review the mifepristone REMS. 2021 REMS 644; 2021 REMS 1568. FDA committed to review "any relevant data and evidence submitted by the plaintiffs." 2021 REMS 644.

42. SFP submitted a summary of peer-reviewed scientific evidence to FDA. 2021 REMS 950–55. With respect to the Prescriber Certification ETASU, SFP highlighted:

- An abstract of a study showing that after Canada deregulated mifepristone and permitted "any physician or nurse practitioner" to prescribe the drug, there was no "clinically significant increase in abortion complications, ongoing pregnancy, or adverse events." 2021 REMS 957 (cited at 2021 REMS 951). Major complication rates in the Canadian study were comparable to those found in a study of a similar dataset from California, 2021 REMS 951 (citing 2021 REMS 686–94), and were consistent with a clinical review of major complication rates across multiple studies, *id.* (citing 2021 REMS 958–65).

- A demographically representative survey of 1,000 ACOG members showing that the Provider Certification ETASU deters providers from providing medication abortion care. 2021 REMS 951 (citing 2021 REMS 966–72). Nine percent of the surveyed members reported that they were deterred from providing medication abortion by the need to register with Danco. 2021 REMS 971. The survey concluded that the REMS "is a barrier to provision of medication abortion." 2021 REMS 971.

- Qualitative studies demonstrating that the ETASU create administrative burdens that challenge providers' ability to incorporate mifepristone into their practice. 2021 REMS 951 (citing 2021 REMS 973–78 and 2021 REMS 979–83).

43. All *Chelius* plaintiffs, including SFP, made a separate written submission to FDA. 2021 REMS 1159–67. With respect to the Prescriber Certification ETASU, the submission offered:

- Another abstract for the Canadian study discussed in the SFP letter. 2021 REMS 1160 (citing 2021 REMS 1172).

- First-hand accounts of otherwise qualified physicians deterred from becoming certified providers because registration with the drug manufacturer and drug distributor could expose them to anti-abortion violence, 2021 REMS 1937–38; 2021 REMS 1962–64; 2021 REMS 1991–92.

- Descriptions of how cumbersome it is for medical offices to develop special systems to track certifications and maintain records of signed Patient Agreement forms, delaying or impeding efforts to dispense mifepristone. 2021 REMS 1989–90; 2021 REMS 980; 2021 REMS 951.

- Statements from medical professional societies explaining how the REMS and its ETASU are medically unnecessary and impede access to the drug. 2021 REMS 139 (AMA); 2021 ED 11–13 (ACOG); 2021 REMS 2051–52 (ACOG); 2021 REMS 1168–71 (AAFP).

44. The submission also included the *Chelius* plaintiffs' sworn, first-hand accounts explaining: (i) why the Patient Agreement form is superfluous since informed consent is a "bedrock of medical care, taught as a core skill in medical school and reinforced by the American Medical Association's Code of Medical Ethics" (2021 REMS 1942); (ii) how the Patient Agreement form can undermine the informed consent process when the provider's evidence-based clinical practice differs from the protocol described in the form (2021 REMS 2006–08); and (iii) how the Patient Agreement form can be "distressing" for patients prescribed mifepristone to treat early pregnancy loss (2021 REMS 2007–08).[2]

45. Planned Parenthood's detailed submission to FDA included a copy of the National Abortion Federation's Clinical Policy Guidelines for Abortion Care. 2021 REMS 668–79; 2021 REMS 782–845. Those guidelines demonstrate how the Prescriber Certification and Patient Agreement ETASU are redundant of existing clinical guidelines. 2021 REMS 789 (provider competency requirement); 2021 REMS 791 (informed consent generally); 2021 REMS 803 (informed consent for medication abortion).

46. On December 16, 2021, FDA informed Danco, GenBioPro and the *Chelius* plaintiffs that the Agency had decided to eliminate the In-Person Dispensing Requirement. 2021 REMS 1803; 2021 REMS 1808; REMS 1812. This conclusion relied upon FDA's finding that

[2] "Mifepristone, in combination with misoprostol, is the most effective regimen for medical management of miscarriage . . . ." 2022 CP 72 (citizens' petition filed by ACOG, AMA, SFP and other groups); *see* 2019 CP 402–11.

"there does not appear to be a difference in adverse events between periods when the in-person dispensing requirement was being enforced and periods when the in-person dispensing requirement was not being enforced," including the period after April 12, 2021, when uncertified mail-order pharmacies could dispense the drug. 2021 REMS 1583.

47. FDA also informed Danco, GenBioPro and the *Chelius* plaintiffs that it had decided to mandate a new Pharmacy Certification ETASU, and to retain the Prescriber Certification and Patient Agreement ETASUs. 2021 REMS 1803–04; 2021 REMS 1808–09; 2021 REMS 1812. FDA's reasoning for these decisions is set forth in a "REMS Modification Rationale Review" (the "2021 REMS Modification Rationale"). 2021 REMS 1561–1609.

