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UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF WASHINGTON

STATE OF WASHINGTON, *et al.*, Plaintiffs, v. U.S. FOOD AND DRUG ADMINISTRATION, *et al.*, Defendants.	No. 1:23-cv-03026 DEFENDANTS' CROSS-MOTION FOR SUMMARY JUDGMENT AND OPPOSITION TO PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT With Oral Argument: TBD (*see* ECF No. 153)

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INTRODUCTION

In 2000, the U.S. Food and Drug Administration approved mifepristone as safe and effective for medical termination of early pregnancy subject to certain restrictions to assure safe use.[1] Since 2008, those restrictions have been called "elements to assure safe use" (ETASU) and are part of a Risk Evaluation and Mitigation Strategy (REMS). Among other things, the restrictions on mifepristone have always required that prescribers certify that they meet certain criteria and that patients sign a Patient Agreement Form disclosing risks of the drug. Until 2023, the restrictions also included a requirement—known as the "in-person dispensing requirement"—that mifepristone be dispensed only in certain healthcare settings by or under the supervision of a certified prescriber.

In 2021, FDA directed the sponsors of mifepristone to submit a proposed modification to the REMS to eliminate the in-person dispensing requirement and add a pharmacy certification requirement. That directive followed FDA's comprehensive review of adverse event reports, literature, and other information

[1] This brief uses "mifepristone" to refer to drug products approved for medical termination of early pregnancy. FDA has also approved another manufacturer's drug, Korlym, which has mifepristone as its active ingredient and is approved for the treatment of Cushing's syndrome. This litigation does not affect Korlym.

available since an earlier modification in 2016. FDA approved the modified REMS on January 3, 2023. As a result, mifepristone may be dispensed in-person or by mail and must be dispensed by or under the supervision of a certified prescriber or by a certified pharmacy. In short, FDA made mifepristone's REMS less burdensome in response to evidence that an existing restriction (the in-person dispensing requirement) was no longer needed if pharmacy certification was added and the other ETASU were followed.

Indeed, the effect of the January 2023 REMS modification was to make mifepristone's REMS (including the ETASU) less burdensome than ever before. Yet in their Amended Complaint, Plaintiffs—seventeen States and the District of Columbia—challenge the January 2023 REMS modification as unjustified. They allege that mifepristone is safe without a REMS, even though FDA—the expert agency charged with reviewing drug safety—has not reached that conclusion. From there, Plaintiffs argue that FDA should have eliminated the REMS entirely, rather than approve modifications to the REMS that had the effect of making it less burdensome. The Court should reject these arguments, deny Plaintiffs' Motion for Summary Judgment, and grant summary judgment to Defendants.

First, Plaintiffs lack Article III standing to challenge the REMS requirements other than the pharmacy certification requirement. States lack *parens patriae* standing to sue the Federal Government on behalf of their citizens. *Murthy v.*

Missouri, 603 U.S. 43, 76 (2024); *Washington v. FDA (Washington II)*, 108 F.4th 1163, 1177 (9th Cir. 2024). And Plaintiffs' theories of "direct" standing to challenge the prescriber certification requirement and Patient Agreement Form, *see Washington v. FDA (Washington I)*, 668 F. Supp. 3d 1125, 1137 (E.D. Wash. 2023), are also defective.

Second, Plaintiffs failed to administratively exhaust their claims by filing a citizen petition. Doing so would have given the agency an opportunity to apply its expertise in the first instance. Neither FDA's 2020 response to the States' letter, nor its 2021 REMS review, nor its response to a 2022 citizen petition demonstrates that exhaustion would be futile.

Third, Plaintiffs' APA claims fail on the merits. FDA may not approve a modification to a REMS unless the agency determines that, with the change, the drug's benefits outweigh its risks. Here, applying that standard, FDA determined that there was insufficient evidence to eliminate the REMS entirely. Plaintiffs disagree, faulting FDA for supposedly failing to consider relevant statutory factors. But each statutory factor that Plaintiffs identify either was considered by FDA or was not relevant to the modification decision.

Nor do Plaintiffs' attacks on FDA's consideration of the evidence or the agency's reasoning have merit. FDA considered all evidence before it relevant to whether the ETASU are necessary to maintain a favorable benefit/risk (safety)

profile for mifepristone. FDA found insufficient evidence to demonstrate that mifepristone would continue to have a favorable safety profile if the prescriber certification requirement or Patient Agreement Form were eliminated. But FDA found that there was sufficient evidence supporting removal of the in-person dispensing requirement, provided that all other REMS requirements were met and a pharmacy certification requirement was added.

Finally, Plaintiffs' constitutional claims also fail. Plaintiffs do not have Fifth Amendment rights of their own and, in any event, their equal protection claims would be subject to rational basis review. FDA's determination that the REMS is necessary to assure safe use of mifepristone supplies that rational basis.

BACKGROUND

I. Statutory and Regulatory Background

The Federal Food, Drug, and Cosmetic Act (FDCA) generally prohibits the interstate distribution of new drugs that have not received FDA approval. 21 U.S.C. §§ 331(d), 355(a). FDA approves a new drug application if the drug is shown to be safe and effective for its intended use. *Id.* § 355(d); *see also* 21 C.F.R. §§ 314.50, 314.105(c). Similarly, when a drug's sponsor proposes changes to the drug's conditions of approval (such as changes to labeling or to restrictions relating to its distribution or use), FDA reviews the scientific evidence submitted in support of the proposal to determine whether it should be approved. *See* 21 C.F.R.

