January 31, 3025

CITIZEN PETITION

Pursuant to 21 C.F.R. § 10.30, the American College of Obstetricians and Gynecologists, Society of Family Planning, and Society for Maternal-Fetal Medicine submit this petition, together with an appendix of supporting studies and documents, to request that the Food and Drug Administration ("FDA"): (1) remove the Mifepristone Shared System Risk Evaluation and Mitigation Strategy ("REMS"), including all of its Elements to Assure Safe Use ("ETASU"); or (2) in the alternative, at a minimum, refrain from taking any action that would further reduce patient access to mifepristone[1] and/or increase the burdens associated with prescribing or dispensing mifepristone.

Over more than two decades, hundreds of medical studies and vast amounts of data have confirmed that mifepristone, in combination with misoprostol, is a safe and effective way to terminate an early pregnancy. The scientific evidence is overwhelming: major adverse events occur in ***less than 0.32%*** of patients.[1] The risk of death is almost non-existent. Few drugs have been so extensively studied after their approval by FDA and few can boast such a clear and compelling record of safe use. Access to mifepristone enables practitioners to provide safe, medically-appropriate, evidence-based, and effective care. Indeed, mifepristone, in combination with misoprostol, constitutes the most common form of abortion in the United States, accounting for nearly two out of every three abortions.

[1] Petitioners use "mifepristone" herein to refer to both Mifeprex (NDA 020687) and its generic (ANDA 091178).

FDA itself determined in 2016, based on more than 2.5 million uses, that the drug's "efficacy and safety have become well established by both research and experience, and serious complications have proven to be extremely rare."[2] Yet, despite this record, FDA continues to subject mifepristone to unique regulatory requirements that impose burdens on health care providers and hamper patients' access to this medication. Particularly in light of rising maternal mortality across the country, access to mifepristone is a crucial component of comprehensive reproductive health care. Leading medical associations agree that, given mifepristone's outstanding safety record and its critical importance for reproductive health care, it is past time for FDA to fully lift the mifepristone REMS.[3] Consistent with this medical community consensus, Petitioners respectfully request that FDA eliminate its existing medically unnecessary barriers to mifepristone, or at minimum, take no further steps that would reduce access to this safe, essential medication.

ACTION REQUESTED

Petitioners request that FDA remove the Mifepristone Shared System REMS Program, including but not limited to the three ETASU requiring prescriber certification, pharmacy certification, and a patient agreement form. In the alternative, Petitioners request that FDA, at a minimum, take no action imposing greater burdens on patient access to mifepristone, and no action increasing burdens on the health care system relating to the provision of mifepristone, including but not limited to (a) adding new ETASU, (b) reinstating former mifepristone ETASU that are not currently part of the January 2023 REMS, (c) making the existing ETASU more onerous, or (d) modifying the REMS or labeling for mifepristone in a manner inconsistent with prevailing standards of evidence-based care.

STATEMENT OF GROUNDS

A. Mifepristone is extremely safe

Twenty-five years ago, FDA approved mifepristone (under the brand name Mifeprex) as part of a two-drug regimen for medication abortion.[4] In that regimen, which now is FDA-approved through ten weeks of pregnancy, mifepristone blocks a hormone necessary to sustain pregnancy, and misoprostol causes contractions and bleeding that empty the uterus.[5] As of December 31, 2024, approximately 7.5 million U.S. patients had used this regimen for medication abortion.[6] High-quality studies also support the use of mifepristone with misoprostol specifically for managing early pregnancy loss.[7]

While all abortion is very safe, FDA acknowledges that medication abortion with mifepristone provides a "meaningful therapeutic benefit" to some patients and may be "preferable and safer in [a patient's] particular situation."[8] Some patients, for instance, who have been the victims of rape or sexual assault may prefer to avoid the use of medical instruments in a procedural abortion; others may have uterine abnormalities that are contraindications for procedural abortion; still others may use medication abortion to avoid the risks of any anesthesia or sedation associated with abortion procedures.

As is the case for all drugs sold in the United States, the FDA-approved labeling for mifepristone warns of the drug's risks.[9] For mifepristone, the boxed warning in the labeling lists: "serious and sometimes fatal infections or bleeding," both of which FDA accurately described in 2016 as "exceedingly rare, generally far below 0.1% for any individual adverse event."[10] As the labeling makes plain, these risks arise whenever the pregnant uterus is evacuated, whether by "miscarriage, surgical abortion, medical abortion, or childbirth."[11] The labeling confirms: "[n]o causal relationship between the use of [Mifepristone tablets 200mg] and misoprostol and [serious infections and bleeding] has been established."[12] Indeed, FDA concluded in 2016 that the "critical

risk factor" for certain rare serious infections following mifepristone use "[wa]s pregnancy itself," not the medication.[13] After nearly 25 years of mandatory reporting of deaths potentially associated with mifepristone, the associated fatality rate is 0.00048%—and not one of the infinitesimally small number of deaths can be "causal[ly]" attributed to mifepristone.[14]

Mifepristone is as safe or safer than common drugs like Tylenol, Viagra, and penicillin—some of which are sold without a prescription and none of which has a REMS.[15] And mifepristone is far safer than hundreds of opioid analgesics that are subject to *less stringent* ETASU than mifepristone, even as opioids claim lives at such "a staggering rate" that they are "reducing life expectancy in the United States."[16]

B. Mifepristone's safety profile has remained strong and stable even after FDA removed certain medically unnecessary restrictions

Mifepristone's safety record has remained remarkably stable since FDA's original approval in 2000, including after FDA lifted some of its initial restrictions on the drug.

Since acknowledging in 2016 that mifepristone's safety profile is "well-characterized" and "has not changed over the period of surveillance,"[17] FDA has made three principal changes to the mifepristone REMS: (1) in 2016, FDA allowed all health care professionals with prescriptive authority under state law to become certified prescribers; (2) that same year, FDA eliminated the requirement that prescribers report serious adverse events potentially associated with mifepristone other than death; and (3) in 2021, FDA suspended and then, in 2023, permanently lifted the requirement that mifepristone be dispensed to patients only in person at a hospital, clinic, or medical office. In addition, in 2016, FDA made numerous changes to mifepristone's labeling, including updating the dosing and the route of misoprostol administration, removing the indication for multiple follow-up visits, and changing the gestational age indication from 49 days to 70 days.

There is no evidence that eliminating any of the former REMS restrictions (or changing

the label indications) reduced mifepristone's safety.[18] To the contrary, and as further detailed below, high-quality research and real-world data from both the United States and globally confirm that mifepristone remains one of the safest medications used in medical practice.[19]

1. Mifepristone is safe when prescribed and dispensed by qualified advanced practice clinicians

In 2016, FDA correctly concluded that advanced practice clinicians ("APCs") with prescriptive authority under state law could safely prescribe and dispense mifepristone. When FDA implemented this change, it relied upon three randomized controlled studies[20] and one comparative study[21] to support the conclusion that medication abortion is safe and effective when provided by APCs.[22] The success rates for medication abortions provided by APCs were greater than 96% across all the studies, and were similar to the success rates for physician-prescribed abortions.[23]

Since then, additional high-quality, peer reviewed studies further confirm FDA's 2016 finding that mifepristone remains safe and effective when prescribed and dispensed by qualified nonphysicians. A comprehensive, peer-reviewed review of the safety and effectiveness of medication abortion, conducted by the National Academies of Science, Engineering, and Medicine—an independent organization dedicated to providing objective expert advice on scientific, engineering and medical issues to inform public policy—concluded that "both trained physicians (OB/GYNs, family medicine physicians, and other physicians) and advanced practice clinicians (APCs) (physician assistants, certified nurse-midwives, and nurse practitioners) can provide medication and aspiration abortions safely and effectively."[24] A retrospective observational cohort study of medication abortion between 2009 to 2018 concluded that the safety and effectiveness of APC-provided medication abortion are within the established medical benchmarks.[25] And in the event that uterine aspiration is needed to complete the evacuation of a patient's uterus, studies show that the very low complication rate for aspiration procedures is "not

significantly different" whether performed by an APC or by a doctor.[26] The latter finding is consistent with research comparing the safety of aspiration abortion procedures when performed by physicians and APCs.[27]

Moreover, rescinding the ability of APCs to prescribe mifepristone would burden patient access by reducing the number of certified prescribers without increasing safety or efficacy.[28] And the burden would fall most heavily on underserved rural and remote populations.[29] Given the significant data showing that APCs offer improved access without compromising safety or efficacy, there is no reason for FDA to restrict the ability of APCs to provide medication abortions where permitted by state law.

