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IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF HAWAII

HEIDI PURCELL, *et al*., Plaintiffs, v. XAVIER BECERRA, *et al*., Defendants.	CIV. NO. 1:17-00493-JAO-RT **DEFENDANTS' CONCISE STATEMENT OF FACTS IN SUPPORT OF MOTION FOR SUMMARY JUDGMENT**

Pursuant to Local Rule 56.1(1), Defendants respectfully submit this Concise Statement of Facts in Support of Motion for Summary Judgment.[1]

As a preliminary matter, Defendants note that this case "does not require fact finding on behalf of this court." *Northwest Motorcycle Ass'n v. U.S. Dept. of Agriculture*, 18 F.3d 1468, 1472 (9th Cir. 1994). "[I]n the context of reviewing an administrative decision under the APA, 'there are no disputed facts that the district court must resolve.'" *Conservation Council for Haw. v. Nat'l Marine Fisheries Serv.*, 97 F. Supp. 3d 1210, 1218 (D. Haw. 2015) (quoting *Occidental Eng'g Co. v. INS*, 753 F.2d 766, 769 (9th Cir. 1985)). Rather, the agency "is *itself* the finder of fact," and "the function of the district court 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*, 753 F.2d at 769-70 (emphasis added); *accord City & Cnty. of S.F. v. United States*, 130 F.3d 873, 877 (9th Cir. 1997). Accordingly, the facts set forth below describe the relevant regulatory history and FDA's findings.

1. In 2000, FDA approved mifepristone (under the brand name Mifeprex) in a regimen with misoprostol for medical termination of intrauterine pregnancy

[1] Under the stipulated schedule entered by this Court, the parties agreed to provide record materials to the Court through a Joint Appendix to be filed at the conclusion of briefing. Accordingly, to avoid overburdening the Court's docket, Defendants do not file the record excerpts at this time, but will include them in the Joint Appendix with relevant material highlighted.

through 49 days gestation. 2021 REMS 001566; FDA 0003-5; FDA 0009.

2. At the time of approval, to assure mifepristone's safe use, FDA placed restrictions under Subpart H on the distribution and use of the drug product. 2021 REMS 001566; FDA 0003-5.

3. The restrictions imposed at the time of approval in 2000 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. 2021 REMS 001566; FDA 0004.

4. 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. 2021 REMS 001566; FDA 0003.

5. Because these restrictions under Subpart H were in place when the Food and Drug Administration Amendments Act of 2007 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); 2021 REMS

001566; FDA 1281; PCSF ¶ 27.

6. In 2011, in response to a supplemental application submitted by the sponsor, FDA approved the Mifeprex REMS after determining that restrictions remained necessary to ensure the benefits of mifepristone outweigh the risks. FDA 1281; 2021 REMS 001565, 1566.

7. In 2016, FDA approved 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. 2021 REMS 001565; FDA 0371-381.

8. 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. 2021 REMS 001565; PCSF ¶ 43.

9. 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. 2021 REMS 001565, 1568; 2021 REMS 000643-650.

10. FDA's 2021 REMS review encompassed "multiple different sources

of information," including "published literature," "safety information," adverse event reports, a "REMS assessment report" submitted by the sponsors, "information provided by advocacy groups, individuals, and the [sponsors]," and "an examination of literature references provided by plaintiffs in the *Chelius v. Becerra* litigation." 2021 REMS 001570.

11. The agency's 2021 literature review covered material published between March 29, 2016 (the date of an earlier REMS modification) and July 26, 2021, and 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." 2021 REMS 001570.

12. FDA "focused on publications containing safety data related to outcomes of medical abortion (objective safety data) obtained from [FDA's] literature search and from the references proved to [FDA] relevant to the REMS ETASUs." 2021 REMS 001571.

13. "Appendix A" to FDA's 2021 REMS review memo, entitled "References Cited in Letters from Plaintiffs," contains a chart that lists the references that FDA "excluded" from the review, describes the contents of the listed references, and briefly notes the reason that FDA did not give the item weight in making its determination. 2021 REMS 001604-1608.

14. 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 the American College of Obstetricians and Gynecologists and the Society of Family Planning, and data relating to an increase in new providers for this care obtained from well-conducted surveys. 2021 REMS 001572, 1577.