§ 314.70. And in determining whether a drug is "safe," FDA examines whether the benefits of the drug outweigh the risks. *See* FDA Guidance for Industry, *Benefit-Risk Assessment for New Drug and Biological Products* (Oct. 2023) ("Because all drugs can have adverse effects, the demonstration of safety requires a showing that the benefits of the drug outweigh its risks.").[2]

In 1992, FDA promulgated regulations (the Subpart H regulations) providing for the imposition of conditions "needed to assure safe use" of certain new drugs that satisfy the other requirements for approval under the FDCA. Final Rule, 57 Fed. Reg. 58,942, 58,958 (Dec. 11, 1992) (codified at 21 C.F.R. § 314.520). In the Food and Drug Administration Amendments Act of 2007 (FDAAA), Congress codified and expanded the Subpart H regulations by giving FDA authority to require a REMS when it determines that restrictions are necessary to ensure that the benefits of a drug outweigh the risks. *See* Pub. L. No. 110-85, tit. IX, § 901 (codified at, *inter alia*, 21 U.S.C. § 355-1). FDA may require that a REMS include ETASU if necessary to mitigate a serious health risk and if certain statutory criteria relating to ensuring safety and minimizing the burden of restrictions are satisfied. 21 U.S.C. § 355-1(f). ETASU may include requirements that a drug's prescribers have particular training or are specially certified, that a drug be dispensed only in certain settings or by certified pharmacies, and that the drug be dispensed to

[2] Available at https://www.fda.gov/media/152544/download.

patients only with evidence or other documentation of safe-use conditions. *See* 21 U.S.C. § 355-1(f)(3).

FDAAA expressly incorporated drugs with existing Subpart H restrictions to assure safe use into the new REMS framework. *See* Pub. L. No. 110-85, tit. IX, § 909 (21 U.S.C. § 331 note). Specifically, Congress "deemed" such drugs to have a REMS in effect, with the Subpart H restrictions serving as ETASU. *Id.* § 909(b). Thereafter, sponsors for such drugs were required to submit supplemental new drug applications with a proposed REMS, which FDA then reviewed. *See id.*

FDAAA also provided standards for modifying an existing REMS. *See* 21 U.S.C. § 355-1(g)(4). As relevant here, FDA may require a sponsor to "submit a proposed modification" to a REMS if the agency "determines that 1 or more goals or elements should be added, modified, or removed" from the approved REMS to "ensure the benefits of the drug outweigh the risks of the drug" or "minimize the burden on the health care delivery system of complying with the strategy." *Id.* § 355-1(g)(4)(B).

II. Factual and Procedural Background

In 2000, FDA approved mifepristone (under the brand name Mifeprex) in a regimen with misoprostol for medical termination of intrauterine pregnancy through 49 days gestation. EAR155; Defendants' Excerpts of Administrative Record (DEAR) 1-3, 7. At the same time, to assure mifepristone's safe use, FDA

placed restrictions under Subpart H on the distribution and use of the drug product. EAR155; DEAR1-3. These included requirements that (1) prescribers certify that (among other things) they have the ability to accurately date pregnancies and diagnose ectopic pregnancies, and will either provide surgical intervention or arrange for others to provide it if necessary; (2) the drug be dispensed only in certain healthcare settings, by or under the supervision of a specially certified prescriber (the in-person dispensing requirement); and (3) patients sign a Patient Agreement Form. EAR155; DEAR2. FDA concluded based on a review of clinical trials and other scientific evidence that, under those conditions, mifepristone was safe and effective, in a regimen with misoprostol, to terminate early pregnancy. EAR155; DEAR1.

Because these restrictions under Subpart H were in place when FDAAA took effect, Mifeprex was "deemed to have in effect an approved [REMS]" that continued these restrictions as "elements to assure safe use." Pub. L. No. 110-85, § 909(b)(1); *see also* EAR155; DEAR42. In 2011, in response to a supplemental application submitted by the sponsor, FDA approved the Mifeprex REMS after determining that certain restrictions remained necessary to ensure the benefits of mifepristone outweigh the risks. DEAR42; EAR154, 155. In 2016, FDA approved a supplemental application from the sponsor proposing modifications to the conditions of approval (including the REMS) for Mifeprex, to lower the dose of

mifepristone, increase the gestational age limit from 49 to 70 days, reduce the number of required in-person clinic visits from three to one, remove the requirement that mifepristone be taken at a clinic, and to allow mifepristone to be prescribed by non-physician healthcare providers licensed under state law to prescribe drugs. EAR154; DEAR31-41. When FDA approved a generic version of the drug in 2019, it approved a single, shared system REMS, known as the Mifepristone REMS Program, for both Mifeprex and the generic version. EAR154.

FDA has since reviewed and approved modifications to the Mifepristone REMS Program that are consistent with decades of experience reflecting that, with the REMS in effect, the benefits of mifepristone outweigh the risks. As relevant here, on May 7, 2021, FDA announced that it would review the elements of the Mifepristone REMS Program to determine whether those elements should be modified. EAR154, 157; DEAR46-53. FDA's review encompassed "multiple different sources of information," including "published literature," "safety information," adverse event reports, a "REMS assessment report" submitted by the sponsors, and "information provided by advocacy groups, individuals, and the [sponsors]." EAR159; *see also* DEAR285-288. The time period for the agency's literature search was March 29, 2016 (the date of the 2016 REMS modification) to July 26, 2021, and the search included publications found on PubMed and Embase as well as those provided by "advocacy groups, individuals, plaintiffs in [*Chelius v.*

Becerra, No. 1:17-493-JAO-RT (D. Haw.)]," the sponsors, and "healthcare providers and researchers." EAR159.

On December 16, 2021, FDA announced its conclusion that "mifepristone will remain safe and effective for medical abortion if the in-person dispensing requirement is removed, provided all the other requirements of the REMS are met, and pharmacy certification is added." EAR188; *see also* EAR190. Specifically, because FDA found insufficient evidence to demonstrate that the drug would be safe without them, FDA determined that the prescriber certification and Patient Agreement Form requirements continued to be necessary components of the REMS to mitigate risks related to heavy bleeding, missed ectopic pregnancy, and other issues. EAR161-167, 185-186.