48. The 2021 REMS Modification Rationale justifies FDA's decision to retain the Prescriber Certification ETASU by asserting that "[n]one of the publications we reviewed would support a conclusion that a healthcare provider who prescribes mifepristone does not need to meet the qualifications" set forth in the Prescriber Agreement. 2021 REMS 1596. FDA faulted the record for lacking "studies comparing providers who met these qualifications with providers who did not," and opined that in the absence of such studies, "there is no evidence to contradict our previous finding" that provider qualifications are "necessary to mitigate the serious risks associated with the use of mifepristone." 2021 REMS 1573. In addition, FDA believed that removal of the In-Person Dispensing ETASU could increase the number of prescribers and claimed that maintaining the prescriber certification was necessary to ensure that the new prescribers "meet the necessary qualifications and adhere to the guidelines for use" and that "the benefits of mifepristone for medical abortion outweigh the risks." 2021 REMS 1574; *see also* 2021 REMS 1597 ("We have determined that healthcare provider certification continues to be necessary to ensure the benefits outweigh the risks. . . ."). FDA did not address the medical professional societies' conclusion that

prescriber *certification* was not needed to assure prescriber *qualification*, given the extensive legal, ethical and professional guidelines that govern medical care.

49. The 2021 REMS Modification Rationale acknowledges CDER's 2016 recommendation that the Patient Agreement ETASU be lifted (2021 REMS 1575), that "informed consent in medicine is an established practice" (2021 REMS 1577), that medical professional guidelines from the National Abortion Federation, ACOG and SFP support "detailed patient counseling" (*id.*), and that a study confirms "strong adherence to evidence-based guidelines" among providers in North America (*id.*). FDA justifies the Patient Agreement ETASU by asserting that a projected increase in the number of providers after removal of the In-Person Dispensing ETASU requires "standardizing the medication information on the use of mifepristone that prescribers communicate to their patients." 2021 REMS 1578. FDA did not explain why the label's prescribing information or the Medication Guide—which addresses the same risks as the Patient Agreement and is distributed to each patient—would not suffice to provide such standardization. 2021 REMS 1574–78; 2021 REMS 1597; FDA 616; 2023 SUPP 1505–08; 2023 SUPP 1486–89; 2023 SUPP 1510.

50. FDA's stated justification for the Pharmacy Certification ETASU is to prevent pharmacies from fulfilling prescriptions written by uncertified providers after the In-Person Dispensing ETASU was removed: "Given this modification to the dispensing requirements in the REMS, it is necessary to add a requirement for certification of pharmacies." 2021 REMS 1600. FDA did not address whether pharmacy certification would impede access to mifepristone or burden the health care system. *Id.*

51. The 2021 REMS Modification Rationale focused on what the FDA termed "objective safety data related to outcomes of medical abortion" (2021 REMS 1571). On that basis, FDA excluded the following evidence:

- "Qualitative" studies or surveys assessing "US clinicians' perspectives on how mifepristone regulations affect access to medication abortion," which evaluated the REMS from the vantage point of providers, clinic staff and pharmacists. 2021 REMS 1571.[3]
- Data on "the logistics of accessing abortion care" or "service availability." 2021 REMS 1572.[4]
- Statements by professional medical societies such as ACOG, AMA, and AAFP regarding provider qualifications and the effects of the REMS, which the review derided as "policy/advocacy statements." 2021 REMS 1571.[5]
- The NASEM Report, on the ground that it offered "only general statistics about abortion care in the United States" and "[d]id not provide safety data relevant to the elements of the REMS." 2021 REMS 1571; *see* 2021 REMS 1607.
- Sworn declarations from providers discussing how the ETASU impeded patient access and burdened the health care delivery system. 2021 REMS 1570–71 (FDA considered only certain "literature references" submitted by the *Chelius* plaintiffs).

52. FDA's guidance to drug manufacturers encourages them to "identify complementary data sources that provide a combination of *qualitative* and quantitative information about the REMS" and to seek "input from the key stakeholders affected by the REMS, including prescribers, pharmacists, other healthcare professionals, and patients," in preparing their proposals for periodic REMS assessments. FDA, *REMS Assessment: Planning and Reporting Guidance for Industry* 7, 12 (2019) ("REMS Assessment Guidance") (emphasis added),

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[3] *See* 2021 REMS 1607 (excluding Srinivasalu [2021 REMS 973–78] and Calloway [2021 REMS 979–83] studies); 2021 REMS 1608 (excluding Munro [2021 REMS 984–92] study).

[4] *See* 2021 REMS 1605 (excluding Fuentes [2021 REMS 339–47], Bearak [2021 REMS 1177–84], Cartright [2021 REMS 1185–97], Barr-Walker [2021 REMS 313–38], Grossman [2021 REMS 1227–29], Dobie [2021 REMS 1230–34], Shelton [2021 REMS 1251–54], Norris [2021 REMS 1255–61], and Upadhyay [2021 REMS 1262–69] studies); 2021 REMS 1606 (excluding Jones, Guttmacher Institute, and Johns studies); 2021 REMS 1608 (excluding Jones [2021 REMS 1030–51] and Ely [2021 REMS 1052–60] studies).