2. The elimination of the in-person dispensing ETASU did not impact the safety of mifepristone

Telehealth for medication abortion is now a standard method of providing abortion care in the United States and around the world.[30] As in other areas of medicine provided by telehealth, reproductive health clinics and providers have developed specific protocols and technologies for telehealth care to ensure adequate patient contact and monitoring, such as health questionnaires, specialized patient platforms (*e.g.*, a patient "portal"), messaging and chat functions, and phone or video calls, all of which enable care to be provided with fewer or no in-person visits.

Critically, telehealth protocols for medication abortion offer the same patient protections as in-person dispensing and provide an equivalent level of patient care. Just as would happen during in-person care, patients are evaluated by a clinician who screens the patient to confirm pregnancy (relying on, *e.g.*, medical history, self-reported symptoms, and results of an at-home pregnancy test), assesses the duration of pregnancy, and identifies contraindications such as a potential ectopic pregnancy or other medical conditions or drug allergies.[31] Where clinically appropriate, the patient is advised to obtain in-person testing before proceeding.[32]

After the patient's eligibility for medication abortion has been confirmed and the patient has provided informed consent, the clinician either sends the appropriate medications to the patient directly or transmits a prescription to a mail-order or retail pharmacy.[33] And just as would happen during in-person care, the clinician advises the patient about follow-up care, including instructions for confirming that the pregnancy has terminated and what to do if they experience signs and symptoms of complications.[34] The percentage of patients that visit an emergency room for *any* abortion-related reason is exceedingly small,[35] and, as detailed below, the manner in which mifepristone is prescribed or dispensed does not alter its safety profile.

a. *Telehealth medication abortion is safe and effective*

After reviewing (a) REMS assessment data, (b) data from FDA's Adverse Event Reporting System ("FAERS") during the period when the in-person dispensing ETASU was not being enforced during the COVID-19 pandemic, and (c) numerous published studies, FDA concluded in December 2021 that "mifepristone will remain safe and effective for medication abortion if the in-person dispensing requirement is removed."[36] Specifically, FDA's analysis relied upon six studies that "generally support a conclusion that dispensing by mail is safe."[37] FDA stated that it would permanently remove the in-person dispensing requirement to "render the REMS less burdensome to healthcare providers and patients," enabling prescribers to provide medication abortion by telehealth where permitted by state law.[38] FDA formalized that change when it published the updated REMS in January 2023.

FDA's decision to eliminate this ETASU was strongly supported by the scientific evidence available as of December 2021. Research published since then further confirms that direct-to-patient telemedicine for medication abortion is safe and effective.[39]

For instance, a peer-reviewed study of over 6,000 telehealth patients in 20 states and Washington DC treated by three different online clinics between April 2021 and January 2022 found that "telehealth for abortion is effective and safe, with [safety and efficacy] rates similar to in-person care."[40] This study evaluated both "synchronous" telehealth care (where the provider communicates with the patient either by video or phone call) and "asynchronous" telehealth care (where the communication is by text message),[41] and further found that both "synchronous and asynchronous care are comparably effective and safe."[42] Specifically, the rates for both serious adverse events (0.25%) and ectopic pregnancy (0.14%) were "similar to previous studies of in-person medication abortion care," published in 2013 to 2015, which had found adverse event rates of 0.2–0.5%, and ectopic pregnancy rates of 0.2%.[43]

Other high-quality studies have come to similar conclusions. For instance, one study that compared in-person medication abortion care with telehealth care without in-person diagnostic or screening tests concluded that "medication abortion [performed through] telehealth screening and mail-order pharmacy dispensing of medications was associated with similar rates of complete abortion as in-person care with ultrasonography, met the prespecified threshold for noninferiority, and had low rates of [adverse events] overall."[44] A smaller study of medication abortion in primary care settings found that medication abortion provided by telehealth was "as effective, timelier and potentially more accessible than in-clinic care."[45] Another study comparing abortion outcomes between screening approaches across five telehealth sites showed no difference in serious adverse events between patients who received pre-abortion ultrasound or pelvic exams and those who did not.[46] And a systematic review and meta-analysis of the literature on medication abortion by telehealth confirms that telehealth abortion care is as safe and effective as in-person care, with a "shorter waiting time for medication delivery."[47]

All of these studies confirm that FDA was correct in determining that removal of the in-person dispensing requirement did not impact the safety and effectiveness of medication abortion.

b. *Telehealth for medication abortion improves access to care with high patient satisfaction*

At the same time, research also confirms that the availability of medication abortion by telehealth improves patient access to mifepristone and reduces burdens on the health care delivery system while maintaining or improving patient satisfaction. Accordingly, any reversion to an in-person dispensing requirement would burden patient access and the health care system, contrary to the statutory standards that govern FDA's imposition of ETASU. *See* 21 U.S.C. § 355-1(f)(2).

Telehealth increases access to abortion care by eliminating the need to travel to a health care provider. Thus, it offers a particular benefit for patients living in rural and medically underserved areas where there is no access to in-person abortion care,[48] as well as for patients who find it challenging to take time off from work or arrange for childcare in order to travel for abortion care.[49] Without associated travel, patients do not have to incur any expenses for transportation, gas, and lodging, incur fewer expenses for child care, and lose fewer wages.[50] In other words, telehealth eliminates or mitigates many of the burdens that can deter and delay abortion access for the low-income populations that comprise a majority of abortion seekers.[51] Telehealth also reduces delays in obtaining care because it enables patients to avoid long wait times at physical clinics[52]—a particularly urgent concern since *Dobbs v. Jackson Women's Health Organization*, as state abortion bans have increased demand for abortion care in many states where abortion remains lawful.[53] Reinstating in-person dispensing—which would lead to even more in-person visits at brick-and-mortar clinics already stretched thin—would increase burdens on the health care system and impede patient access.

Even without considering the time and expense of having to travel for abortion care, medication abortion care is typically more affordable for patients when provided through telehealth than through in-person care.[54] In 2023, pricing data collected from brick-and-mortar clinics that offered both in-person and telehealth care revealed that they were able to offer telehealth abortion services at a lower rate than in-person medication abortion services.[55] Given the longstanding prohibition on using federal funds to pay for abortion, managing the cost of abortion care is essential to ensure that patients with fewer resources are able to access the care they need.

In general, telehealth offers many opportunities for patients and providers to build trust and rapport—and that observation holds true in the context of medication abortion. In a qualitative study of 1,600 patients who received abortion care through telemedicine, "nearly all participants were very satisfied with telehealth abortion," with 98% of those surveyed reporting that they trusted their provider.[56] Patients further reported that choosing telehealth not only made abortion care more accessible, but also allowed them to receive care more quickly and with greater privacy in the comfort of their own home.[57]

Studies also show that telehealth abortion care offers patients other significant advantages. In a survey of medication abortion patients, those who received services by telehealth felt that the option "allowed them to talk more freely and openly, and feel more confident about the privacy of their abortion decision."[58] Indeed, a recent qualitative study of telehealth patients found that telehealth mitigates some manifestations of abortion stigma by eliminating the need to visit a physical clinic and thus reducing the visibility of one's abortion decision.[59] This benefit is all the more essential given increased rates of anti-abortion violence and harassment at brick-and-mortar clinics—violence and harassment specifically designed to deter or prevent access to reproductive

care.[60] In short, depriving mifepristone patients of the telehealth option would impede patient access in violation of FDA's congressional mandate not to impede access.