At the same time, FDA determined that the REMS "must be modified" to remove the requirement that mifepristone be dispensed only in certain healthcare settings because this requirement is "no longer necessary to ensure that the benefits of the drug outweigh the risks." DEAR54-62. FDA also determined that because the in-person dispensing requirement was being removed, it was necessary to add a new requirement that pharmacies that dispense the drug be certified. EAR189-190. FDA reasoned that "[a]dding the pharmacy certification requirement incorporates pharmacies into the REMS, ensures that pharmacies are aware of and agree to follow applicable REMS requirements, and ensures that mifepristone is only

dispensed pursuant to prescriptions that are written by certified prescribers." EAR189. "[M]ifepristone will remain safe and effective" with these REMS modifications, FDA concluded, "provided all the other requirements of the REMS are met and pharmacy certification is added." EAR188; *see also* EAR190.

FDA directed the mifepristone sponsors to submit supplemental applications proposing these modifications to the REMS. DEAR54-62. The sponsors submitted their supplemental applications on June 22, 2022, and FDA approved them on January 3, 2023. DEAR63-245. Plaintiffs challenge that decision.

STANDARD OF REVIEW

In reviewing agency action under the APA, "the function of the district court" at summary judgment "is to determine whether or not as a matter of law the evidence in the administrative record permitted the agency to make the decision it did." *Occidental Eng'g Co. v. INS*, 753 F.2d 766, 769 (9th Cir. 1985)). That inquiry requires the Court to determine, based on the administrative record, *Camp v. Pitts*, 411 U.S. 138, 142 (1973), whether the challenged agency action was "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law," 5 U.S.C. § 706(2)(A), or "in excess of statutory jurisdiction, authority, or limitations," *id.* § 706(2)(C).

Review under the arbitrary-and-capricious standard is "at its most deferential" with respect to an agency's scientific determinations within its area of expertise.

Balt. Gas & Elec., Co. v. Nat. Res. Def. Council, Inc., 462 U.S. 87, 103 (1982). "[FDA's] judgments as to what is required to ascertain the safety and efficacy of drugs fall squarely within the ambit of the FDA's expertise and merit deference from [courts]." *Schering Corp. v. FDA*, 51 F.3d 390, 399 (3d. Cir. 1995); *see also FDA v. Am. Coll. Of Obstetricians & Gynecologists*, 141 S. Ct. 578, 579 (2021) (Roberts, C.J., concurring in the grant of application stay).

ARGUMENT

I. Plaintiffs Lack Standing

To meet the "irreducible constitutional minimum of standing," *Lujan v. Defs. of Wildlife*, 504 U.S. 555, 560 (1992), Plaintiffs "must show (i) that [they] suffered an injury in fact that is concrete, particularized, and actual or imminent; (ii) that the injury was likely caused by the defendant[s]; and (iii) that the injury would likely be redressed by judicial relief," *TransUnion LLC v Ramirez*, 594 U.S. 413, 423 (2021). "In order to have standing at the summary judgment stage, plaintiffs must 'set forth by affidavit or other evidence specific facts' . . . showing that they have suffered an 'injury in fact' that is fairly traceable to the action they seek to challenge." *Arakaki v. Hawaii*, 314 F.3d 1091, 1098 (9th Cir. 2002) (quoting *Lujan*, 504 U.S. at 561). Moreover, "standing is not dispensed in gross." *Lewis v. Casey*, 518 U.S. 343, 358 n.6 (1996). "Rather, a plaintiff must demonstrate standing for

each claim he seeks to press and for each form of relief that is sought." *Davis v. FEC*, 554 U.S. 724, 734 (2008) (internal quotation marks omitted).

Plaintiffs have failed to show standing to challenge the prescriber certification requirement and Patient Agreement Form through any of their various theories. *First*, Plaintiffs contend that they have *parens patriae* standing. *See, e.g.*, Am. Compl. ¶ 16; *Washington I*, 668 F. Supp. 3d at 1136-37. But "States do not have standing as *parens patriae* to bring an action against the Federal Government." *Murthy*, 603 U.S. at 76. That holds true when States challenge REMS decisions under the APA. *Washington II*, 108 F.4th at 1177.

Second, Plaintiffs argue that they have standing because the REMS causes more patients to choose surgical abortion over mifepristone, thereby indirectly increasing the costs of Medicaid and other state-funded healthcare programs. *See, e.g.*, Birch Decl. ¶¶ 3-18; *Washington I*, 668 F. Supp. 3d at 1137. But "an alleged uptick in Medicaid costs is exactly the kind of 'indirect effect[] on … state spending' that the Supreme Court has rejected as a basis for standing." *Washington II*, 108 F.4th at 1176. A contrary conclusion would lead to the untenable proposition that "every entity that provides health insurance or subsidized medical care" has standing to challenge the indirect effects of FDA regulation. *Id.*; *see also FDA v. Alliance for Hippocratic Medicine*, 602 U.S. 367, 392 (2024).

Moreover, Plaintiffs have provided no evidence that the Mifepristone REMS Program causes more patients to choose higher-cost surgical abortion over mifepristone. *Cf.* Nelson Decl. ¶ 13 (offering only speculation). Indeed, they acknowledge that the number of surgical abortions *decreased* during the period from 2015 to 2022—before FDA approved a modification in January 2023 that made the REMS *less* burdensome. Birch Decl. ¶ 8, 13. Plaintiffs also assert that increasing the restrictions on mifepristone would cause an increase in surgical abortion. *See, e.g.*, Birch Decl. ¶ 10. But Plaintiffs challenge only the existing REMS, not a hypothetical future modification. Plaintiffs' "purely speculative" assertion that the REMS indirectly causes increased healthcare costs cannot support standing. *See Simon v. E. Kentucky Welfare Rights Org.*, 426 U.S. 26, 42-43 (1976).