[5] *See* 2021 REMS 1604 (excluding statements by AMA [2021 REMS 139], ACOG [2021 ED 11–13] and AAFP [2021 REMS 1168–71]).

https://www.fda.gov/media/119790/download (last accessed Oct. 23, 2024).[6] FDA expressly allows drug manufacturers to "use a range of methods to identify burdens and opportunities to reduce them, including interviews with stakeholders or use of focus groups." REMS Assessment Guidance at 13. And in determining whether a REMS is necessary, FDA guidance provides that it "may take into consideration" the views of such "professional societies." FDA, *REMS: FDA's Application of Statutory Factors in Determining When a REMS is Necessary* 4–5 (2019) ("REMS Guidance"), https://www.fda.gov/media/100307/download (last accessed Oct. 23, 2024).

53. The 2021 REMS Modification Rationale excluded from consideration the study showing that after Canada deregulated mifepristone, adverse events had not increased. 2021 REMS 1604 (referring to Schummers study [2021 REMS 1172]); 2021 REMS 1607 (referring to Schummers study [2021 REMS 956–57]). This critical data was excluded on the ground that FDA could not "conduct a full review of the methods or results," since they were reported only in study abstracts. 2021 REMS 1571.

54. When FDA decided to remove the In-Person Dispensing ETASU and add a Pharmacy Certification ETASU, it directed Danco and GenBioPro to submit a new proposed REMS implementing these changes. 2021 REMS 1804; 2021 REMS 1809. Their submissions were made on June 22, 2022. 2023 SUPP 257–350; 2023 SUPP 351–439.

55. On June 21, 2022, ACOG, joined this time by AMA, urged FDA to reconsider the mifepristone REMS by eliminating the ETASU. 2023 SUPP 34. These medical professional societies urged that "[b]arriers to accessing mifepristone do not make care safer, are not based on medical evidence, and create barriers to patient access to essential reproductive health care." 2023

[6] The Court may take judicial notice of these agency documents on a government website. *See Charlene B. v. Soc. Sec. Admin.*, No. 4:21-cv-00019, 2022 WL 509340, at *2 (W.D. Va. Jan. 25, 2022); *Mays v. Smith*, 70 F.4th 198, 206 n.4 (4th Cir. 2023).

SUPP 33. Specifically, they anticipated that the undefined pharmacy certification process would "serve as a deterrent to pharmacies' decisions to stock and dispense mifepristone." 2023 SUPP 34.

56. On October 4, 2022, ACOG, AAFP, AMA, the American College of Nurse Midwives and the Society for Maternal-Fetal Medicine filed a citizen's petition with the FDA asking the Agency to eliminate or modify the REMS as part of an effort to broaden the use of mifepristone for miscarriage management. 2022 CP 71–98. Among other things, their petition relied upon a complete, peer-reviewed publication of the Schummers study demonstrating that Canada's deregulation of mifepristone did not adversely affect the drug's safety. 2022 CP 87 (citing 2022 CP 99–109). The petition also urged FDA not to include a certification requirement for pharmacies because "research . . . suggests that the pharmacy requirement is unnecessary," 2022 CP 85, and "the burdens associated with the certified pharmacy requirement will also fall disproportionately on poor and rural [patients], contrary to the REMS statute." 2022 CP 86.

57. FDA, Danco and GenBioPro engaged in several rounds of communications regarding the proposed REMS. 2023 SUPP 1117–19. During those discussions, the drug manufacturers informed FDA that "most stakeholders—particularly [health care providers]—continue to request the removal of both the Prescriber Agreement and Patient Agreement to reduce the burden on them and their patients." 2023 SUPP 462.

58. On January 3, 2023, FDA approved the modified REMS. 2023 SUPP 1451–60; 2023 SUPP 1461–65. FDA's reasoning is contained in a "Joint Summary Review" (the "2023 Joint Summary Review") which repeats FDA's bare conclusion in the 2021 REMS Modification Rationale that a Pharmacy Certification ETASU was needed to "ensure[] that mifepristone is only dispensed pursuant to prescriptions that are written by certified prescribers." 2023 SUPP 1124.

FDA acknowledged that the requirement that pharmacies verify prescriber certification "will likely limit the types of pharmacies that will choose to certify in the REMS." 2023 SUPP 1125.

59. The 2023 Joint Summary Review does not address the full Schummers study (2022 CP 99–109) showing that Canada had deregulated mifepristone without adversely affecting patient safety. 2023 SUPP 1112–50. Nor does it articulate a reason for maintaining the Prescriber Certification and Patient Agreement ETASUs, other than to assert that the Patient Agreement form "continues to be an important part of standardizing" the information given to patients. 2023 SUPP 1122. The 2023 Joint Summary Review did approve revising the Patient Agreement to remove a reference to ectopic pregnancy from the list of mifepristone risks: "The reference to ectopic pregnancy has been reorganized in the document since it is not a risk of the drug." 2023 SUPP 1123; *see* 2023 SUPP 1510 (listing possible symptoms of ectopic pregnancy).

60. When FDA issued the modified REMS, the Agency also denied the 2022 citizen's petition filed by ACOG, AMA, AAFP and other medical professional societies. 2022 CP 110–13.

61. FDA's post-marketing surveillance of adverse events among U.S. women who used mifepristone to terminate pregnancies did not identify any new safety issues after 2005. FDA 336; FDA 365–66; 2021 ED 436; 2021 REMS 1524; 2023 SUPP 1047; 2023 SUPP 1131. The total number of deaths occurring among U.S. patients who took mifepristone is tiny—28 out of the approximately 5.6 million patients who took mifepristone from 2000 through 2022—and FDA acknowledges that none of them can "with certainty be causally attributed to mifepristone." 2023 SUPP 1052. Pregnancy-related mortality numbers are much higher. 2021 REMS 85.

