Attachment 2
3/13/17

Statement of Mailee R. Smith
Staff Counsel, Americans United for Life
On Regulation of Chemical Abortion
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I am Mailee Smith, staff counsel with Americans United for Life (AUL), a national public interest law firm with a practice in abortion and bioethics law. I have extensive experience in constitutional law and abortion jurisprudence, including legislative work and litigation related to chemical abortion.

There are two general types of abortion: surgical and chemical (or "medical"). Surgical abortion involves the use of instruments to empty the uterus. Examples include aspiration and dilation and evacuation (D&E). Abortion providers consider surgical abortion in the first trimester "extremely safe." *See, e.g.*, *Planned Parenthood v. DeWine*, 696 F.3d 490, 494 (6th Cir. 2012); *see also* Planned Parenthood, *In-Clinic Abortion Procedures* (2014).[1] According to the Guttmacher Institute, the vast majority of first-trimester abortions are surgical abortions. *See* Guttmacher Institute, *Fact Sheet: Induced Abortion in the United States* (July 2014).[2]

Chemical abortion, on the other hand, involves the use of abortion-inducing drugs. The recommended method of chemical abortion in the United States is the combined use of mifepristone and misoprostol. In the United States, mifepristone is marketed under the brand name "Mifeprex." *Mifeprex Final Printed Labeling* ("*Mifeprex FPL*").[3] Together, the administration of Mifeprex and the second drug, misoprostol, is the only method of chemical abortion approved by the Food and Drug Administration (FDA) and is known as the "RU-486 (or Mifeprex) regimen." The Guttmacher Institute reports that chemical abortion accounts for only 36 percent of abortions before nine weeks gestation. Guttmacher Institute, *supra*.

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[1] http://www.plannedparenthood.org/health-topics/abortion/in-clinic-abortion-procedures-4359.asp. All websites were last visited on January 29, 2015.

[2] http://www.guttmacher.org/pubs/fb_induced_abortion.html.

[3] http://www.accessdata.fda.gov/drugsatfda_docs/label/2005/020687s013lbl.pdf.

Despite the fact that the FDA approved administration of the RU-486 regimen with clear restrictions, abortion providers admittedly flout those requirements and administer the drugs in a manner that has not been approved by the FDA.

The states have an interest in protecting maternal health through regulations that rein in the abortion industry's misuse of such drugs. The Supreme Court has repeatedly held that states have an interest in protecting maternal health from the outset of pregnancy.[4] Further, the Court has explicitly held that state and federal legislatures are given "wide discretion to pass legislation in areas where there is medical and scientific uncertainty."[5] In the context of chemical abortion, these holdings by the Supreme Court provide strong support for regulations requiring abortion providers to abide by the protocol approved by the FDA. Women's lives are endangered by misuse of abortion-inducing drugs. Even if abortion proponents argue that their misuse is "safe," courts are to give deference to states in regulating a potentially deadly abortion practice.

Regulation of chemical abortion, and particularly requirements that a physician examine a woman prior to abortion and dispense the drugs in accordance with the FDA protocol, are supported by the FDA's restrictions on distribution and use of the RU-486 regimen, by the known risks involved in chemical abortion, and by known contraindications for the RU-486 regimen.

The FDA's restrictions on distribution and use of the RU-486 regimen support regulation of chemical abortion

Even before the approval of mifepristone for termination of pregnancy, the FDA treated the drug regimen differently than the vast majority of drug approvals. In its "Approvable Letter" of February 2000, the FDA informed the drug sponsor that restrictions on the distribution and use of mifepristone were needed to assure safe use. FDA, Feb. 2000 Approvable Letter, at 5.[6]

The FDA subsequently approved the RU-486 regimen under the rubric of "Subpart H," a special provision in the Code of Federal Regulations for drugs that "can be safely used ***only if*** distribution or use is ***restricted***." 21 C.F.R. § 314.520 (emphasis added). Under Subpart H, the FDA can "require such postmarketing restrictions as are needed to assure safe use" of the drug approved. *Id.*

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[4] *Gonzales v. Carhart*, 550 U.S. 124, 145 (2007); *Casey*, 505 U.S. 833, 846 (1992) (both citing *Roe v. Wade*).