Third, Plaintiffs argue that the REMS restricts their employees' practices, *see Washington I*, 668 F. Supp. 3d at 1137, which they say affects their generalized "proprietary interests in delivering high-quality patient care," Am. Compl. ¶ 14. This vague theory fails to identify a concrete injury to their providers' interests in practicing medicine. *See Spokeo, Inc. v. Robins*, 578 U.S. 330, 340-41 (2016) (to be concrete, an injury must be "real, not abstract" (citation and quotation marks omitted)). Plaintiffs do not—and cannot—allege, for example, that the Patient Agreement Form actually prevents state healthcare providers from communicating

what they believe is medically sound advice to patients. Nor do they explain how state-employed prescribers who are already certified have a redressable injury stemming from the prescriber certification requirement.

Finally, at most, Plaintiffs have standing to challenge only the particular REMS requirements that they have shown cause them redressable actual or imminent injury. *See Davis*, 554 U.S. at 734. While Defendants do not dispute that one Plaintiff (Washington) has met this requirement with respect to the pharmacy certification requirement, *see* Dasgupta Decl. ¶¶ 8-14, 19, Plaintiffs have not met that burden for any other REMS requirement.

II. Plaintiffs Failed To Administratively Exhaust Their Claims

Plaintiffs also failed to administratively exhaust their claims through a citizen petition. *See* 21 C.F.R. §§ 10.45(b), (f), 10.25(a), 10.30. This Court previously noted that Plaintiffs did not pursue their claims through a citizen petition. *Washington I*, 688 F. Supp. 3d at 1138. It found, however, that "exceptional circumstances" excuse that failure because exhaustion would have been futile. *Washington I*, 688 F. Supp. 3d at 1138. Respectfully, Defendants disagree with that conclusion.

Exhaustion requirements "avoid premature claims and [] ensure that the agency possessed of the most expertise in an area be given first shot at resolving a claimant's difficulties." *Idaho Sporting Cong., Inc. v. Rittenhouse*, 305 F.3d 957,

965 (9th Cir. 2002). In particular, requiring a plaintiff challenging FDA approval of a drug application to first file a citizen petition is necessary to "prevent[] premature interference with agency processes so that the agency may function efficiently and so that it may have an opportunity to correct is own errors, to afford the parties and courts the benefit of its experience and expertise, and to compile a record which is adequate for judicial review." *Center for Food Safety v. Hamburg*, 696 F. App'x 302, 303 (9th Cir. 2017).

Plaintiffs' claims turn on issues within the agency's expertise. They involve technical and factual assertions about, for example, safety comparisons of mifepristone to other drugs and alleged burdens of REMS requirements on the healthcare delivery system—including burdens that Plaintiffs allege have arisen only after FDA's 2021 REMS review. *See, e.g.*, Am. Compl. ¶¶ 3, 25, 147, 176, 178-88, 212, 219. Their claims also rely on studies that were not before the agency at the time of that determination. *See, e.g.*, Am. Compl. ¶¶ 141 n.62, 143 n.66, 149 n.79, 150 n.80; Godfrey Decl. ¶ 22 n.21; Janiak Decl. ¶ 15 n.7. Requiring exhaustion will ensure that these "technical and policy questions" will be "addressed in the first instance by the agency with regulatory authority over the relevant industry rather than by the judicial branch." *See Astiana v. Hain Celestial Grp., Inc.*, 783 F.3d 753, 760 (9th Cir. 2015). This will "afford the parties and courts the benefit of [FDA's] experience and expertise, and [allow it] to compile a

record which is adequate for judicial review." *Center for Food Safety*, 696 F. App'x at 303. That is why courts (including this one) have required a party challenging FDA's approval of a drug application or other marketing authorization to first file a citizen petition presenting the challenge to the agency. *See, e.g.*, *Jensen v. Biden*, No. 4:21-cv-5119, 2021 WL 10280395 (E.D. Wash. Nov. 19, 2021) (Rice, J.); *Ass'n of Am. Physician & Surgeons, Inc. v. FDA (AAPS)*, 539 F. Supp. 2d 4, 21-24 (D.D.C. 2008), *aff'd*, 358 F. App'x 179 (D.C. Cir. 2009); *see also Doe #1-#14 v. Austin*, 572 F. Supp. 3d 1224, 1234 (N.D. Fla. 2021).

None of FDA's previous actions demonstrates that the futility exception applies. *First*, FDA never considered Plaintiffs' 2020 letter in connection with a REMS modification decision. That letter was submitted to a public docket for guidance regarding FDA's policy for certain REMS requirements during the COVID-19 public health emergency, *see* FDA-2020-D-1106-0061, and did not contain all of Plaintiffs' present arguments or the studies Plaintiffs rely on. FDA's response to that letter therefore does not demonstrate that it would have been futile for Plaintiffs to have presented their arguments to the agency during the 2021 REMS review or now through a new citizen petition.

Second, FDA's conclusion in 2021 that the REMS must be modified but not eliminated likewise does not excuse Plaintiffs' failure to exhaust. Plaintiffs' challenge raises points that could not have been considered in 2021, including their

arguments about post-*Dobbs* developments and a 2022 Canadian study. Indeed, Plaintiffs' argument that it would have been futile to ask FDA to consider the Canadian study cannot be squared with their argument that FDA's failure to consider that study warrants remand. After all, if it is certain that the outcome would have been the same had FDA considered the study, then any failure to consider it would be harmless error. *See* 5 U.S.C. § 706 ("due account shall be taken of the rule of prejudicial error").