62. FDA has never explained how the mifepristone REMS and its ETASU satisfy the statutory requirements of 21 U.S.C. § 355-1(a) & (f), other than by bare assertions that they are

needed to ensure the benefits of mifepristone outweigh its risks and do not burden patient access. FDA 231–36; FDA 342–60; FDA 698–709; 2021 REMS 1561–1609; 2023 SUPP 1112–50.

6. FDA's inconsistent treatment of other drugs with no ETASU or REMS

63. FDA has approved over 20,000 prescription drugs. FDA at a Glance (Nov. 2020), https://www.fda.gov/media/143704/download (last visited Oct. 21, 2024. The FDA's website identifies 73 REMS programs, including the one for mifepristone. https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=RemsData.page (last visited Oct. 23, 2024).

64. Evidence presented to FDA in the course of the 2023 REMS review showed that other commonly-prescribed drugs are comparably safe or less safe than mifepristone but do not have REMS. 2021 REMS 85 (penicillin and phosphodiesterase type-5 inhibitors such as Viagra); 2021 REMS 1169 (acetaminophen, aspirin, loratadine, and sildenafil); 2021 ED 240 (NSAIDs and aspirin); FDA 1256 (Accutane); 2021 REMS 1161 (Jeuveau, Propecia, NuvaRing, Coumadin).

65. Evidence presented to FDA in the course of the 2023 REMS review showed that other commonly-prescribed drugs require careful patient screening but do not have REMS. FDA 1247 (referring to cardiovascular drugs, anti-psychotics and antibiotics).

66. In 2012, FDA approved a new drug application for 300 mg tablets of mifepristone, under the brand name "Korlym," for treatment of certain patients with Cushing's syndrome. FDA 307–30. For those patients, Cushing's syndrome is a chronic condition that could entail decades of daily treatment. FDA 297. FDA considered each of the six statutory factors set out in 21 U.S.C. § 355-1(a) and concluded that a REMS was unnecessary. FDA 296–302; FDA 327–29. FDA also considered a non-statutory factor, whether a REMS for Korlym would be appropriate because of "the more controversial use of [mifepristone] for medical termination of pregnancy." FDA 310;

FDA 327–29. Since its approval, Korlym has resulted in many more adverse events than mifepristone used for pregnancy termination. 2021 REMS 1393; 2023 SUPP 1042.

C. Procedural History

On April 7, 2023, the Northern District of Texas issued a preliminary injunction staying the effective date of FDA's 2000 approval of mifepristone and all subsequent FDA actions to regulate the drug in *Alliance for Hippocratic Med. v. U.S. Food and Drug Admin*., No. 2:22-cv-223, 2023 WL 2825871 (N.D. Tex. Apr. 7, 2023). Plaintiffs filed this case and moved for a preliminary injunction to maintain the 2023 REMS during this lawsuit.

On August 21, 2023, this Court denied Plaintiffs' motion because the Supreme Court had stayed the *Alliance* injunction. *Whole Woman's Health Alliance v. U.S. Food and Drug Admin.*, No. 3:23-cv-00019, 2023 WL 5401885 at *8 (W.D. Va. Aug. 21, 2023). In its opinion, this Court held that Plaintiffs had standing and that administrative exhaustion was futile. *Id.* at *5, *7. After the Supreme Court issued its opinion in the *Alliance* case, the parties jointly requested that this Court schedule briefing on cross-motions for summary judgment. Dkt. 56, *Whole Woman's Health Alliance v. U.S. Food and Drug Admin.*, No. 3:23-cv-00019 (W.D. Va. Jul. 12, 2024).

Argument

The APA requires courts to "hold unlawful and set aside agency action, findings, and conclusions" that are found to be, among other grounds, (1) "in excess of statutory jurisdiction, authority, or limitations," 5 U.S.C. § 706(2)(C), or (2) "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law," 5 U.S.C. § 706(2)(A). Here, the undisputed material facts establish that FDA's 2023 REMS Decision violates the APA in both ways. Plaintiffs are therefore "entitled to judgment as a matter of law" pursuant to Fed. R. Civ. P. 56(a). *Casa de Maryland v. Dep't of Homeland Sec.*, 924 F.3d 684, 703 (4th Cir. 2019).

I. The 2023 REMS Decision Exceeds FDA's Statutory Authority

When it issued the 2023 REMS Decision, FDA blew past the clear Congressional guardrails— set out in 21 U.S.C. § 355-1(a)(1) and (f)(1)—that limit the Agency's authority to issue a REMS or ETASU. Those guardrails also constrain the Agency's authority when modifying a REMS or ETASU under 21 U.S.C. § 355-1(g)(4)(B). *See Washington v. U.S. Food and Drug Admin*., 668 F. Supp. 3d 1125, 1140–41 (E.D. Wash. 2023) (holding that it would be "contrary to the plain language of the statute" to relieve the Agency of its obligation to consider the § 355-1(a)(1) and (f)(1) criteria when modifying a REMS).