[5] *Gonzales*, 550 U.S. at 163.

[6] http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2000/20687approvable00.pdf

To put this into perspective, out of almost 1,800 New Drug Applications (NDAs) approved between 1992 and 2011, only 69 were approved under Subpart H.[7] Thus, mifepristone is not comparable to the vast majority of drugs approved by the FDA between 1992 and 2011.

Per the Subpart H approval, the FDA's September 2000 "Approval Letter" restricted the distribution of Mifeprex by requiring that it be provided by or under the supervision of a physician who has the ability to assess the duration of pregnancy accurately, diagnose ectopic pregnancies, provide surgical intervention in cases of incomplete abortion or severe bleeding (or has made plans to provide such surgical intervention through other qualified physicians), and assure patient access to medical facilities equipped to provide blood transfusions and resuscitation. FDA, Sept. 2000 Approval Letter, at 2.[8]

Under the Subpart H restrictions, providers who wish to prescribe the RU-486 regimen must first sign a "Prescriber's Agreement" which reiterates the restrictions and attests that the provider meets the prescribed qualifications. Mifeprex (Mifepristone) Tablets, 200 mg Prescriber's Agreement.[9]

The fact that the FDA has restricted the distribution and use of the RU-486 regimen is confirmed by a Department of Health and Human Services (HHS) memorandum on the approval of Mifeprex. Memorandum of Department of Health and Human Services to "NDA 20-687 MIFEPREX (mifepristone) Population Counsel" (Sept. 28, 2000).[10] HHS determined that "goals of safe and appropriate use" of the RU-486 regimen can be achieved through the requirements that physicians be able to accurately date pregnancies and diagnose ectopic pregnancies:

> By coupling professional labeling with other educational interventions such as the Medication Guide, Patient Agreement, and Prescriber's Agreement, along with having physician qualification requirements of abilities to date pregnancies

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[7] *See CDER Drug and Biologic Accelerated Approvals as of September 30, 2011*, http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/UCM278506.pdf; FDA, *Summary of NDA Approvals & Receipts, 1938 to the present* (updated 2013), http://www.fda.gov/AboutFDA/WhatWeDo/History/ProductRegulation/SummaryofNDAApprovalsReceipts1938tothepresent/default.htm

[8] http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2000/20687appltr.pdf

[9] http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111364.pdf

[10] http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111366.pdf

> accurately and diagnose ectopic pregnancies (and other requirements), goals of safe and effective use may be achieved.

Id. at 2. That memo demonstrates the FDA's concern for an ongoing relationship between the patient and the physician administering the drugs, noting that returning to the health clinic for misoprostol "has the *additional advantage of contact between the patient and health care provider* to provide ongoing care." *Id.* at 3 (emphasis added).

Additionally, the FDA explicitly left room for states to require that physicians *directly* dispense the RU-486 regimen to patients. In its memo, HHS commented that the physician qualifications do "not preclude another type of health care provider, acting under the supervision of a qualified physician, from dispensing the drug to patients, *provided state laws permit this*." *Id.* at 5 (emphasis added).

The significance of the FDA's restrictions is also evidenced by the enrollment of Mifeprex on the list of medications which require a Risk Evaluation and Management Strategy (REMS)—the category of drugs identified by the FDA as at high risk of post marketing complications. *See* FDA, *Approved Risk Evaluation and Mitigation Strategies (REMS).*[11]