Third, ACOG's 2022 citizen petition did not relate to the agency's 2021 review of the REMS or to the January 2023 REMS modification. Rather, it asked FDA to request that the sponsor of Mifeprex submit a supplemental new drug application proposing to (1) add miscarriage management as an approved indication and (2) eliminate or modify the REMS so that it would not be unduly burdensome for *that* use. EAR210-337. FDA denied the citizen petition because it is up to the sponsor to decide whether to seek approval for a new indication. EAR240-243.

Citing the Canadian study, that petition also urged FDA to exercise enforcement discretion with respect to the REMS requirements as they pertain to miscarriage management, while such a supplemental new drug application was being considered. EAR240-243. FDA denied this request because the management of miscarriage is not a currently approved indication for mifepristone. It thus would be premature for FDA to consider any impact that the addition of this

indication would have on the REMS, including whether the REMS is unduly burdensome for that use. EAR240-243. This disposition of the petition made it unnecessary for the agency to consider the Canadian study.

In short, nothing demonstrates that it would have been futile for Plaintiffs to present their claims (including about the Canadian study) to FDA. While it is not a foregone conclusion that FDA would find that the study supports the result Plaintiffs seek, it is also not certain that FDA would reject Plaintiffs' arguments.

III. Plaintiffs' APA Claims are Meritless

A. FDA reasonably applied the REMS modification statutory factors

As explained above, FDA's decision to modify a REMS is governed by § 355-1(g)(4). That paragraph is titled "[m]odification" and, among other things, sets forth the factors that FDA considers when determining whether to require a sponsor to propose a REMS modification. FDA may require that a sponsor propose a modification to an existing REMS in a supplemental application to "ensure the benefits of [a] drug outweigh the risks of the drug" or to "minimize the burden on the health care delivery system." 21 U.S.C. § 355-1(g)(4)(B). FDA may not approve a supplemental application modifying a REMS unless the agency is satisfied that the evidence shows that the drug will remain safe with the modification. *Id.* §§ 355-1(g)(4)(B), 355(d); 21 C.F.R. §§ 314.1 (new drug

application requirements apply to supplemental applications), 314.105(c) (approval contingent on meeting statutory standards for safety and effectiveness).

Here, FDA appropriately applied the § 355-1(g)(4)(B) factors to determine that the REMS must be modified in certain respects and that, as modified, the drug would remain safe, while minimizing the burden of the REMS. In reaching that determination, FDA did not reassess information it already considered in coming to its then-existing safety determination. Rather, it based that determination on its 2021 review of information generated after the 2016 REMS modification. EAR159-160, 161, 166, 193-197.

Specifically, FDA carefully examined hundreds of publications to determine whether they supported modifications to the REMS that would continue to assure safe use of the drug. EAR159-160, 161, 166, 193-197. The agency also reviewed information from a wide variety of other sources, including healthcare providers, advocacy groups, and Plaintiffs. EAR159-160, 161, 166, 193-197. FDA also considered safety information from time periods in which the in-person dispensing requirement was not being enforced during the COVID-19 public health emergency, including information from the sponsors and adverse event reports. EAR159. Additionally, in assessing whether to maintain the Patient Agreement Form, FDA considered the National Abortion Federation's 2020 Clinical Policy Guidelines for Abortion Care, as well as Practice Bulletins from ACOG and the

Society of Family Planning, and data relating to an increase in new providers for this care obtained from well-conducted surveys. EAR161, 166.

Based on its review, FDA found evidence sufficient to support eliminating the in-person dispensing requirement, so long as pharmacy certification was added and the other existing REMS elements were retained. EAR188; *see also* EAR191. FDA's determination with respect to each element was reasonable.

1. Prescriber certification. FDA explained that the evidence was insufficient to show that the benefits of mifepristone would continue to outweigh its risks if the prescriber certification requirement was removed. EAR162, 186. Specifically, the agency's literature review did not identify any studies comparing providers who met the qualifications that must be certified to with providers who did not, and thus found "no evidence to contradict [its] previous finding that prescribers' ability to accurately date pregnancies, diagnose ectopic pregnancies, and provide surgical intervention or arrange for such care through others if needed, is necessary to mitigate the serious risks associated with" the drug. EAR162. In addition, by requiring prescribers to acknowledge that they "must report patient deaths associated with mifepristone to the manufacturer," the prescriber certification requirement "ensures that the manufacturer receives all reports of patient deaths and, in turn, fulfills its regulatory obligations to report those deaths to the FDA." EAR163. Moreover, FDA anticipated a "potential for doubling" the number of

prescribers due to the agency's removal of the in-person dispensing requirement. EAR163; *see also* EAR186. In view of that potential, the agency determined that it was important to retain the prescriber certification to ensure that providers meet the necessary qualifications and adhere to the guidelines for use. EAR163; *see also* EAR186.

FDA therefore concluded that prescriber certification "continues to be a necessary component of the REMS to ensure the benefits of mifepristone for medical abortion outweigh the risks." EAR163; *see also* EAR186. At the same time, it noted that "[t]he burden of prescriber certification has been minimized to the extent possible" because each provider need only provide one certification to each of the two drug sponsors for mifepristone. EAR163; *see also* EAR186.

2. Patient Agreement Form. FDA similarly concluded that the single-page Patient Agreement Form, which "ensures that patients are informed of the risks of serious complications associated with" use of mifepristone for this indication, "does not impose an unreasonable burden on providers or patients" and "remains necessary to assure the safe use of Mifepristone." EAR163, 167; *see also* EAR186. FDA explained that "literature that focused on the informed consent process" "d[id] not provide evidence that would support removing" the Patient Agreement Form requirement. EAR165, 166; *see also* EAR186. Specifically, the agency found "no publications which directly addressed" the Patient Agreement Form. EAR165.

