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Modified REMS, Clarification on Mailing Drugs, and Movement in Texas Case Mark Significant Weeks in the Reproductive Health Legal Sphere

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With the approval of the modified mifepristone Risk Evaluation and Mitigation Strategy (REMS), it has been a momentous few weeks in the reproductive health legal space.

Modification to the REMS for Mifepristone

Mifeprex (mifepristone), used together with misoprostol to end an early pregnancy, is one of a relatively small number of medications deemed by the US Food and Drug Administration (FDA) to require a REMS – a drug safety program aimed at ensuring that the benefits of a medication with "serious safety concerns" outweigh its risks. Per FDA:

REMS are designed to reinforce medication use behaviors and actions that support the safe use of that medication . . . REMS are not designed to mitigate all the adverse events of a medication, these are communicated to health care providers in the medication's prescribing information. Rather, REMS focus on preventing, monitoring and/or managing a specific serious risk by informing, educating and/or reinforcing actions to reduce the frequency and/or severity of the event.

The requirement of a REMS for mifepristone is itself somewhat controversial. Certain parties, such as the American College of Obstetricians and Gynecologists, have long maintained that the weight of medical evidence stands against the need for a REMS for the drug. Nonetheless, mifepristone has had a REMS since it was first approved by FDA in 2000. The REMS was subsequently updated in 2016 to extend the gestational age for which the drug was approved and to allow for the administration of misoprostol at home, in addition to in a clinical setting.

In 2021, FDA determined that it was necessary to again modify the REMS "to reduce burden on the

health care delivery system and to ensure the benefits of the product outweigh the risks." Following this determination, on December 16, 2021, FDA announced that the REMS would be modified to (1) remove the requirement that mifepristone be dispensed in person, and (2) allow for pharmacies to dispense the drug if certified pursuant to requirements enumerated in the REMS. Following its standard procedure for REMS modifications, FDA sent REMS Modification Notification letters to the companies that hold the drug approvals for Mifeprex and mifepristone, who then submitted proposed REMS modifications to the Agency.

On January 3, 2023, two years after announcing the proposed modifications, FDA approved the modifications to the REMS and published them here. Consistent with the 2021 proposed modifications, the approved modified REMS permanently removed the in-person dispensing requirement and allows for the dispensing of mifepristone by certified pharmacies. As before, mifepristone remains available only by prescription.

In a marked change from the previous REMS — under which retail pharmacies were prohibited from dispensing mifepristone — the modified REMS allows for any pharmacy to become certified so long as it meets certain requirements. Namely, the pharmacy must:

- Be able to receive Prescriber Agreement Forms by email and fax;
- Be able to ship mifepristone using a shipping service that provides tracking information;
- Designate an authorized representative to carry out the certification process on behalf of the pharmacy; and
- Ensure the authorized representative oversees implementation and compliance with the REMS.

In the wake of the recent REMS modification, at least two major pharmacy retail chains — Walgreens and CVS Health — have stated that they will seek certification to allow for dispensing mifepristone.

It is yet to be determined the precise impact the modified REMS will have on access to mifepristone in states where medical termination of a pregnancy has been made illegal. Per FDA, the Agency is coordinating with the US Department of Justice (DOJ) "and others across the government" on such legal issues, and "[a]ny questions regarding preemption of state law should be directed to [DOJ]."

Mailing Mifepristone and Misoprostol

In a related development, on December 23, 2022, the US Department of Justice (DOJ) Office of Legal Counsel (OLC) published a memorandum opinion for the General Counsel of the US Postal Service (USPS) regarding the mailing of mifepristone and misoprostol. The opinion was issued by OLC in response to USPS' inquiry as to whether 18 U.S.C. § 1461 — originally enacted as part of the Comstock Act — prohibits the mailing of either mifepristone or misoprostol. Under the Act, "[e]very article or thing designed, adapted, or intended for producing abortion" and "[e]very article, instrument, substance, drug, medicine, or thing which is advertised or described in a manner calculated to lead another to use or apply it for producing abortion" is "declared to be nonmailable matter and [may] not be conveyed in the mails or delivered from any post office or by any letter carrier." Nonetheless, OLC concluded that 18 U.S.C. § 1461 does not prohibit the mailing of either mifepristone or misoprostol "where the sender lacks the intent that the recipient of the drugs will use

them unlawfully." OLC explained that "the mere mailing of such drugs to a particular jurisdiction is an insufficient basis for concluding that the sender intends them to be used unlawfully."

Meanwhile, 20 attorneys general issued letters to CVS and Walgreens warning against mailing "abortion pills" to their respective states. Despite OLC's memorandum opinion, the February 1, 2023 letters state that 18 U.S.C. § 1461 "expressly prohibits" using the mail to send or receive drugs that will be "used or applied for producing abortion." Indeed, the letters note that the attorneys general "reject [OLC's] bizarre interpretation" and that they "expect courts will as well."

Litigation Against HHS and FDA Administrative Actions

Finally, there has been recent movement on the docket in *Alliance for Hippocratic Medicine, et al. v. US Food and Drug Administration, et al.*, 2:22-cv-00223, filed in the US District Court for the Northern District of Texas on November 18, 2022. As we reported previously, the plaintiffs in this matter — a collection of organizations and providers that oppose abortion — filed suit against the FDA and the US Department of Health and Human Services (HHS) to challenge six administrative actions taken by FDA related to the Mifeprex approval, generic mifepristone approval, and REMS under the Administrative Procedure Act (5 U.S.C. § 706). Among other things, the plaintiffs seek a preliminary and permanent injunction ordering FDA and HHS to withdraw FDA's approval of both mifepristone and misoprostol for use in the provision of abortion and to withdraw FDA's actions "to deregulate" these drugs.

Concurrent with the Complaint, the plaintiffs also filed a motion for a preliminary injunction ordering FDA and HHS to withdraw or suspend, among other things:

- FDA's approvals of Mifeprex and generic mifepristone;
- FDA's 2021 decision to exercise enforcement discretion with respect to the in-person dispensing requirement under the REMS; and
- FDA's 2021 denial of a 2019 citizen petition raising concerns regarding the updated REMS and petitioning for further clinical studies.

The last several weeks have seen a flurry of activity in this matter. The court has stayed the deadline to answer the Complaint until the motion for a preliminary injunction is resolved. Danco Laboratories (the manufacturer of Mifeprex) has been granted leave to intervene in the case.
Additionally, *amicus* briefs have been filed by numerous entities, including private organizations, US States, Members of Congress, and food and drug scholars. The parties have additionally filed briefs on whether the court should consolidate the injunction hearing and the trial on the merits. Lastly, the court has ordered that the plaintiffs may file a consolidated reply to the response briefs filed by FDA/HHS and Danco on the motion for a preliminary injunction. ArentFox Schiff will be closely monitoring the docket and providing substantive updates as the case continues forward.

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