3. Evidence supports FDA's elimination of non-fatal mandatory adverse event reporting for mifepristone

FDA determined in 2016 that it was unnecessary to require prescribers of mifepristone to report non-fatal adverse events following the use of mifepristone given mifepristone's stable risk profile reflected in 15 years of mandatory serious-adverse-event reporting.[61] Since then, multiple data sources confirm that mifepristone continues to be extremely safe. FDA correctly lifted the broad adverse-event reporting requirement in 2016, and the ongoing requirement that mifepristone prescribers report the miniscule number of deaths following mifepristone use is extraneous.

First, FDA continues to collect data on adverse events for mifepristone through multiple data sources, including FAERS and case reports in published medical literature, just as it does for other drugs. *See* 21 U.S.C. § 355(k); 21 C.F.R. §§ 314.80, 314.81. FDA regularly relies upon stable FAERS data in determining whether a REMS may be removed.[62] Second, the medical literature shows an adverse event rate for mifepristone when prescribed pursuant to updated standards of evidence-based care, and in the absence of prior REMS requirements, that is comparable to the real-world clinical data reported to FDA prior to 2016. For example, a recent large prospective cohort study of over 6,000 patients who obtained medication abortion by telehealth had a serious adverse event rate of only 0.25%, comparable to the rate for in-person care included in the mifepristone labeling based on pre-2016 studies.[63] In other words, there is no reason to believe that the complication rate materially changed following the elimination of the pre-2016 adverse event reporting requirement. And, given the infinitesimal death rate associated with (and not proven to be caused by) mifepristone after millions of uses and decades of mandatory reporting, there is likewise no reason to maintain this special REMS reporting requirement.

C. A REMS is not necessary to ensure that mifepristone's benefits outweigh its risks, and the mifepristone ETASU do not fit the statutory profile

Given mifepristone's safety, FDA has not gone far enough in eliminating burdensome, medically unnecessary restrictions on this safe medication. As detailed below, the prescriber certification, patient agreement, and pharmacy certification ETASUs do not enhance safety—but *do* impede patient access and burden the health care delivery system. Indeed, FDA still regulates mifepristone more stringently than nearly any other of the 20,000 drugs it regulates. Unlike the 97% of prescription drugs without a REMS—including, to take just two examples, Viagra (with a fatality rate six-times that of mifepristone) and Jeuveau (a drug that temporarily improves the appearance of wrinkles and whose labeling features a black-box warning of "life threatening" breathing difficulties)—mifepristone is among the tiny fraction of medications subject to such regulation, alongside highly addictive and dangerous opioids.

A REMS is not necessary for mifepristone under the statutory scheme Congress has mandated to guide FDA's balancing of a medication's risks and benefits. Specifically, a REMS is permitted only if "necessary to ensure that the benefits of [a] drug outweigh [its] risks…." 21 U.S.C. § 355-1(a)(1); *accord id.* § 355-1(g)(4)(B)(i). Among other factors, Congress directed FDA to consider the "seriousness of any known or potential adverse events" and "the background incidence of such events in the population likely to use the drug, *id*.—a particularly meaningful consideration here since the serious adverse events associated with mifepristone are risks of "pregnancy itself."[64] Congress further limited FDA's authority to impose ETASU, permitting them only where "necessary to assure safe use of the drug, because of its inherent toxicity or potential harmfulness," and only where "required as part of [a] strategy to mitigate a specific serious risk listed in the labeling of the drug." 21 U.S.C. §355-1(f)(1). Moreover, ETASU may be imposed only when they are "commensurate with the specific serious risk[s] listed in the labeling"; must,

"to the extent practicable," "conform with [ETASU] for other drugs with similar, serious risks"; and may "not be unduly burdensome on patient access," "considering in particular … patients who have difficulty accessing health care (such as patients in rural or medically underserved areas)." *Id.* §355-1(f)(1)-(2). Petitioners respectfully submit that the mifepristone REMS and ETASU do not meet these statutory requirements.

1. Prescriber Certification

The Prescriber Certification ETASU requires would-be prescribers to fax a form to the drug distributor attesting that they can date a pregnancy and diagnose an ectopic pregnancy; can ensure patient access to a uterine evacuation procedure in cases of incomplete abortion or severe bleeding and to medical facilities equipped to provide blood transfusions and resuscitation if necessary; and have read and understood the prescribing information. Clinicians also agree to review the Patient Agreement with the patient, answer the patient's questions, obtain a signature, retain the signed form, and provide the patient a copy; and (as discussed in Section B.3, above), to report any patient deaths to the drug sponsor. As of 2023, this ETASU also requires clinicians to fulfill certain obligations if a pharmacy will dispense the mifepristone, including providing the pharmacy with their signed Prescriber Certification form and communicating directly with the pharmacy if the pharmacy cannot ensure delivery within four calendar days.

For 99.5% of the over 20,000 prescription drugs it regulates, FDA does not impose a prescriber certification ETASU.[65] This is true even for drugs that, unlike mifepristone, require diagnostic tests or special screening before they can be safely prescribed. FDA has retained the Prescriber Certification ETASU because it assumes that certification is necessary to assure that only qualified providers will prescribe mifepristone.[66] The facts, however, show otherwise. For instance, in 2017, Canada removed its REMS-like requirements, which included a prescriber certification requirement. While eliminating those restrictions significantly increased access to

mifepristone, it had no negative impact on mifepristone's safety or efficacy.[67]

Contrary to FDA's assumption, the Prescriber Certification ETASU is unnecessary to assure that health care professionals prescribe mifepristone only when competent to do so because *all* clinicians are ethically obligated to provide only medically necessary and appropriate care within the scope of their training and competence.[68] There are countless medications not subject to a Prescriber Certification ETASU that can be safely prescribed only when the clinician makes a proper diagnosis, screens for contraindications, and provides instructions for any necessary follow-up or emergency care—and there is nothing unique about prescribing mifepristone that makes this burdensome ETASU necessary. To the contrary, as Petitioner ACOG noted in a letter to FDA nearly a decade ago, "[a] standard clinical license should be sufficient to ensure that a practitioner meets qualifications for prescribing mifepristone."[69] Nor is it necessary to assure that a health care professional will obtain a patient's informed consent for mifepristone when medical ethics and professional guidelines already require informed consent as an essential practice across all areas of medicine, including abortion care.[70] Indeed, FDA has recognized that there is "strong adherence to evidence-based guidelines" by clinicians who provide abortion care.[71]

The Prescriber Certification ETASU also impedes patient access to mifepristone by chilling a health care provider's decision to offer this medication. Nearly one in ten OBGYNs responding to a survey of Petitioner ACOG's members were deterred from prescribing mifepristone because of the requirement that they register with the drug sponsor.[72] A qualitative survey of family practitioners concluded that removal of the in-person dispensing requirement would not eliminate the distinct deterrent effect of prescriber certification on would-be prescribers.[73]

It is well-documented that many would-be prescribers do not register to prescribe mifepristone because they fear anti-abortion threats and violence if their registrations became

public.[74] Moreover, the Pharmacy Certification ETASU requires prescribers to send their certification form to every pharmacy that will dispense mifepristone to their patients and requires the pharmacy to keep that form on file. Notwithstanding the important confidentiality safeguards contained in the Pharmacy Certification's ETASU requirement, this protocol multiplies the possibility of a data breach and amplifies providers' concerns for their safety and the safety of their families. In the aftermath of the *Dobbs* decision, acts of anti-abortion violence and harassment have increased dramatically in states where abortion access is protected by state law.[75] The Prescriber Certification ETASU persists in deterring providers from prescribing mifepristone and impeding patient access.