REMS Prerequisites. In 21 U.S.C. § 355-1(a)(1) and (g)(4)(B), Congress mandated that when modifying a REMS, FDA "shall" consider six statutory factors to determine 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)(A)–(E). Nowhere in the 2023 REMS Decision did FDA consider those factors. If FDA had considered them, it necessarily would have concluded that after 23 years of use with an excellent safety record, mifepristone did not meet the statutory threshold for a REMS: (1) mifepristone is used by millions of patients, SMF ¶ 1; (2) all patients who take mifepristone for medication abortion already are pregnant, a condition that itself can entail severe medical risks, SMF ¶¶ 1–2; (3) mifepristone "provides a meaningful therapeutic benefit" over the alternative way of ending an early pregnancy, procedural abortion, SMF ¶ 2, and is far safer than childbirth, SMF ¶¶ 2, 61; (4) patients take only one mifepristone pill to terminate a pregnancy, SMF ¶ 1; (5) the only serious adverse events are "exceedingly rare," are not proven to be caused by mifepristone and are also associated with other pregnancy outcomes, SMF ¶¶ 3–4, 17; and (6) mifepristone has been marketed in the U.S. for decades with no new safety concerns since 2005, SMF ¶¶ 15, 61.

ETASU Prerequisites. To impose or maintain an ETASU, FDA must first determine that the drug "can be approved only if, or would be withdrawn unless" there were an ETASU. 21 U.S.C.

§ 355-1(f)(1)(A), (g)(4)(B). The grounds for withdrawing approval of a drug are set forth in 21 U.S.C. § 355(e). Under that statute, FDA would have to show that the withdrawn drug was "unsafe" or "not safe" without the ETASU. FDA has never claimed, even in a conclusory way, that any of the mifepristone ETASU could meet that high bar. Nor could it, given the record evidence—which FDA outright ignored—of a study showing that Canada deregulated mifepristone without adversely affecting safety. SMF ¶¶ 42, 53, 56, 59. But the 2023 REMS Decision did not determine, for *any* ETASU, whether mifepristone's approval would have to be withdrawn without it.

Exclusion of data relevant to statutory limits on ETASU. Congress also directed that each ETASU imposed by FDA "shall" comply with specific limitations. 21 U.S.C. §355-1(f)(2). Of relevance here, an ETASU must "not be unduly burdensome on patient access," with particular regard for "patients who have difficulty accessing health care," and must be "compatible with established distribution, procurement and dispensing systems for drugs" so as to "minimize the burden on the health care delivery system." 21 U.S.C. § 355-1(f)(2)(A), (C)(ii), (D)(i). But the most probative evidence on these subjects was shut out from consideration when FDA excluded all publications addressing "the logistics of accessing abortion care" and "service availability," all of the sworn provider declarations detailing how the ETASU impeded patient access and burdened the health care delivery system, and all "qualitative" studies of the impact of the mifepristone ETASUs. SMF ¶ 51. Indeed, FDA acknowledged that the Pharmacy Certification ETASU would "likely limit the types of pharmacies that will choose to certify in the REMS," without addressing whether limiting the number of pharmacies that dispense mifepristone would unduly burden patient access. SMF ¶ 58.

When a federal agency does not adhere to statutory requirements mandated by Congress, it "fail[s] in its statutory duty." *Friends of Buckingham v. State Air Pollution Control Bd.*, 947 F.3d

68, 93 (4th Cir. 2020). The Court should vacate the 2023 REMS Decision as "inconsistent with the statutory mandate[s]" of 21 U.S.C. § 355-1(a)(1), (f)(1), and (g)(4)(B). *SEC v. Sloan*, 436 U.S. 103, 118–19 (1978).

II. The 2023 REMS Decision Was Arbitrary and Capricious

While deferential in some circumstances, the arbitrary and capricious standard does not "reduce judicial review to a rubber stamp of agency action." *Wild Va. v. U.S. Forest Serv.*, 24 F.4th 915, 926 (4th Cir. 2022) (quoting *Friends of Back Bay v. U.S. Army Corps of Eng'rs,* 681 F.3d 581, 587 (4th Cir. 2012)). Federal agencies must both "examine the relevant data" and "supply a reasoned analysis" for their decisions. *Motor Vehicle Mfrs. Ass'n of U.S., Inc. v. State Farm Mut. Auto. Ins. Co.*,463 U.S. 29, 42–43 (1983). This reasoned analysis must include "a rational connection between the facts found and the choice made." *Sierra Club v. W. Va. Dep't of Env't Prot.*, 64 F.4th 487, 502 (4th Cir. 2023) (quoting *Friends of Buckingham*, 947 F.3d at 83) (cleaned up) (vacating agency action under APA arbitrary and capricious standard). In reviewing agency action, the court "must conduct a searching and careful review" to determine whether the agency's decision meets these standards. *Id.* at 501.