15. Laure Schummers et al., *Abortion Safety and Use with Normally Prescribed Mifepristone in Canada*, 386 New Eng. J. Med. 57-67 (2022) ("the Canadian study") was published in 2022, after FDA completed its 2021 REMS review and directed the sponsors to propose a modified REMS. 2022 CP 000099-109.

16. The Canadian study was cited to FDA in a 2022 citizen petition asking 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. 2022 CP 000071-98.

17. FDA denied the citizen petition because it is up to the sponsor to decide whether to seek approval for a new indication.

18. The 2022 citizen 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. 2022 CP 000110-113.

19. FDA denied this request because the management of miscarriage is not a currently approved indication for mifepristone, and it would be premature for FDA to consider the impact that the addition of this indication would have, if any, on the REMS so that it is not unduly burdensome for that use. 2022 CP 000110-113.

20. 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." 2021 REMS 001599; *see also* 2021 REMS 001601.

21. FDA found 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. 2021 REMS 001572-1578, 1596-1597.

22. 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. 2021 REMS 001573-1574, 1597.

23. FDA's 2021 literature review did not identify any studies comparing

providers who met these qualifications 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. 2021 REMS 001573.

24. FDA found that 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." 2021 REMS 001574.

25. FDA anticipated a "potential for doubling" the number of prescribers due to the agency's removal of the in-person dispensing requirement and, in view of that potential, 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. 2021 REMS 001574; *see also* 2021 REMS 001597.

26. FDA 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." 2021 REMS 001574; *see also* 2021 REMS 001597.

27. FDA found 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. 2021 REMS 001574; *see also* 2021 REMS 001597.

28. FDA 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." 2021 REMS 001574, 1578; *see also* 2021 REMS 001597.

29. 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. 2021 REMS 001576, 1577; *see also* 2021 REMS 001597.

30. FDA found "no publications which directly addressed" the Patient Agreement Form. 2021 REMS 001576.

31. FDA found that 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." 2021 REMS 001576-1577.

32. The Patient Agreement Form may be signed electronically. 2023 SUPP 001122.

33. As with prescriber certification, FDA found that the "potential doubling of medical abortion providers" weighed in favor of retaining the Patient Agreement Form. 2021 REMS 001597; *see also* 2021 REMS 001578.

34. 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," a need the Patient Agreement Form fulfills by "standardizing the medication information that prescribers communicate to their patients, including new prescribers." 2021 REMS 001597; *see also* 2021 REMS 001575, 1578.

35. FDA found that the Patient Agreement Form provides that information in a "brief and understandable format," thus minimizing the burden of this requirement. 2021 REMS 001578.

36. 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 the benefits of mifepristone outweigh the risks of serious complications associated with mifepristone that are listed in the labeling of the drug." 2021 REMS 1803-1807; 1808-1811.

37. FDA 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. 2021 REMS 001600-1601.

38. The pharmacy certification requirement permits pharmacies to dispense mifepristone upon prescription by a certified prescriber if the pharmacies become certified. 2021 REMS 001600-1601.

39. 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." 2021 REMS 001600.

40. FDA acknowledged prescriber (and patient) 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. 2023 SUPP 1124-1125.

41. In light of the labeled indication and gestational age, pharmacies must ensure delivery within four days of receiving a prescription or make contact with the prescriber who can agree to another timeline. 2023 SUPP 1122.

42. FDA directed the mifepristone sponsors to submit supplemental applications proposing these modifications to the REMS. 2021 REMS 001803-1807, 1808-1811.

43. The sponsors submitted their supplemental applications in 2022, and

FDA approved them on January 3, 2023. 2023 SUPP 000257-350, 351-439; 2023 SUPP 001448-1460, 1461-1465.

44. FDA found that Korlym does not require a REMS to assure safe use of the drug to treat Cushing's syndrome, including that women with Cushing's syndrome are "unlikely to be pregnant" due to the underlying disease and the sponsor voluntarily distributes Korlym exclusively through specialty pharmacies. FDA 298, 304; *see generally* FDA 292-306.

Dated: December 3, 2024

Respectfully submitted,

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Certificate of Compliance

I hereby certify that this document complies with the word-count limits set by the Court in Dkt. 82 and 211 because, excluding parts of the document exempted by Local Rule 7.4(d), it contains 2,135 words. In compliance with Local Rules 7.4(e) and 10.2(a), I further certify that this document has been prepared using Microsoft Word in 14-point Times New Roman font.

Dated: December 3, 2024

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