2. Pharmacy Certification

The Pharmacy Certification ETASU is largely a means of enforcing the Prescriber Certification requirement by "ensur[ing] that mifepristone is only dispensed pursuant to prescriptions that are written by certified prescribers."[76] As detailed above, there is no valid reason for maintaining Prescriber Certification, undermining any justification for this derivative ETASU. Meanwhile, the Pharmacy Certification ETASU compounds the burdens on providers and the health care delivery system. As Petitioners and other commenters have previously warned, the extra costs and administrative burdens that this ETASU imposes on pharmacies disincentivizes pharmacies from dispensing mifepristone—an assessment that FDA seemingly shared when it found that the Pharmacy Certification would "likely limit" "pharmacies choosing to certify."[77]

Critically, FDA has not reckoned with the significant burdens the Pharmacy Certification ETASU imposes on patients—particularly those who already face significant obstacles in obtaining needed health care—despite a statutory requirement to assess those burdens. *See* 21 U.S.C. §355-1(f)(2)(C)(ii). First, the strong disincentivizing effect of the ETASU on brick-and-mortar pharmacies leaves telehealth patients dependent on mail-order (*i.e.*, online) pharmacies to

access mifepristone. While it is critical that patients retain the option to have their mifepristone mailed to them, this model does not work for everyone, as Petitioners' members see in their practices. Individuals who lack stable housing may not have a physical address to which a package can be securely and confidentially mailed. Patients experiencing abuse in their household may not be able to rely on mail delivery if they need to keep their pregnancy and abortion decision confidential for their own safety. Patients who lack facility with computers[78] or who lack reliable internet access, such as those living in rural areas, are more likely to depend on neighborhood retail pharmacies to access mifepristone. In such situations, the inability to use an online pharmacy may impede access altogether.

Moreover, the Pharmacy Certification ETASU places significant burdens on the health care delivery system by, for example, mandating that pharmacies either ensure delivery to the patient within four days of receiving the prescription or contact the prescriber to confirm that later delivery is acceptable. In their discussions with FDA, the drug sponsors noted that this means a default of "two-day or next day shipping," and noted concerns about the resulting "affordability of shipping services."[79] Indeed, this four-day requirement makes expedited delivery the default option—effectively increasing shipping costs for all patients—even when delivery on a longer timeline is clinically appropriate. To be sure, Petitioners are deeply invested in ensuring timely access to health care. But mifepristone is no different from the countless other time-sensitive medications dispensed through pharmacies without a Pharmacy Certification ETASU mandating such deadlines.[80] As the sponsors made clear, "the professional practice of pharmacy requires that pharmacies promptly dispense products to patients upon receiving the prescription or swiftly communicate with the patient and prescriber if that is not possible within the appropriate clinical window."[81] And FDA found no increase in adverse events when mail-order pharmacies dispensed

mifepristone during the COVID-19 pandemic with no delivery-date mandate.[82] At bottom, while timely access to health care is certainly critical, it is not in mifepristone patients' best interests for FDA to impose delivery restrictions that needlessly increase the cost of abortion care and deter pharmacies from dispensing this medication.

Additionally, the Pharmacy Certification ETASU means that prescribers cannot simply issue a prescription to the patient's preferred pharmacy location, as they do with virtually all other medications (including other time-sensitive medications). Instead, they have to contact any pharmacy their patients may seek to use in order to identify one that is certified to dispense mifepristone. As a practical matter, since so few pharmacies are certified, the Pharmacy Certification ETASU results in additional burdens and delay.

3. Patient Agreement

The Patient Agreement ETASU requires the patient to sign an FDA-approved form stating that they are taking mifepristone because they have "decided ... to end [their] pregnancy," that they will follow a particular clinical protocol, and that they understand when and how to seek follow-up or emergency care. Notably, in 2016, FDA's own scientific review team determined that this ETASU was "duplicative" of the Medication Guide that every patient receives and "does not add to safe use conditions" and, accordingly, recommended its elimination.[83] However, FDA's Commissioner at the time overrode the review team's recommendation, leading FDA to maintain this ETASU.[84]

In choosing to again retain this requirement in 2023, FDA speculated that *new* mifepristone prescribers might not provide appropriate counseling and obtain informed consent absent the Patient Agreement ETASU.[85] FDA's speculation, however, cannot be reconciled with the Agency's recognition that, in general, "informed consent in medicine is an established practice."[86] As noted above in Section C.1, informed consent is part of the professional guidelines governing abortion

care.[87] And, as FDA recognizes, the "same risk information" contained in the Patient Agreement is contained in the Medication Guide that all patients receive.[88] FDA did not identify any evidence suggesting that new prescribers of mifepristone would shirk these professional norms; in fact, the Agency routinely approves entirely new drugs without a patient agreement ETASU, even though every prescriber will be unfamiliar with that new medication. This evidence justifies "remov[ing] this REMS requirement[] . . . based on the integration of the REMS safe use condition into clinical practice,[89] as the Agency has done for other drugs.

FDA acknowledged in 2016 that the Patient Agreement ETASU "is a burden for patients."[90] It can also be a burden for qualified health care providers who seek to prescribe mifepristone, since they often must struggle with administrative complexities associated with integrating the Patient Agreement form into existing clinical record systems.[91] In the course of its reviews of the mifepristone REMS, the Agency has never explained why it believes this ETASU's burdens are essential to ensure that mifepristone's benefits outweigh its risks.

D. FDA should have reviewed *all* relevant data in its most recent REMS review

During FDA's most recent REMS review, FDA excluded from consideration information that was directly relevant to the Agency's statutory obligation to ensure that an ETASU is "not … unduly burdensome on patient access" (especially for those patients in "rural or medically underserved areas"), as well as the requirement that FDA "minimize the burden on the health care delivery system" when imposing ETASU. 21 U.S.C. §§ 355-1(f)(2)(C), (D).[92] That information included input from Petitioners and other associations of health care professionals on the burdens imposed by the REMS, as well as "[d]ata on the logistics of accessing abortion care in general, such as time to appointment or the distance traveled to obtain care."[93]

These exclusions prevented FDA from accurately assessing the burdens that the mifepristone ETASU impose on patient access and the health care system. Petitioners respectfully

submit that this was a significant misstep, which deprived FDA of information directly relevant to the applicable statutory requirements. Petitioners therefore urge FDA to revisit this highly relevant evidence from 2022 or earlier as well as the more recent evidence cited above confirming that mifepristone remains extremely safe and effective after FDA's 2016 and 2023 changes to the REMS and mifepristone label and that those regulatory updates reduced needless burdens.

E. In the alternative, and at an absolute minimum, FDA must maintain the status quo with respect to mifepristone

At the very minimum, based on the evidence detailed above of mifepristone's ongoing safety and efficacy, there is no medical basis to further restrict access beyond the status quo as of January 2023 by, for instance, reinstating any previously withdrawn ETASU; increasing the burdens of the existing ETASU; imposing a new ETASU; or modifying the mifepristone labeling to be inconsistent with prevailing standards of evidence-based care. As discussed in Section B, numerous high-quality studies show that mifepristone's safety profile remained strong and stable even after FDA removed the special non-fatal adverse-event reporting requirement, permitted APCs to independently prescribe mifepristone where permitted by state law, and eliminated the in-person dispensing requirement. To be sure, anti-abortion activists have pointed to other publications in support of their efforts to reinstate previous, superseded ETASU, such as the five articles attached to the complaint in *Alliance v. Hippocratic Medicine*, No. 2:22-cv-00223-Z (N.D. Tex.). But as FDA recognized at the time, none of these articles contains "safety data relevant to" the removal of the in-person dispensing requirement.[94]

Conversely, the evidence is clear that reinstating the prior ETASU would impede patient access. For example, one recent study found that telehealth plays an "instrumental role in obtaining an abortion among patient populations who are known to face the most structural barriers to abortion care," particularly "those residing in rural areas, and those who resided far from an

abortion facility."[95] Reinstating the prior ETASU would demonstrably impede patient access, particularly for "patients who have difficulty accessing health care," in violation of the statutory command of 21 U.S.C. § 355-1(f)(2).