FDA did not come close to fulfilling these obligations when it made the 2023 REMS Decision: (a) FDA purposefully excluded key categories of data from consideration; (b) the only rationales that FDA did proffer for its ETASU rest on "pure speculation," *Appalachian Voices v. U.S. Dep't of Interior*, 25 F.4th 259, 274 (4th Cir. 2022), and are "so implausible that [they] could not be ascribed to a difference in view or the product of agency expertise," *State Farm*, 463 U.S. at 43; and (c) FDA did not even acknowledge, much less explain, its inconsistent regulation of mifepristone relative to comparably safe or less safe drugs. Importantly, the Fourth Circuit has held that where an agency departs from the consensus of medical professional societies on

questions of professional practice, it must explain its reasoning—something FDA never did. *Mayor of Baltimore v. Azar*, 973 F.3d 258, 276–77 (4th Cir. 2020) (holding agency action to be arbitrary and capricious where it "fail[ed] to address head-on the arguments of [several of the country's leading] medical organizations" on medical ethics).

A. FDA Categorically Excluded Several Critical Categories of Relevant Data from Consideration

It was arbitrary and capricious for FDA to exclude evidence directly relevant to the mandates of 21 U.S.C. § 355-1(a)(1), (f)(2)(A), and (C). An agency cannot choose to disregard record evidence contrary to its conclusion. *See Sierra Club*, 64 F.4th at 502 ("[r]ecord evidence contrary to an agency's conclusion requires 'further elaboration' and must be 'grapple[d] with'").

Statements by medical professional societies. FDA excluded statements by prominent medical professional societies urging that the mifepristone REMS were medically unnecessary and impeded patient access to the drug. SMF ¶ 51. For years, these groups have told FDA that its mifepristone restrictions are "outdated," "not based on scientific evidence and cause significant barriers to accessing abortion care." SMF ¶ 33 (ACOG); SMF ¶ 34 (AAFP). Their consensus was bolstered by the authoritative NASEM Report, by the former FDA Commissioner who had initially imposed marketing restrictions on mifepristone in 2000, and by the medical researchers and academics who made up the Mifeprex Study Group. SMF ¶¶ 30–31, 35.

The evidence from these medical societies and other professionals refutes FDA's unproven speculation that the "empty formality" of provider certification is necessary to assure that new providers have the qualifications that FDA deems necessary to prescribe mifepristone. SMF ¶¶ 21–22, 35, 48. But FDA reviewed none of it, explicitly declining to consider publications from ACOG, AMA, AAFP, and other medical associations that FDA deemed "opinions, commentaries, or policy/advocacy statements." SMF ¶ 51.

FDA's excuse was that the medical professional societies' positions did not constitute "objective safety data," SMF ¶ 51 (at 2021 REMS 1571), but that is a spurious distinction. FDA's own guidance documents state that the Agency may consider input from "professional societies" as well as "prescribers … and other healthcare professionals" in determining whether a REMS meets the statutory criteria or fulfills its stated objectives. SMF ¶ 52. At a bare minimum, FDA was required to respond to evidence from the nation's leading medical professional associations demonstrating their consensus that a REMS with ETASU is inappropriate for mifepristone. *See Mayor of Baltimore*, 973 F.3d at 276.

Safety data from Canada's deregulation of mifepristone. After declaring that its inquiry focused solely on "objective safety data related to outcomes of medical abortion," SMF ¶ 51 (2021 REMS 1571), FDA ignored the data showing that when Canada stopped requiring provider certification and began regulating mifepristone like other drugs, there was no decline in safety. SMF ¶¶ 42, 53, 56, 59. Initially, FDA refused to consider abstracts of a study that examined the impact when Canada removed its REMS-like restrictions and concluded that the change did not increase the incidence of serious adverse events. SMF ¶ 53. But even after ACOG submitted a complete, peer-reviewed publication of the same study to FDA, FDA said nothing about it in the 2023 REMS Decision, SMF ¶ 59, notwithstanding that Canada's experience with deregulation is directly relevant to whether a REMS is "necessary to ensure that the benefits of the drug outweigh the risks" and whether an ETASU is "required … to mitigate a specific serious risk listed in the labeling of the drug," 21 U.S.C. § 355-1(a)(1), (f)(1). The Agency's failure to "examine the relevant data" on these central issues is arbitrary and capricious. *Sierra Club*, 64 F.4th at 502.

Qualitative studies and healthcare professional narratives. The FDA is required to assess burdens on patient access and on the health care delivery system when it imposes, modifies or

removes any ETASU. 21 U.S.C. §355-1(f)(2)(C), (f)(2)(D), (g)(4)(B). But FDA refused to consider any information on these subjects on the pretext that they were not "objective safety data." SMF ¶ 51. For instance, FDA excluded a qualitative study of "US clinicians' perspectives on how mifepristone regulations affect access to medication abortion." *Id.* (referring to 2021 REMS 973–78). FDA also did not examine sworn physician narratives from the *Chelius* case discussing how legal and ethical guidelines governing medical care make the ETASUs superfluous; how fear of public disclosure deters qualified healthcare professionals from seeking certification to prescribe mifepristone;[7] how the ETASUs burden patient access, especially in rural areas; and how the Patient Agreement ETASU undermines informed consent by, among other things, requiring patients who take mifepristone for miscarriage management to attest that they are using it to end their pregnancies. *See* SMF ¶ 44.

