Society of Family Planning & SFP RESEARCH FUND

August 11, 2021

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Urology, Obstetrics, and Gynecology
5901-B Ammendale Road
Beltsville, MD 20705-1266

Re: US Food and Drug Administration's review of the risk evaluation and mitigation strategy for mifepristone

Dear Dr. Catherine Sewell:

On May 7, 2021, the US Food and Drug Administration (FDA) announced a review of the risk evaluation and mitigation strategy for the drug mifepristone (hereafter, the mifepristone REMS). On behalf of the Society of Family Planning, the academic society for Complex Family Planning subspecialists and over 1,000 academicians, scientists, and partners focused on abortion and contraception research and clinical care, we write to share relevant evidence to support your review of the mifepristone REMS. We appreciate the opportunity to lend the expertise of the Society and its members to this process and applaud your efforts, as a science-based agency, to center sound medical evidence in the decision-making process related to mifepristone and its distribution and use.

As the organization representing Complex Family Planning Fellowship-trained obstetrician-gynecologists—the leaders in clinical care and medical education related to complex abortion and contraception—we conclude the additional controls provided by the REMS are not medically necessary to ensure patient safety. Our 30 years of experience within the Fellowship providing abortion and pregnancy loss care in complex cases, as well as the existing evidence on this topic described in detail below, does not support requiring provider certification and registration to prescribe mifepristone or restricting the healthcare professionals that can prescribe mifepristone. Mifepristone is extremely safe and highly effective when provided via a health center, pharmacy, or home delivery, and does not require a clinician to oversee dispensing.

On behalf of our expert membership, we offer the following summary of peer-reviewed scientific evidence related to the mifepristone REMS, with a focus on research published since the most recent FDA-approved labeling change in 2016. **We conclude that the current REMS, specifically the provisions that require provider certification and registration and restrict where mifepristone may be dispensed, confers no benefit in terms of safety, efficacy, or acceptability of the drug mifepristone and instead creates barriers to use that negatively impact public health and equity in access to care.**

Requiring provider certification and registration to prescribe mifepristone is unnecessary because it does not increase patient safety and constrains abortion provision.

- **The mifepristone REMS currently requires that providers are specially certified to prescribe the drug and must register as prescribers directly with the manufacturer(s); however, there is no evidence this requirement increases abortion safety**. In Canada, mifepristone-specific requirements for provider certification were lifted in November 2017. According to a comprehensive analysis of linked medical and financial records in Ontario, medication abortion remained extremely safe after deregulation, with a major complication rate of 0.33% compared to a rate of 0.31% in an analysis of a similar administrative dataset from California under the REMS, and consistent with a clinical review finding major complication rates <1% across multiple studies of mifepristone use for early abortion.[1–3]

- **Requiring provider certification and registration prevents many providers from incorporating mifepristone into their scope of practice**. In a representative national population-based survey of obstetrician-gynecologists, Grossman and colleagues found that 28% of obstetrician-gynecologists who did not currently provide care using mifepristone would do so if they could prescribe it similarly to other drugs.[4] Several recent, rigorous qualitative studies with diverse groups of clinicians have also demonstrated how the REMS creates barriers to incorporation of mifepristone into practice by creating administrative burdens that clinical champions are unable to overcome.[5,6]

The current restrictions on where mifepristone may be dispensed are unnecessary because mifepristone dispensing in clinical care settings is not associated with higher efficacy, greater safety, or greater acceptability compared to dispensing in brick-and-mortar pharmacies or via postal mail or delivery service.

- **The requirement for in-person dispensing of mifepristone in certain health care settings confers no safety benefit**. Through the mifepristone labeling change approved in 2016, the FDA recognized that requiring misoprostol be administered in clinical settings as part of early abortion care is unnecessary. As the summary of the peer-reviewed literature below suggests, patient self-administration of mifepristone at home is effective, safe, and acceptable. However, the current mifepristone REMS further require that mifepristone be distributed “only in…clinics, medical offices, and hospitals.”