ENVIRONMENTAL IMPACT

Petitioners' proposal is categorically exempt from the requirement of an environmental impact statement under 21 C.F.R. § 25.31(a) or 21 C.F.R. § 25.31(b).

ECONOMIC IMPACT

No information required at this time.

CERTIFICATION

Petitioners certify that, to the best of our knowledge and belief, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioners which are unfavorable to the petition.

Signed:

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[1] Ushma D. Upadhyay et al., *Incidence of Emergency Department Visits and Complications After Abortion*, 125 Obstetrics & Gynecology 175, 181 (2015) (study of nearly 55,000 abortions found a major complications rate of 0.31% for medication abortion).

[2] U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Rsch., No. 020687Orig1s020, Mifeprex Medical Review(s) 1, 12 (Mar. 29, 2016).

[3] Am. Coll. of Obstetricians & Gynecologists et al., *Leading Medical Organizations Call for the FDA to Permanently Remove Restrictions on Mifepristone* (June 18, 2024), https://www.acog.org/news/news-releases/2024/06/leading-medical-organizations-call-for-fda-to-permanently-remove-restrictions-on-mifepristone.

[4] U.S. Food & Drug Admin., Mem. re approval action concerning NDA 20-687 MIFEPREX (mifepristone) 1, 1-8 (Sept. 28, 2000).

[5] U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Rsch., U.S. Food & Drug Admin., Joint Summary Review for Mifepristone REMS, at 4 (Jan. 3, 2023); World Health Org., *Medical Management of Abortion*, at 1 (2018).

[6] U.S. Food & Drug Admin., NDA 020687 & ANDA 091178, Mifepristone U.S. Post-Marketing Adverse Events Study through 12/31/2024 (2025).

[7] Courtney A. Schreiber et al., *Mifepristone Pretreatment for the Medical Management of Early Pregnancy Loss*, 378 N. Eng. J. Med. 2161 (2018); Justin J. Chu, et al., *Mifepristone and misoprostol versus misoprostol alone for the management of missed miscarriage (MifeMiso): a randomised, double-blind, placebo-controlled trial*, 396 Lancet 770 (2020).

[8] Janet Woodcock, M.D., Dir., Ctr. for Drug Evaluation & Rsch., Citizen Petition Denial, at 5 (Mar. 29, 2016); *see also* Am. Coll. of Obstetricians & Gynecologists & Soc'y of Family Planning, Prac. Bull. No. 225, *Medication Abortion Up to 70 Days of Gestation*, 136 Obstetrics & Gynecology 1 (Oct. 2020, *reaff'd* 2023); Nathalie Kapp & Patricia A. Lohr, *Modern methods to induce abortion: Safety, efficacy and choice*, 63 Best Prac. & Rsch. Clinical Obstetrics & Gynaecology 37 (2020); World Health Org., *Medical Management of Abortion* (2018); Elizabeth G. Raymond & David A. Grimes, *The Comparative Safety of Legal Induced Abortion and Childbirth in the United States*, 119 Obstetrics & Gynecology 215 (2012).

[9] U.S. Food & Drug Admin., Development & Approval Process (Aug. 8, 2022), https://www.fda.gov/drugs/development-approval-process-drugs.

[10] U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Research, Application No. 020687Orig1s020 Medical Review(s), at 47 (Mar. 29, 2016).

[11] Mifepristone 2023 Labeling and Medication Guide, at 16.

[12] Mifepristone 2023 Labeling and Medication Guide, at 2, 5.

[13] Janet Woodcock, M.D., Dir., Ctr. for Drug Evaluation & Rsch., U.S. Food & Drug Admin., Citizen Petition Denial, at 25-26 (Mar. 29, 2016).

[14] Mifepristone 2023 Labeling and Medication Guide, at 1-2, 5; U.S. Food & Drug Admin., NDA 020687 & ANDA 091178, Mifepristone U.S. Post-Marketing Adverse Events Study through 12/31/2024 (2025) (36 reported deaths after approximately 7.5 million uses of mifepristone for medical termination of pregnancy).

[15] Nat'l Acad. of Sci., Eng'g & Med., *The Safety & Quality of Abortion Care in the United States*, at 79 (2018) (risks of mifepristone are "similar in magnitude" to "antibiotics and NSAIDs"); Advancing New Standards in Reprod. Health, UCSF, *Analysis of Medication Abortion Risk and the FDA report "Mifepristone U.S. Post-Marketing Adverse Events Summary through 12/31/2022,"* Issue Brief, at 3 (May 2024) (Viagra and penicillin have fatality rates "several times higher" than mifepristone); Gregory Lowe, et al., *10-Year analysis of adverse event reports to the Food and Drug Administration for phosphodiesterase type-5 inhibitors* 9 J. of Sexual Med. 265 (2012) (fatality rates for Viagra); Alfred Neugut, et al., *Anaphylaxis in the United States: an investigation into its epidemiology*, 161 Archives of Internal Med. 15 (2001) (fatality rates for penicillin).

[16] U.S. Food & Drug Admin., *Opioid Medications*, (2021), https://www.fda.gov/drugs/information-drug-class/opioid-medications; U.S. Food & Drug Admin., *REMS Document*, *Opioid Analgesic REMS Program*, (2021),

https://www.accessdata.fda.gov/drugsatfda_docs/rems/Opioid_Analgesic_2021_04_09_REMS_Document.pdf; U.S. Food & Drug Admin., *Opioid Analgesic REMS*, https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=RemsDetails.page&REMS=17 (last updated Oct. 31, 2024) ("Products" tab).

[17] U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Rsch., No. 020687Orig1s020, Mifeprex Medical Review(s), at 88 (Mar. 29, 2016).

[18] *See, e.g.*, U.S. Food & Drug Admin., REMS Modification Rationale Review (Dec. 16, 2021), at 12 (noting that the results of two pre-2016 studies "not captured in [FDA's] 2016 literature search . . . are consistent with the existing safety profile of the approved medical abortion regimen."); *id.* at 21-22 (finding "no new safety concerns with the use of mifepristone for medical termination of pregnancy" between January 2020 and September 2021 based on data from the FDA Adverse Event Reporting System or the "published medical literature"); U.S. Food & Drug Admin., *Pharmacovigilance Memorandum: Mifepristone, All Adverse Events* (Apr. 12, 2022) at 6 (same as to period from October 2021 to December 2022).

[19] *See. e.g.*, Laura Schummers et al., *Abortion Safety and Use with Normally Prescribed Mifepristone in Canada*, 386 New Eng. J. Med. 57, (2022) (in Canada, lifting all REMS-like restrictions resulted in no change to mifepristone's safety profile); Ushma Upadhyay et al., *Effectiveness and Safety of Telehealth Medication Abortion in the United States*, 30 Nature Medicine 1191, 1191 (2024) (in US, "[t]elehealth medication abortion is effective, safe and comparable to safety and efficacy of in-person medication abortion care.").