There can be no genuine dispute that this evidence was probative to the required statutory analysis of the burdens resulting from the mifepristone ETASUs. FDA routinely relies on "key stakeholders" for input on the impact of a REMS, "including prescribers, pharmacists, other healthcare professionals, and patients." SMF ¶ 52 (quoting Assessment Guidance 12). This includes "surveys, focus groups, and interviews" to "inform the applicant and the Agency about the impact of the program on the healthcare delivery system and on patient access to the drug, as well as opportunities for program improvement." *Id.* FDA specifically encourages the use of "complementary data sources that provide a combination *of qualitative* and quantitative information about the REMS." *Id.* (quoting Assessment Guidance 7) (emphasis added). By encouraging manufacturers to submit stakeholder data, FDA necessarily implies that such data is relevant to REMS assessment. FDA could not flout its own guidance without a reasoned

[7] FDA must credit those fears, for it refuses to disclose the names of its own employees who review mifepristone even under the restrictions of a protective order. *See* 2021 REMS 1163.

explanation for the discrepancy. *See Def. of Wildlife v. U.S. Dep't of Interior*, 931 F.3d 339, 358 (4th Cir. 2019) (arbitrary of agency to contravene its own guidance without a discernible explanation); *Contractors Transport Corp. v. United States*, 537 F.2d 1160, 1162 (4th Cir. 1976) ("Patently inconsistent application of agency standards to similar situations lacks rationality and is arbitrary.").

Data on the "logistics of accessing abortion care." Congress directed FDA to ensure that ETASU are not "unduly burdensome on patient access …, considering in particular … patients who have difficulty accessing health care (such as patients in rural or medically underserved areas)." 21 U.S.C. § 355-1(f)(2)(C)(ii). Nonetheless, FDA excluded all "[d]ata on the logistics of accessing abortion care," again on the trumped-up ground that it was not "objective safety data." SMF ¶ 51. The excluded materials included a study of "Time to appointment and delays in accessing care among U.S. abortion patients" and another on "Distance Traveled to Obtain Clinical Abortion Care in the United States." *Id.* (referring to 2021 REMS 1030–51 and 2021 REMS 339–47). The Agency's failure to "examine the relevant data" on this central issue of burdens on patient access to mifepristone is arbitrary and capricious. *Sierra Club*, 64 F.4th at 502.

B. FDA's Rationales for the 2023 REMS Are Unreasonable

FDA's explanations for maintaining the Prescriber Certification and Patient Agreement ETASUs and imposing a Pharmacy Certification ETASU bristle with groundless assumptions, logical inconsistencies, and legal errors. None of them can withstand judicial review.

1. Prescriber Certification ETASU

FDA's central justification for maintaining the Prescriber Certification ETASU was that the Agency did not find "any studies comparing providers who met" the qualifications set out in the prescriber certification form "with providers who did not," and thus "no evidence to contradict

[its] previous finding" that "a healthcare provider who prescribes mifepristone should meet th[ose] … qualifications." SMF ¶ 48. FDA's "previous finding," in turn, merely recited that prescriber qualifications "continue to be necessary to ensure the benefits outweigh the risks" of mifepristone, SMF ¶ 25—which is the standard for a REMS under 21 U.S.C. § 355-1(a), not the more demanding standard for an ETASU under 21 U.S.C. § 355-1(f). FDA expressed particular concern that "new prescribers" might not "meet the necessary qualifications" absent the Prescriber Certification ETASU. SMF ¶ 48. On this basis, FDA concluded that the Prescriber Certification ETASU was necessary "to ensure the benefits of mifepristone for medical abortion outweigh the risks." *Id.*

No part of this explanation holds water.

First, FDA acknowledges that there is no proven link between mifepristone and the two serious risks listed in the mifepristone label: heavy bleeding and serious infection. SMF ¶ 4. In the absence of proof that these "extremely rare" risks are caused by mifepristone, as opposed to pregnancy itself, SMF ¶¶ 3–4, FDA cannot connect the dots between the qualifications on the Prescriber Certification Form and mitigation of those risks.[8] And even if FDA could connect a listed risk to a prescriber *qualification*, FDA never explains why an unverified and unaudited self-*certification* might be "required" when legal, ethical and professional guidelines *already* constrain healthcare providers to offer patients care only when qualified to do so. SMF ¶¶ 20–21, 35, 44–45. Other drugs also require careful patient screening, but unlike mifepristone, they are not subject to a REMS. SMF ¶¶ 22, 65. Where, as here, an agency does not draw a logical connection between its premise and its conclusion, its decision is arbitrary and capricious. *See Dow AgroScis. LLC v. Nat'l Marine Fisheries Serv.*, 707 F.3d 462, 472 (4th Cir. 2013).

[8] Indeed, one of the stated qualifications on the Prescriber Certification Form is the ability to diagnose ectopic pregnancy, SMF ¶ 7, but missed ectopic pregnancies are not one of the two serious risks listed on the mifepristone label, SMF ¶ 4, and FDA expressly acknowledges that ectopic pregnancies are "not a risk of the drug," SMF ¶ 59.

Second, FDA speculates that absent certification, "new prescribers" might flout their professional obligations by prescribing a drug without adequately screening for patient eligibility, but that speculation has no factual basis. SMF ¶ 48. FDA compounded the error when it refused to grapple with the evidence from multiple professional medical societies rebutting the Agency's speculation: "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"; and "[c]linicians with routine professional training can provide [mifepristone] appropriately." SMF ¶¶ 20–21. FDA's "pure speculation" is not a reasoned explanation for its decision. *Appalachian Voices*, 25 F.4th at 274.