- **Mifepristone can be safely dispensed in brick-and-mortar pharmacies**. Pharmacists are well qualified to assure safe dispensing of medications with a comparable safety profile to the 200 mg mifepristone tablet, including the 300 mg formulation of mifepristone for Cushing’s syndrome, which is not subject to a REMS. Evidence from high-income countries with health care infrastructure comparable to the US has demonstrated the acceptability of pharmacy dispensing of mifepristone. For example, mifepristone is currently distributed by pharmacists in Canada, a practice that Canadian physicians report facilitates the provision of medication abortion with mifepristone.[7] In the

US, physicians support pharmacy dispensing of mifepristone. In a qualitative study of primary care providers' perceptions of and experiences with mifepristone, Rasmussen and colleagues found that primary care providers in Illinois support pharmacy dispensing of mifepristone, describing it as a more patient-centered approach to administration of this drug.[8] Further, a recent US study demonstrated that pharmacy dispensing of mifepristone is safe and effective. In a study that included eight pharmacies in California and Washington state, Grossman and colleagues demonstrated that mifepristone dispensing by pharmacists in the pharmacy setting after the patient received counseling from a clinician is as effective (93.5% abortion completion with medication alone) as in-clinic dispensing efficacy reported by Winikoff and colleagues in a large multi-site national trial.[9,10] In Grossman and colleagues' study, only three (1.3%) participants visited an emergency department during the study follow up period, a lower proportion than most clinical trials of medication abortion using in-clinic mifepristone administration (range 2.9-4.1%).[10,11]

- **Mifepristone can also be safely dispensed by mail**. In a large (N=1,157 abortions) national US-based clinical trial of mifepristone dispensing by mail (the Teleabortion study), Chong and colleagues also found that mifepristone dispensing by direct mail to consumers is effective (95% abortion completion with medication alone), with only 0.9% experiencing any serious adverse event compared to an adverse event rate of 0.65% in a large (N=233,805 medication abortions) retrospective cohort study of in-clinic mifepristone administration.[12,13]

- **Retrospective analyses of rapid practice adaptations in the context of the COVID-19 pandemic further demonstrate the safety, efficacy, and acceptability of mifepristone dispensing by mail**. In a large (N=52,218) retrospective cohort study, Aiken and colleagues reported on the safety, efficacy, and acceptability of telemedicine abortion at Britain's largest abortion providers, which rapidly adapted to provide medication abortion using telemedicine during the spring and summer of 2020.[14] Following a telehealth consultation, individuals with a last menstrual period dating the pregnancy up to 69 days and without symptoms of ectopic pregnancy were able to receive both mifepristone and misoprostol for home administration. Investigators found that while medication abortion was equally effective in the telemedicine model (98.8%) vs the traditional in-clinic mifepristone administration model (98.2%, p=1.0), individuals using telemedicine had a shorter wait time between first contact and initiating the medication abortion (6.5 days vs. 10.7 days, p<0.001).

- **Whether patients receive mifepristone at a pharmacy or by mail, they report high acceptability**. In their pharmacy dispensing study, Grossman and colleagues report that 74.3% of patients would recommend pharmacy dispensing of mifepristone to a friend in a similar situation, and 65.4% were highly satisfied with their abortion experience.[9] Hyland and colleagues report that 97% of women cared for by an Australian telemedicine medication abortion service report high satisfaction, and Chong and colleagues report that 85% of participants in the Teleabortion study found their abortion experience "very satisfactory".[12,15]

Requiring provider certification and registration to prescribe mifepristone and mifepristone dispensing restrictions may lead to abortions happening later in pregnancy. Unfortunately, abortions become more socially and clinically complicated the further along in a pregnancy the abortion occurs.[2,16–18] Thus, restrictions such as the mifepristone REMS that limit people's ability to access abortion as soon as they discover they are pregnant negatively impact public health. Delays are particularly problematic for people with low incomes as abortions after the first trimester are more expensive and often result in even further delays in obtaining a desired abortion.[19–21] In Canada, where abortions are covered as part of universal health care, the proportion of abortions in the second trimester decreased by approximately 12% after mifepristone deregulation.[1] In the US, where limited access and cost are major contributors to delays in abortion, lifting the REMS may result in an even greater shift in abortions to earlier gestational ages.

The National Academies of Science, Engineering, and Medicine defines quality abortion care as safe, effective, patient-centered, timely, efficient, and equitable.[16] **By unnecessarily limiting the number of mifepristone providers in the US, the mifepristone REMS adversely impacts timeliness and equity in access to care.** As the academic society representing Complex Family Planning subspecialists, scientists, and partners focused on abortion and contraception research and clinical care, we hope this sound medical evidence is held central in your review of the mifepristone REMS. We appreciate your commitment to centering science and ensuring that policy decisions are based on the latest evidence.

Sincerely,

The Society of Family Planning Board of Directors

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