[20] Claudia D. Olavarrieta et al., *Nurse versus physician-provision of early medical abortion in Mexico: a randomized controlled non-inferiority trial*, 93 Bull World Health Org. 249 (2015); H. Kopp Kallner et al., *The Efficacy, Safety and Acceptability of Medical Termination of Pregnancy Provided by Standard Care by Doctors or by Nurse-Midwives*, 122 BJOG: Int'l J. Obstetrics & Gynecology 510 (2015); IK Warriner et al., *Can Midlevel Health-Care Providers Administer Early Medical Abortion as Safely and Effectively as Doctors? A Randomised Controlled Equivalence Trial in Nepal*, 377 Lancet 1155 (2011).

[21] Mahesh Puri et al., *The role of auxiliary nurse-midwives and community health volunteers in expanding access to medical abortion in rural Nepal*, 22 Reprod. Health Matters 94 (2015).

[22] U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Research, Application No. 020687Orig1s020 Cross Discipline Team Leader Review (Mar. 29, 2016), at 16-17.

[23] *Id*. at 17.

[24] Nat. Acad. Sci., Eng'g, & Med., *The Safety and Quality of Abortion Care in the United States* 1, 165 (2018).

[25] L. Porsch et al., *Advanced Practice Clinicians and Medication Abortion Safety: A 10-Year Retrospective Review*, 101 Contraception 357 (2020).

[26] Amy Levi et al., *Training in Aspiration Abortion Care*, 88 Int'l J. Nursing Studies 55, 57 (2018).

[27] Eva Patil et al., *Aspiration Abortion with Immediate Intrauterine Device Insertion: Comparing Outcomes of Advanced Practice Clinicians and Physicians*, 61 J. Midwifery & Women's Health 325 (2016).

[28] L. Porsch et al., *Advanced Practice Clinicians and Medication Abortion Safety: A 10-Year Retrospective Review*, 101 Contraception 357 (2020).

[29] Lydia Mainey, et al., *The Role of Nurses and Midwives in the Provision of Abortion Care: A Scoping Review*, 29 J. of Clinical Nursing 1513 (2020); Nat. Acad. Sci., Eng'g, & Med., *The Safety and Quality of Abortion Care in the United States* 1, 114-17 (2018).

[30] Am. Coll. Obstetricians & Gynecologists, *Medication Abortion Up to 70 Days of Gestation*, Practice Bulletin No. 225, at e35 (Oct. 2020, *reaff'd* 2023), https://www.acog.org/clinical/clinical-guidance/practice-bulletin/articles/2020/10/medication-abortion-up-to-70-days-of-gestation ("Medication abortion can be provided safely and effectively by telemedicine with a high level of patient satisfaction"); World Health Organization, Abortion Care Guideline, 95 (March 8, 2022), https://www.who.int/publications/i/item/9789240039483 (recommending the option of telemedicine to deliver medical abortion services).

[31] Elizabeth G. Raymond et al., *Commentary: No-Test Medication Abortion: A Sample Protocol Increasing Access During a Pandemic and Beyond*, 101 Contraception 361, 362 (2020).

[32] *Id*. at 362-63 (recommending in-person testing for patients with significant symptoms of or risk factors for ectopic pregnancy; recent vaginal bleeding or pelvic pain, prior permanent contraception, prior ectopic pregnancy, or intrauterine device in place at conception); *id.* at 363 (in a small number of cases, the clinician may advise the patient to obtain Rh testing for the purpose of determining whether treatment with Rh D immune globulin is appropriate); *see also* Am. Coll. Obstetricians & Gynecologists, *RhD Immune Globulin Administration After Abortion or Pregnancy Loss at Less Than 12 Weeks of Gestation*, Clinical Practice Update, at e140 (Dec. 2024) (suggesting that "Rh testing and RhIg administration can be considered on an individual basis" for patients at less than 12 weeks gestation and need not be performed routinely); Nat'l Abortion Fed., *Clinical Policy Guidelines for Abortion Care* at 12 (2024) ("Below 12 weeks from the last menstrual period, patients and providers may forego Rh testing and anti-D immune globulin for patients who are Rh negative").

[33] Elizabeth G. Raymond et al., *Commentary: No-Test Medication Abortion: A Sample Protocol Increasing Access During a Pandemic and Beyond*, 101 Contraception 361, 364 (2020); Alice Mark et al., *The Future Of Abortion Is Now: Mifepristone By Mail And In-Clinic Abortion Access In The United States,* 104 Contraception 38 (2021).

[34] Elizabeth G. Raymond et al., *Commentary: No-Test Medication Abortion: A Sample Protocol Increasing Access During a Pandemic and Beyond*, 101 Contraception 361, 363–64 (2020).

[35] Ushma Upadhyay et al., *Abortion-Related Emergency Department Visits in the United States: An Analysis of a National Emergency Department Sample*, 16 BMC Med. 1, 7-10 (2018). The majority of these visits involved "observation care only," likely because some patients do not appreciate that normal post-abortion symptoms include "ongoing uterine cramping and bleeding." *Id*. at 9.

[36] U.S. Food & Drug Admin., REMS Modification Rationale Review, NDA 020687 & 91178, at 39 (Dec. 16, 2021).

[37] *Id*. (referring to Holly A. Anger et al., *Clinical and Service Delivery Implications Of Omitting Ultrasound Before Medication Abortion Provided Via Direct-To-Patient Telemedicine And Mail In The U.S.*, 104 Contraception 659 (2021); Elizabeth Raymond et al., *TelAbortion: evaluation of a direct to patient telemedicine; abortion service in the United States*, 100 Contraception 173 (2019); Erica Chong et al., *Expansion of a direct-to-patient telemedicine abortion service in the United States and experience during the COVID-19 pandemic*, 104 Contraception 43 (2021); Daniel Grossman et al., *Mail-order pharmacy dispensing of mifepristone for medication abortion after in-person clinical assessment*, 107 Contraception 36 (2021); Courtney Kerestes et al., *Provision of medication abortion in Hawai'i during COVID-19: Practical experience with multiple care delivery models*, 104 Contraception 49 (2021); Paul Hyland et al., *A direct-to-patient telemedicine abortion service in Australia: Retrospective analysis of the first 18 months*, 58 The Austl. & N.Z. J. of Obstetrics & Gynaecology 335 (2018); Courtney Kerestes et al., *Provision of medication abortion in Hawai'i during COVID-19: Practical experience with multiple care delivery models*, 104 Contraception 49 (2021); Paul Hyland et al., *A direct-to-patient telemedicine abortion service in Australia: Retrospective analysis of the first 18 months*, 58 The Austl. & N.Z. J. of Obstetrics & Gynaecology 335 (2018)).

[38] *Id*.

[39] *See*, *e.g*., Ushma Upadhyay et al., *Effectiveness and safety of telehealth medication abortion in the USA*, 30 Nature Med. 1191 (2024); Lauren J. Ralph et al., *Comparison of No-Test Telehealth and In-Person Medication Abortion*, 332 JAMA 898 (2024), https://jamanetwork.com/journals/jama/article-abstract/2820321; Silpa Srinivasulu et al., *Telehealth Medication Abortion in Primary Care: A Comparison to Usual in-Clinic Care*, 37 J. of the Am. Board of Fam. Med. 295 (2024).

[40] Ushma Upadhyay et al., *Effectiveness and safety of telehealth medication abortion in the USA*, 30 Nature Med. 1191, 1197 (2024).

[41] *Id*.

[42] *Id.* at 1197.

[43] *Id*. at 1194.

[44] Lauren J. Ralph et al., *Comparison of No-Test Telehealth and In-Person Medication Abortion*, 332 JAMA 898, 903 (2024).