Finally, FDA's demand for safety data from hypothetical "studies comparing providers who met" the qualifications set out in the prescriber certification form "with providers who did not" makes no sense. SMF ¶ 48. Assuming that any provider who wished to prescribe mifepristone lacked the qualifications set out in the Prescriber Certification form—an assumption refuted by copious record evidence that any clinician who cares for pregnant patients would have those basic qualifications, SMF ¶¶ 20–21, 35, 44–45—that unqualified provider could not prescribe mifepristone for a real patient without abrogating the fundamental ethical obligation to exercise "sound medical judgment." SMF ¶ 20. It is irrational for FDA to effectively condition the removal of a burdensome ETASU on the performance of a chimerical study. *See Dow AgroScis.*, 707 F.3d.at 471–72 (arbitrary to rely on unsupported assumption).

2. Patient Agreement ETASU

In 2016, the FDA Commissioner overruled the unanimous recommendation of FDA staff that the Patient Agreement ETASU be removed as redundant of existing informed consent practices, based solely on his own *ipse dixit* that it "would not interfere with access and would

provide additional assurance that the patient is aware of the nature of the procedure, its risks, and the need for appropriate follow-up care." SMF ¶¶ 26–28. In its 2023 REMS Decision, FDA again recognized, as Agency staff had done in 2016, that "informed consent in medicine is an established practice," and more specifically that informed consent is embedded in professional guidelines for abortion care in the United States. SMF ¶ 49. Nonetheless, FDA retained the Patient Agreement ETASU because it wanted to "standardiz[e] the medication information on the use of mifepristone that prescribers communicate to their patients" in light of an anticipated influx of new prescribers upon the upcoming removal of the In-Person Dispensing ETASU. *Id.*

It is hard to imagine a more arbitrary rationale. "Standardizing" medication information is not a permissible basis for an ETASU under 21 U.S.C. § 355-1(f). Nor is the Patient Agreement Form needed to achieve that end because FDA concedes that the Patient Agreement Form addresses *exactly the same risks* as the Medication Guide given to each patient when mifepristone is dispensed. SMF ¶ 26. And FDA's reference to new prescribers is a red herring; FDA has "removed REMS requirements in other [drug] programs based on the integration of the REMS safe use condition into clinical practice," notwithstanding that those drugs too inevitably are prescribed by new providers. SMF ¶ 27. Whenever FDA approves a new drug, *every* prescriber initially will be unfamiliar with it, but patient agreement ETASUs are rare.[9] FDA's inconsistent reasoning, and its failure to "dispel [these] tension[s]," is emblematic of arbitrary action. *Sierra Club*, 64 F.4th at 502.

[9] Indeed, FDA issues REMS for only a tiny percentage of the drugs it approves. According to the FDA website, FDA has approved over 20,000 drugs, but there are only 73 REMS programs. SMF ¶ 63.

3. Pharmacy Certification ETASU

FDA's principal justification for imposing the Pharmacy Certification ETASU is that it is needed to "ensure[] that mifepristone is only dispensed pursuant to prescriptions that are written by certified prescribers." SMF ¶¶ 50, 58. Since FDA's justification for the Pharmacy Certification ETASU rests on the flawed justification for the Prescriber Certification ETASU, *see* Section II.B.1., FDA's imposition of the Pharmacy Certification ETASU is equally arbitrary and capricious. Nor is there a statutory basis for it. When FDA suspended enforcement of the In-Person Dispensing ETASU in April, 2021, resulting in dispensing by mail-order pharmacies, FDA did not then require those pharmacies to be certified or to deliver mifepristone within four days. SMF ¶ 40. Nonetheless, FDA found that there was no increase in adverse events during that period. SMF ¶ 46. FDA did not make the finding required by 21 U.S.C. § 355-1(f)(1)—that it would have had to withdraw approval for mifepristone absent the Pharmacy Certification ETASU—and it could not have done so in light of that history.

C. FDA Did Not Acknowledge or Address the Record Evidence that Mifepristone Is Subject to More Restrictive Conditions than Comparably Safe Drugs

The administrative record shows that FDA was presented with numerous, specific examples of other drugs that pose comparable or greater risks to patients than mifepristone that FDA approved without a REMS or ETASU. SMF ¶¶ 22, 64–66. FDA never addressed its disparate regulation of mifepristone, either in general or with respect to any of the many specific examples presented to it. As the Fourth Circuit has explained, when "an agency applies different standards to similarly situated entities and fails to support this disparate treatment with a reasoned explanation," its action is arbitrary and capricious. *Kirk v. Comm'r of Soc. Sec. Admin.*, 987 F.3d 314, 321 (4th Cir. 2021) (citation omitted). FDA's failure to explain its differential treatment of mifepristone is itself arbitrary and capricious.

Conclusion

For the foregoing reasons, Plaintiffs respectfully request that their motion for summary judgment be granted, that the court declare that the 2023 REMS Decision violates the APA, and that the Court vacate the 2023 REMS Decision or, in the alternative, remand it to FDA for reconsideration consistent with the statutory requirements.

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Respectfully submitted,

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