Moreover, seven studies focusing on the informed consent process contained "no outcome data" or "other evidence demonstrating that informed consent made the Patient Agreement Form unnecessary." EAR165-166.

Further, as with prescriber certification, FDA found that the potentially significant increase in the number of medical abortion providers weighed in favor of retaining the Patient Agreement Form. EAR186; *see also* EAR185. The agency noted the "continued need to ensure that patients are consistently provided patient education under the Mifepristone REMS Program regarding the use and risks of mifepristone." EAR186; *see also* EAR164, 167. The Patient Agreement Form, FDA explained, fulfills that need by "standardizing the medication information that prescribers communicate to their patients, including new prescribers." EAR186; *see also* EAR164, 167. It also provides that information in a "brief and understandable format," thus minimizing the burden of this requirement. EAR167.

3. Pharmacy certification. FDA determined that the benefits of mifepristone for medical termination of early pregnancy would continue to outweigh the risks if the in-person dispensing requirement was removed, provided all other requirements of the REMS were met and a pharmacy certification requirement was added. EAR188; *see also* EAR189-190. The pharmacy certification requirement permits pharmacies to dispense mifepristone upon prescription by a certified prescriber if the pharmacies become certified. EAR189-190. FDA explained that,

with the removal of the in-person dispensing requirement, the pharmacy certification requirement is necessary to ensure that pharmacies are aware of and agree to follow applicable REMS requirements and that only prescriptions from certified prescribers are filled. EAR189.

B. Plaintiffs fail to identify any relevant statutory factor that FDA did not reasonably consider

1. Plaintiffs disagree with how FDA weighed the § 355-1(g)(4)(B) considerations, but they fail to identify any way in which FDA's consideration was unreasonable. Congress assigned FDA the responsibility to determine the conditions under which drugs are safe. 21 U.S.C. § 355(d). Based on the evidence, FDA concluded that the evidence remains insufficient to find that mifepristone would be safe without the requirements for the prescriber certification, the Patient Agreement Form, and pharmacy certification. That determination is entitled to the utmost deference. *Balt. Gas & Elec., Co.*, 462 U.S. at 103; *Schering Corp.*, 51 F.3d at 399; *see also Am. Coll. Of Obstetricians & Gynecologists*, 141 S. Ct. at 579 (Roberts, C.J., concurring in the grant of application stay) (explaining that the "significant deference" owed to FDA's judgments weighed against "compel[ling] the FDA to alter the regimen for medical abortion").

First, Plaintiffs do not dispute that prescribers should have the qualifications that the prescriber certification requirement ensures. Instead, they argue that the requirement is unnecessary because prescribers may possess those qualifications

without so certifying. Pl. MSJ 19. But FDA did not rest its decision solely on the need for prescribers to have these qualifications. FDA also invoked (1) the absence of new evidence demonstrating a reason to depart from the agency's earlier determination that prescriber certification was necessary to ensure the safe use of mifepristone, (2) the prescriber certification's role in ensuring that patient deaths are reported to FDA, and (3) the potential for a significant increase in the number of prescribers following elimination of the in-person dispensing requirement. EAR162-163; *see also* EAR186. Given these considerations, it was reasonable for FDA to find that the evidence did not support eliminating this requirement.

Plaintiffs also wrongly accuse FDA of ignoring prescribers' alleged fear that certification will cause their identities to be exposed, thus opening them up to threats and stigma. Pl. MSJ 20-21. In fact, FDA acknowledged confidentiality concerns and emphasized those concerns as part of the basis for requiring pharmacy certification in light of the elimination of the in-person dispensing requirement. DEAR258-259. But while FDA acknowledged that the prescriber certification requirement imposes a burden, it concluded that this burden "has been minimized to the extent possible by requiring prescribers to certify only one time for each [sponsor]." EAR163; *see also* EAR186.

Second, Plaintiffs argue that the Patient Agreement Form should be eliminated because the information it provides is also contained in the boxed warning of the

full prescribing information and in the Medication Guide required to be provided to patients. Pl. MSJ 10. But FDA considered the relevant evidence and rejected this argument. EAR165, 166; *see also* EAR186. Notably, Plaintiffs do not dispute that there was an "absence of evidence" to support eliminating the Patient Agreement Form. Pl. MSJ 10. Rather, they appear to fault FDA for failing to point to evidence that mifepristone would be unsafe without a Patient Agreement Form. *Id.* But that flips the burden: under § 355-1(g)(4)(B), FDA determines if an existing REMS should be modified to, among other things, "ensure the benefits of the drug outweigh the risks of the drug." *See supra* pp. 18-19.

Third, Plaintiffs note that FDA acknowledged that the pharmacy certification requirement would likely limit the types of pharmacies that would choose to dispense mifepristone. Pl. MSJ 22. That acknowledgement refutes Plaintiffs' suggestion that FDA ignored the burdens of this requirement.