[45] Silpa Srinivasulu et al., *Telehealth Medication Abortion in Primary Care: A Comparison to Usual in-Clinic Care*, 37 J. of the Am. Board of Fam. Med. 295, 299 (2024). While the study was too small to draw conclusions about safety, its safety data was "within the range of other studies evaluating complete abortion after [medication abortion] in primary care." *Id*. at 299.

[46] Holly A. Anger & Elizabeth G. Raymond, *Clinical and service delivery outcomes following medication abortion provided with or without pretreatment ultrasound or pelvic examination: An updated comparative analysis*, 140 Contraception 1 (2024); *see also* Lauren J. Ralph et al., *Comparison of No-Test Telehealth and In-Person Medication Abortion*, 332 JAMA 898 (2024).

[47] *See* Leonardo Cely-Andrade et al., *Telemedicine For The Provision Of Medication Abortion To Pregnant People At Up To Twelve Weeks Of Pregnancy: A Systematic Literature Review And Meta-Analysis,* 21 Reprod. Health 136, 155 (2024) (meta-analysis of 21 articles published between 2011 and 2022, concluding there are no significant differences in safety, effectiveness, or patient satisfaction when comparing telehealth to in-person abortion care).

[48] Leah R. Koenig et al., *The role of telehealth in promoting equitable abortion access in the United States: spatial analysis,* 9 JMIR Public Health Surveillance e45671 (2023).

[49] Amy Tressan et al., *Telemedicine Abortion in Primary Care: An Exploration of Patient Experiences*, 22 Annals of Fam. Med. 19 (2024) (Table 1); Rachel K. Jones, *Medicaid's Role In Alleviating Some Of The Financial Burden Of Abortion: Findings From The 2021-2022 Abortion Patient Study*, 56 Persp. on Sexual & Reprod. Health 244, 245 (2024) (fifty-five percent of abortion seekers had experienced a prior birth).

[50] Erica Chong et al., *Expansion of a direct-to-patient telemedicine abortion service in the United States and experience during the COVID-19 pandemic*, 104 Contraception 43, 44 (2021).

[51] Guttmacher Inst., *Abortion in the United States* (June 2024), https://www.guttmacher.org/fact-sheet/induced-abortion-united-states (stating that "[s]ome 41% of people obtaining abortions had an income below the federal poverty level (FPL) and 30% had incomes between 100% and 199% of the FPL").

[52] Andréa Becker et al., *"It Was So Easy in a Situation That's So Hard": Structural Stigma and Telehealth Abortion*, 0 J. of Health & Soc. Behav. 1 (2025).

[53] Rachel K. Jones et al., *The Number of Brick-and-Mortar Abortion Clinics Drops, as US Abortion Rate Rises: New Data Underscore the Need for Policies that Support Providers* (June 2024), https://www.guttmacher.org/report/abortion-clinics-united-states-2020-2024 (noting that "[s]ome states that share a border with one or more ban states absorbed the additional patients with little or no increase in the numbers of brick-and-mortar clinics between 2020 and March 2024").

[54] *See* Erica Munson & Kelli S. Hall, *Opportunities for Increasing Access to Person-Centered Abortion Care Through Telehealth,* 114 Am. J. of Public Health 152 (2024).

[55] Ushma Upadhyay et al., *Pricing of medication abortion in the United States, 2021–2023*, 56 Persp. on Sexual & Reprod. Health 282 (2024).

[56] Leah R. Koenig et al., *Patient Acceptability of Telehealth Medication Abortion Care in the United States, 2021-2022: A Cohort Study*, 114 Am. J. Pub. Health 241, 247-248 (2024) (Table 2).

[57] *Id*. at 248.

[58] Emily M. Godfrey et al., *Patient Perspectives Regarding Clinician Communication During Telemedicine Compared With In-Clinic Abortion*, 141 Obstetrics & Gynecology 1139, at 1143 (2023).

[59] Andréa Becker et al., *"It Was So Easy in a Situation That's So Hard": Structural Stigma and Telehealth Abortion*, 0 J. of Health & Social Behav. 1 (2025).

[60] Nat'l Abortion Fed., *2022 Violence & Disruption Statistics Report* at 9, 11(2023).

[61] U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Rsch., No. 020687Orig1s020, Mifeprex Medical Review(s), at 88 (Mar. 29, 2016).

[62] *See*, *e.g.*, U.S. Food & Drug Admin., Lotronex (alosetron hydrochloride) Information at 2-3 (Sept. 8, 2023), https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/lotronex-alosetronhydrochloride-information (citing as support for removing the REMS that reporting of adverse events in FAERS "has been stable since 2002 and an increase in severe outcomes has not been observed"); Chisato Fukazawa et al., *Factors Influencing Regulatory Decision-Making in Signal Management: Analysis Based on the Signals Identified from the FAERS*, 55 Therapeutic Innovation & Regul. Sci. 685 (Mar. 2021) (analyzing regulatory actions taken based on signals FDA identified from FAERS, including labeling changes, REMS modifications, product recall, and withdrawal).

[63] Ushma Upadhyay et al., *Effectiveness and Safety of Telehealth Medication Abortion in the United States*, 30 Nature Med. 1191, 1194 (2024).

[64] Janet Woodcock, M.D., Dir., Ctr. for Drug Evaluation & Rsch., U.S. Food & Drug Admin., Citizen Petition Denial, at 25-26 (Mar. 29, 2016).

[65] U.S. Food & Drug Admin., *Approved REMS*, https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm (sum of drugs with "ETASU A" reflected under REMS Materials, divided by 20,000).

[66] U.S. Food & Drug Admin., REMS Modification Rationale Review, NDA 020687 & 91178, at 13 (Dec. 16, 2021).

[67] Laura Schummers et al., *Abortion Safety and Use with Normally Prescribed Mifepristone in Canada*, 386 New Eng. J. Med. 57, 63-66 (2022). Another Canadian study underscored "the apparent overall short-term safety of accessible first-trimester" abortion, and concluded that serious adverse events associated with the mifepristone/misoprostol regimen were "very rare." Ning Liu et al., *Short-Term Adverse Outcomes After Mifepristone–Misoprostol Versus Procedural Induced Abortion: A Population-Based Propensity-Weighted Study*, 176 Annals of Internal Med. 145, 151 (2023).

[68] Am. Med. Assoc., AMA Principles of Medical Ethics, Principle I ("A physician shall be dedicated to providing competent medical care...").

[69] Hal C. Lawrence, III, MD, Exec. VP & CEO, ACOG, Letter to FDA re recommendations regarding safety, effectiveness, and use of mifepristone, at 2 (Nov. 4, 2015); *see also* Am. Coll. Obstetricians & Gynecologists, *Medication Abortion Up to 70 Days of Gestation, Practice Bulletin No. 225*, at e34 (Oct. 2020, *reaff'd* 2023), https://www.acog.org/clinical/clinical-guidance/practice-bulletin/articles/2020/10/medication-abortion-up-to-70-days-of-gestation ("Any clinician with the skills to screen patients for eligibility for medication abortion and to provide appropriate follow-up can provide medication abortion").

[70] Nat'l Abortion Fed., *2024 Clinical Policy Guidelines for Abortion Care*, at 4 (2024) (at a minimum, patient must be informed of the risks of hemorrhage, infection, continuing pregnancy and death); Am. Coll. of Obstetricians & Gynecologists Comm. Op. No. 819, *Informed Consent and Shared Decision Making in Obstetrics and Gynecology*, 130 Obstetrics & Gynaecology e34 (2021).

[71] U.S. Food & Drug Admin., REMS Modification Rationale Review, NDA 020687 & 91178, at 17 (Dec. 16, 2021).

[72] Daniel Grossman et al., *Induced Abortion Provision Among a National Sample of Obstetrician–Gynecologists*, 133 Obstetrics & Gynecology 477, 482 (2019).