Specifically, one goal of the REMS for Mifeprex is "minimiz[ing] the risk of serious complications by requiring prescribers to certify that they are qualified to prescribe Mifeprex and are able to assure patient access to appropriate medical facilities to manage any complications." *See Risk Evaluation and Mitigation Strategy (REMS) for NDA 20-687 MIFEPREX (mifepristone) Tablets, 200 mg.*[12] In a section entitled "Elements to Assure Safe Use," the REMS highlights that healthcare providers who prescribe Mifeprex will be specially certified, agree that they meet the qualifications, and follow the guidelines in the Prescriber's Agreement. *Id.* at 1. Significantly, Mifeprex is one of only 68 individual drugs for which the FDA is currently requiring a REMS. *See* FDA, *Approved Risk Evaluation and Mitigation Strategies (REMS).*

Thus, as a Subpart H drug, the RU-486 regimen is distinguishable from the vast majority of drugs. The FDA's emphasis on physician qualifications supports regulations that require the physician to examine a woman and be physically present when administering the drugs.

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11 http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111350.htm

12 http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM258412.pdf

The risks involved with administration of the RU-486 regimen support regulation of chemical abortion

The known risks associated with chemical abortion provide a rational basis for requiring a physician be present and examine a woman before administering abortion-inducing drugs. For example, the Mifeprex FPL states that "[n]early all of the women who receive Mifeprex and misoprostol will report adverse reactions, and many can be expected to report more than one such reaction." *Mifeprex FPL, supra*, at 11. These risks include, but are not limited to, uterine hemorrhage, viral infections, and pelvic inflammatory disease. *Id.* at 12.

In July 2011, the FDA reported 2,207 adverse events in the U.S. after women used mifepristone for the termination of pregnancy. FDA, *Mifepristone U.S. Postmarketing Adverse Events Summary Through 04/30/11* (July 2011).[13] Among those were 14 deaths, 612 hospitalizations (excluding deaths), 339 blood transfusions, and 256 infections (including 48 "severe infections"). *Id.* Of the 14 deaths, eight women died following severe bacterial infections, and two died following ruptured ectopic pregnancies.[14]

Significantly, peer-reviewed data demonstrates that surgical abortion is safer than chemical abortion. The largest and most accurate study of medical abortions comes from a large 2009 review of the medical records of 22,368 women who underwent chemical abortions compared with 20,251 women who underwent surgical abortions. That study concluded that the overall incidence of adverse events was fourfold higher with chemical abortions than surgical abortions. M. Niinimäki et al., *Immediate Complications after Medical compared with Surgical Termination of Pregnancy*, OBSTET. GYNECOL. 114:795 (Oct. 2009). *See also* J.T. Jenson et al., *Outcomes of suction curettage and mifepristone abortion in the United States: A prospective comparison study*, CONTRACEPTION 59:153-59 (1999) (finding that chemical abortion failed in 18.3 percent of patients and that surgical abortion failed in only 4.7 percent of patients).

Finally, many potential complications from use of the RU-486 regimen may be unknown, as there are widespread inadequacies in reporting. *See* M.M. Gary & D.J. Harrison, *Analysis of Severe Adverse Events Related to the Use of Mifepristone as an Abortifacient*, ANNALS OF PHARMACOLOGY 40(2):191 (2006). The inadequacies in reporting mean that the prevalence and character of many complications may be unknown.

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http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM263353.pdf

[14] The FDA has not released an adverse event summary since 2011, and the current tally of deaths and complications from mifepristone is not publicly accessible.

In January 2015, Planned Parenthood began touting a study that allegedly supported its misuse of abortion-inducing drugs. However, that study suffers from numerous flaws. For example, one of the most common risks associated with chemical abortion is incomplete abortion. If the drugs do not terminate the pregnancy, a second abortion is necessary—either surgical or an additional chemical abortion. However, the study used a skewed definition of whether the first chemical abortion was "successful": "A successful abortion was defined as expulsion of the pregnancy without the need for aspiration." In other words, only those incomplete abortions that resulted in "aspiration" (*i.e.*, a surgical procedure) were counted among the incomplete abortions. If a woman went on to have a second chemical abortion, the first chemical abortion was included in the "successful" category.