2. Plaintiffs also err by emphasizing the factors in 21 U.S.C. § 355-1(a)(1) that they claim FDA failed to consider. Pl. MSJ 1, 2, 15, 22. As its title ("Initial Approval") suggests, § 355-1(a)(1) governs FDA's decision to require an applicant seeking *initial approval* of a new drug for a particular use to propose a REMS. 21 U.S.C. § 355-1(a)(1). It provides that FDA may require the applicant to propose a REMS if the agency determines that one is "necessary to ensure that the benefits of

the drug outweigh the risks of the drug." *Id.* In making that determination, FDA must consider certain specific factors. These factors do not apply here.[3]

Notably, Plaintiffs are not challenging FDA's "initial approval" of the mifepristone REMS. 21 U.S.C. § 355-1(a)(1). Instead, they challenge only the January 2023 REMS modification, a decision governed by § 355-1(g). As discussed above, § 355-1(g)(4)(B) sets out distinct considerations relevant to an agency decision to propose modifications to a REMS. Moreover, it does not cross-reference or incorporate the factors enumerated in § 355-1(a)(1). Indeed, § 355-1 recognizes an initial determination under subsection (a)(1) as distinct from a later determination to modify the REMS under subsection (g). *See* 21 U.S.C. § 355-1(h)(1) (distinguishing between a "proposed [REMS] for a drug submitted under subsection (a)" and a "proposed modification to an approved [REMS] for a drug submitted under subsection (g)"); *id.* § 355-1(h)(3), (4) (establishing different dispute resolution procedures for decisions under subsections (a)(1) and (g)).

Nor would it make sense to apply the § 355-1(a)(1) factors to a REMS modification decision. Several of those factors are directed at drugs that have not yet been marketed for a particular use subject to a REMS. *See, e.g.*, *id.* § 355-

[3] FDA respectfully disagrees with this Court's preliminary ruling that § 355-1(a)(1) applies to modification decisions. *Washington*, 668 F. Supp. 3d at 1140-41.

1(a)(1)(A) ("*estimated* size of the population *likely* to use the drug") (emphasis added); *id.* § 355-1(a)(1)(B) ("seriousness of the disease or condition that is *to be treated* with the drug") (emphasis added); *id.* § 355-1(a)(1)(C) ("*expected* benefit of the drug") (emphasis added); *id.* § 355-1(a)(1)(E) (referring to "the population *likely* to use the drug") (emphasis added); *id.* § 355-1(a)(1)(F) ("*new* molecular entity") (emphasis added). If Congress intended to require FDA to apply the § 355-1(a)(1) factors when assessing drugs already marketed subject to a REMS, it would have used language more amenable to that assessment.

3. Plaintiffs also argue that FDA failed to apply the factors in § 355-1(f)(1)-(3), which governs FDA's decision whether to require a REMS to include ETASU. Pl. MSJ 1, 12, 14, 16, 18, 21, 22, 24. But subsection (f), like subsection (g), looks to whether ETASU are "necessary to assure safe use of the drug" and are not unduly burdensome. *See id.* § 355-1(f)(1), (2); *accord id.* § 355-1(g)(4)(B)(i) and (ii); *see also id.* § 355-1(f)(1)(A) (permitting FDA to require elements to assure safe use if the drug "can be approved only if, or would be withdrawn unless, such elements are required"). And here, FDA weighed precisely those factors. As discussed, based on its review of the evidence, FDA concluded that (1) there was insufficient evidence to demonstrate that mifepristone would continue to have a favorable safety profile if the prescriber certification requirement or the Patient Agreement Form were eliminated, but (2) there was sufficient evidence supporting removal of

the in-person dispensing requirement, provided that all other REMS requirements were met and a pharmacy certification requirement was added.

Plaintiffs argue that FDA failed to reasonably account for burdens on access, but Plaintiffs do not explain how any of the ETASU could have been modified in a way to make them less burdensome while ensuring the drug's safety. While Plaintiffs contend that FDA should have eliminated the ETASU entirely, that approach is inconsistent with FDA's determination that prescriber certification, the Patient Agreement Form, and pharmacy certification were *necessary* for safety. EAR163, 186, 188, 189-190, DEAR54-62.

Citing § 355-1(f)(2)(D)(i), Plaintiffs fault FDA for requiring a REMS for Mifeprex and its generic when FDA did not require a REMS for Korlym (a different drug product with mifepristone as its active ingredient, *see supra* n.1). In deciding whether to require a REMS for a particular drug, FDA makes a case-by-case determination that involves weighing the drug's risks and benefits in light of its particular conditions of use and other factors. *See* 21 U.S.C. § 355-1(a)(1). Indeed, FDA conducted this case-by-case inquiry for Korlym, explicitly considering the REMS for Mifeprex. FDA explained why Korlym does not require a REMS to assure safe use of the drug to treat Cushing's syndrome. Among other things, FDA noted that women with Cushing's syndrome are "unlikely to be pregnant" due to the underlying disease, and that the sponsor voluntarily

distributes Korlym exclusively through specialty pharmacies. DEAR22, 28; *see generally* DEAR16-30. Because Mifeprex and its generic (on the one hand) and Korlym (on the other) have different approved uses—and different benefits and risks in light of those uses—FDA was not compelled to treat the drugs as the same.

Contrary to Plaintiffs' misrepresentation, FDA did not conclude a REMS was required for Mifeprex and its generic but not for Korlym because abortion is "controversial." Pl. MSJ 1, 6, 24. Rather, FDA simply observed that "the more controversial use of [mifepristone] for medical termination of pregnancy" posed "a regulatory and legal challenge" in terms of whether to also require a REMS for Korlym. EAR310. FDA did not suggest that that "controversy"—let alone "[s]ocial 'controversy,'" Pl. MSJ 24—was a *reason* for requiring a REMS for mifepristone for medical termination of early pregnancy.

4. In any event, even if Plaintiffs were right that FDA did not fully consider particular statutory factors relevant to REMS modification, any such error would be harmless. *See* 5 U.S.C. § 706. Here, FDA determined that the REMS with ETASU is necessary to assure mifepristone's safe use. Because FDA cannot approve a drug for use under conditions that the agency has not determined are safe, 21 U.S.C. § 355(d), none of the factors Plaintiffs identify could have changed the agency's conclusion.