[73] Na'amah Razon et al., *Exploring the impact of mifepristone's risk evaluation and mitigation strategy (REMS) on the integration of medication abortion into US family medicine primary care clinics,* 109 Contraception 19, 23 (2022) ("the physicians we interviewed still encountered a range of barriers to provide medication abortions that the revised REMS will not alleviate").

[74] Citizen Petition from Am. Coll. of Obstetricians & Gynecologists, at 13-14 (Oct. 4, 2022); Dr. Graham Chelius, Soc'y for Fam. Planning & Cal. Acad. of Fam. Physicians, Letter to FDA re: Evidence Supporting Elimination of the Mifepristone REMS, at 5 (Sept. 29, 2021); Suzanne Robottom et al., U.S. Food & Drug Admin., Div. of Risk Management, *Risk Management Review – Korlym (mifepristone*), at 9 (Jan. 27, 2012).

[75] Nat'l Abortion Fed., *2022 Violence & Disruption Statistics Report*, at 8 (2023).

[76] U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Rsch., Joint Summary Review, at 13-14 (Jan. 3, 2023); Citizen Petition from Am. Coll. of Obstetricians & Gynecologists, at 15-16 (Oct. 4, 2022); Letter from Maureen G. Phipps, CEO, Am. Coll. Obstetricians & Gynecologists, & James L. Madara, CEO, Am. Med. Assoc., to Dr. Robert Califf, Comm'r, U.S. Food & Drug Admin. re: Actions Related to Mifepristone, at 3 (June 21, 2022).

[77] U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Rsch, Joint Summary Review, at 14 (Jan. 1, 2023); Citizen Petition from Am. Coll. of Obstetricians & Gynecologists, at 15-16 (Oct. 4, 2022); Letter from Maureen G. Phipps, CEO, Am. Coll. of Obstetricians & Gynecologists, & James L. Madara, CEO, Am. Med. Assoc., to Dr. Robert Califf, Comm'r, U.S. Food & Drug Admin., re: Actions Related to Mifepristone, at 3 (June 21, 2022).

[78] Saida Mamedova et al., *A Description of U.S. adults who are not digitally literate*, Nat'l Ctr. for Educ. Stat., at 5 (2018).

[79] U.S. Food & Drug Admin., *Single Shared System Risk Evaluation & Mitigation Strategy (REMS) Supporting Document* at 7; Sponsors Response to Agency Correspondence Following 9/19/2022 Meeting, at 2 (Oct. 19, 2022); *Mifepristone SSS REMS, Sponsors' Aug. 26, 2022 Resp. to FDA's Information Request Dated July 22, 2022*, at 17 (Aug. 26, 2022).

[80] U.S. Food & Drug Admin., *Approved REMS*, https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm.

[81] U.S. Food & Drug Admin., *Single Shared System Risk Evaluation & Mitigation Strategy (REMS) Supporting Document*, at 7; Sponsors Response to Agency Correspondence Following 9/192022 Meeting, at 2 (Oct. 19, 2022); *Mifepristone SSS REMS, Sponsors' Aug. 26, 2022 Resp. to FDA's Information Request Dated July 22, 2022*, at 17 (Aug. 26, 2022).

[82] U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Rsch., Joint Summary Review, at 5-6 (Jan. 1, 2023); U.S. Food & Drug Admin., REMS Modification Rationale Review (Dec. 16, 2021); U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Rsch., Joint Summary Review, at 23 (Jan. 3, 2023); U.S. Food & Drug Admin., REMS Modification Rationale Review (Dec. 16, 2021); U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Rsch., Joint Summary Review, at 38 (Jan. 1, 2023).

[83] Janet Woodcock, MD, Dir., Ctr. for Drug Evaluation & Rsch., U.S. Food & Drug Admin., Letter re: NDA 020687, Supp 20 (Mar. 28, 2016); U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Rsch., Application No. 020687Orig1s020 Summary Review, at 25 (Mar. 29, 2016).

[84] Janet Woodcock, MD, Dir., Ctr. for Drug Evaluation & Rsch., U.S. Food & Drug Admin., Letter re: NDA 020687, Supp 20 (Mar. 28, 2016).

[85] U.S. Food & Drug Admin., REMS Modification Rationale Review, NDA 020687 & 91178, at 18 (Dec. 16, 2021).

[86] U.S. Food & Drug Admin., REMS Modification Rationale Review, NDA 020687 & 91178, at 17 (Dec. 16, 2021).

[87] Nat. Acad. Sci., Eng'g, & Med., *The Safety and Quality of Abortion Care in the United States,* at 11, 13 (2018); Citizen Petition from Am. Coll. of Obstetricians & Gynecologists, at 13 (Oct. 4, 2022); Citizen Petition Consult re: Prescriber Certification and Adverse Event Reporting, at 8 (Dec. 16, 2021).

[88] U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Rsch., Application No. 020687, Clinical Review, at 89 (Mar. 28, 2016).

[89] U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Rsch., Application No. 020687Orig1s020 Cross Discipline Team Leader Review, at 25 (Mar. 29, 2016).

[90] Janet Woodcock, MD, Dir., Ctr. for Drug Evaluation & Rsch., U.S. Food & Drug Admin., Letter re: NDA 020687, Supp 20 (Mar. 28, 2016); U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Rsch., Application No. 020687Orig1s020 Summary Review, at 25 (Mar. 29, 2016).

[91] Na'amah Razon et al., *Exploring the impact of mifepristone's risk evaluation and mitigation strategy (REMS) on the integration of medication abortion into US family medicine primary care clinics,* 109 Contraception 19, 23 (2022) ("The ongoing requirement for patients to sign a Patient Agreement Form may also limit the ability of family

physicians to provide medication abortion, especially since having this form on site and incorporating it into medical records requires the involvement of clinical administrators.").

[92] U.S. Food & Drug Admin., REMS Modification Rationale Review, NDA 020687 & 91178, at 11-12, 45-49 (Dec. 16, 2021).

[93] U.S. Food & Drug Admin., REMS Modification Rationale Review, NDA 020687 & 91178, at 45-49 (Dec. 16, 2021).

[94] U.S. Food & Drug Admin., Memorandum to File re Referenced Publications, at 2–3 (Dec. 30, 2022) (referring to Studnicki, et al., *A Longitudinal Cohort Study of Emergency Room Utilization Following Mifepristone Chemical and Surgical Abortions, 1999–2015* (2021); Studnicki, et al., *A Post Hoc Exploratory Analysis: Induced Abortion Complications Mistaken for Miscarriage in the Emergency Room are a Risk Factor for Hospitalization* (2022)*;* Rafferty et al., *#AbortionChangesYou: A Case Study to Understand the Communicative Tensions in Women's Medication Abortion Narratives* (2020); Aultman et al., *Deaths and Severe Adverse Events after the use of Mifepristone as an Abortifacient from September 2000 to February 2018* (2019); Cirucci, et al., *Mifepristone Adverse Events Identified by Planned Parenthood in 2009 and 2010 Compared to Those in the FDA Adverse Event Reporting System and Those Obtained Through the Freedom of Information Act* (2021)). The two Studnicki studies were later retracted by the publisher, who relied in part on a post-publication peer review by two independent experts who "identified fundamental problems with the study design and methodology, unjustified or incorrect factual assumptions, material errors in the authors' analysis of the data, and misleading presentations of the data that, in their opinions, demonstrate a lack of scientific rigor and invalidate the authors' conclusions in whole or in part." Retraction Notice, 11 *Health Services Research and Managerial Epidemiology* (2024), https://journals.sagepub.com/doi/10.1177/23333928231216699.

[95] Leah R. Koenig et al., *The role of telehealth in promoting equitable abortion access in the United States: spatial analysis,* 9 JMIR Public Health Surveillance e45671 (2023).