In fact, the study admitted that "information on whether a repeat dose of misoprostol was given is not available" for more than 45 percent of the woman studied. This clearly undermines any purported conclusion that the Planned Parenthood-preferred (and FDA-unapproved) protocol is effective at terminating pregnancy without an additional second abortion.

Significantly, the study also admitted that the effectiveness of Planned Parenthood's protocol was highest at 29 to 35 days and 36 to 42 days gestation (which falls within the FDA's approved 49-day window), but efficacy was "lowest at 57 to 63 days (95.5 %)" (gestational ages which fall outside the FDA's restrictions). Taken at face value, this means that 4 or 5 out of every 100 women using the drugs past the FDA's restrictions will experience (and be subjected to the risks of) two abortions. But as discussed already, that number cannot be taken at face value, because it excludes data on women who had two chemical abortions, meaning that the efficacy is actually lower than 95 percent. It also excludes a large percentage of women who were lost to follow-up. Specifically, 15.5 percent of the patients "studied" did not return for follow-up. This means that no data on subsequent complications or incomplete abortion is available for these women.

In sum, the medical data on the risks inherent in chemical abortion confirms the need for direct physician involvement.

Known contradictions for the RU-486 regimen support regulation

Use of the RU-486 regimen for chemical abortion is contraindicated in a number of situations, all of which bolster requiring physician involvement and presence before administering abortion-inducing drugs.

First, the Mifeprex FPL states explicitly that the regimen is "contradicted if a patient does not have adequate access to medical facilities equipped to provide emergency treatment of incomplete abortion, blood transfusions, and emergency resuscitation during the period from the

first visit until discharged by the administering physician." *Mifeprex FPL*, at 5. Women are instructed that they should not take Mifeprex if they cannot easily get such emergency help in the two weeks following ingestion. *Id.* at 17. Notably, all of the patients in the U.S. clinical trial reviewed by the FDA prior to approval of RU-486 regimen were within one hour of emergency facilities or the facilities of the "principle investigator." Memorandum of Department of Health and Human Services, *supra*, at 5.

HHS has stated that the Mifprex labeling "makes it clear that if there isn't adequate access to emergency services, the medication is contraindicated." *Id.*; *see also id.* at 3 ("The labeling has a contraindication if there is no access to medical facilities for emergency services."). Thus, the very women that abortion providers claim need telemedicine for abortion, because of travel and other potential obstacles, are actually the very women for whom the drugs are contraindicated.

Second, gestational age can be a contraindication for use of abortion-inducing drugs. The drugs become less effective as gestational age increases, and medical evidence demonstrates that complications increase as gestational age advances. *See, e.g.*, M.J. Mentula et al., *Immediate adverse events after second trimester medical termination of pregnancy: results of a nationwide study*, Human Reprod. 26:927-32 (2011). Thus, accurately assessing gestational age is of great import.

Third, the drugs are also contraindicated for women with ectopic pregnancies. Clearly, the FDA was concerned with the potential adverse effects of an undiagnosed ectopic pregnancy "treated" with the RU-486 regimen when it restricted administration to only those physicians able to determine whether there is an ectopic pregnancy.

Importantly, because symptoms of ectopic pregnancy mimic the symptoms of completed mifepristone abortions, ectopic pregnancies can go easily undiagnosed. Improper screening (*i.e.*, failure of a physician to examine the patient) places the life of a woman with an unknown ectopic pregnancy at even greater risk of death by ruptured ectopic pregnancy. The FDA has reported 58 adverse events related to ectopic pregnancies in women using the RU-486 regimen, and 2 of the 14 U.S. women reported to have died after using the regimen died from ruptured ectopic pregnancies. FDA, *Mifepristone U.S. Postmarketing Adverse Events Summary Through 04/30/11*.

Finally, the safety of the RU-486 regimen has not been tested on a large population of women, including minors or women who are heavy smokers. *Mifeprex FPL*, *supra*, at 3, 7.