C. FDA considered all relevant evidence

Plaintiffs' attack on FDA's consideration of the evidence likewise fails. Pl. MSJ 22-24. As explained above, FDA reviewed evidence from a wide variety of sources, including "advocacy groups," "healthcare providers and researchers," and Plaintiffs themselves. FDA did not ignore relevant evidence.

1. As noted, published literature was only one of several types of information that FDA considered. With respect to that literature, the agency's decision to focus on objective safety data when considering whether the evidence supported modifying the REMS with regard to the prescriber certification and in-person dispensing requirements was plainly reasonable. To determine whether to modify an existing REMS, FDA must assess whether the evidence before it shows that the drug would remain safe with the contemplated modification. Objective safety data, which here included, among other things, data regarding safety outcomes during the period in which in-person dispensing was not being enforced, was the evidence most relevant to these modifications, and Plaintiffs do not contend otherwise.

Plaintiffs misunderstand the import of FDA's focus on such evidence. They contend that FDA "*intentionally excluded* reams of relevant information from its review." Pl. MSJ 11. But FDA considered all relevant evidence before it. *See supra* pp. 19-20. The agency generally focused on "objective safety data" because that was the kind of evidence most germane to its safety analysis.

Here, context makes plain that FDA's statements that it "excluded" certain types of evidence meant only that it concluded that such evidence did not bear on evaluation of some of the modifications it was considering. EAR193-197. The APA's requirement that an agency consider all relevant evidence before it does not oblige it to agree that any particular type of evidence should be given weight in its determination. Indeed, "Appendix A" to FDA's 2021 REMS review memorandum contains a chart that lists the references that FDA "excluded" from the review. The chart describes the contents of the listed references and briefly notes the reason that FDA did not give the item weight in making its determination. EAR193-197. The very existence of the chart belies Plaintiffs' contention that FDA did not "consider" the references in the APA sense.

Nor are Plaintiffs correct that FDA refused to consider anything but objective safety data. The 2021 REMS review memorandum makes equally clear that FDA did not "categorically" refuse to consider qualitative data, such as practice guidelines and data from practitioner surveys regarding provider volume. To the contrary, FDA reviewed and considered practice guidelines and survey data in evaluating the Patient Agreement Form ETASU because of the relevance of the practice guidelines, the quality of the survey data, and the relevance of likely changes in provider volume. EAR161, 166.

2. The only evidence Plaintiffs point to (Pl. MSJ 23-24) that FDA did not

consider is the Canadian study referenced above. *See supra* pp. 16-18. But, as noted, that study was not published until 2022—*after* FDA completed its 2021 REMS review and directed the sponsors of mifepristone to propose a modified REMS. ECF No. 157-1, at 8. FDA reasonably imposed a cut-off date of July 2021 for its systematic review of the literature. EAR159. Indeed, had FDA declined to establish a cut-off date, it would never have completed its review. *See Ferguson v. Dep't of Educ.*, No. 09-cv-10057-FM, 2011 WL 4089880, at *10 (S.D.N.Y. Sept. 13, 2011) (finding it reasonable" for agency "to restrict the temporal scope" of inquiry to avoid "'never-ending process.'") (quoting *Coven v. OPM*, No. 07-cv-1831-PHX-RCB, 2009 WL 3174423, at *7 (D. Ariz. Sept. 29, 2009)).

Perhaps Plaintiffs mean to suggest that FDA was required to review any evidence published before the actual *approval* of the proposed modification. But that would open the door to the same "never-ending process." The statute provides that a sponsor has 120 days or a "reasonable time[]" to propose a modified REMS after being directed to do so. 21 U.S.C. § 355-1(g)(4)(B). FDA then generally has 180 days to act on that proposal. *Id.* § 355-1(h)(2)(A). If the agency had to reevaluate its decision to request a modification every time a new, potentially relevant study is published in that long gap and notify the sponsor to amend its pending request for modification based on that study, the evaluation would never be completed. In any event, FDA was never asked to consider the Canadian study

in connection with the January 2023 REMS modification. *See supra* pp. 16-18.

IV. Plaintiffs' Constitutional Claims Fail

Finally, Defendants are entitled to summary judgment on Counts III and IV of the Amended Complaint, which invoke the equal protection component of the Fifth Amendment's Due Process Clause. Plaintiffs (as States) have no rights under that provision. *South Carolina v Katzenbach*, 383 U.S. 301, 323-24 (1966).

In any event, it is unclear what "similarly situated parties," Am. Compl. ¶ 266, Plaintiffs claim to be treated differently from. And even if cognizable, Plaintiffs' claims would be subject to rational-basis review. *Dobbs v. Jackson Women's Health Org.*, 597 U.S. 215, 300 (2022). The Court must therefore reject Plaintiffs' constitutional claims if the January 2023 REMS modification "furthers any legitimate governmental purpose and is rationally related to that goal." *Raidoo v. Moylan*, 75 F.4th 1115, 1121 (9th Cir. 2023). The government has a legitimate interest in protecting public health. *Seaplane Adventure, LLC v. Cnty. of Marin*, 71 F.4th 724, 730 (9th Cir. 2023). For the reasons explained above, FDA's decision to approve modification but not elimination of the Mifepristone REMS Program is rationally related to that interest. Therefore, FDA is entitled to summary judgment on Plaintiffs' constitutional claims.

CONCLUSION

For the foregoing reasons, the Court should grant Defendants' Cross-Motion for Summary Judgment and deny Plaintiffs' Motion for Summary Judgment.

December 11, 2024

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CERTIFICATE OF SERVICE

I hereby certify that, on December 11, 2024, I electronically filed the foregoing with the Clerk of the Court using the CM/ECF system, which will send notification of such filing to all counsel of record.

/s/ Noah T. Katzen
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