**Senator Ben Watson, Chair and Ranking Member Senator Dean Burke, Vice Chair**
**Senate Health and Human Services Committee**
**Senate Bill 456: The Women's Health and Safety Act**
**Testimony In Favor**

## Chairman Ben Watson and Ranking Member Dean Burke,

Thank you for the opportunity to testify on this important bill, SB 456, The Women's Health and Safety Act. I am a board-certified obstetrician gynecologist and CEO of the American Association of Pro-Life Obstetricians and Gynecologists, the largest non-sectarian professional organization of reproductive health professionals in the world. I am also an Associate Research Scholar with the Charlotte Lozier Institute, an organization committed to bringing the power of science, medicine, and research to bear in life-related policy making, media, and debates to promote a culture and polity of life. In that capacity, I have published research for the last decade on the adverse events following mifeprex abortions in peer reviewed medical literature.

In a medical abortion, per the current FDA protocol, women are instructed to take 200 mg of mifepristone on day one, then 24–48 hours later "place two 200 [microgram] misoprostol tablets in each cheek pouch (the area between the cheek and gums) for 30 minutes and then swallow any remnants."[1] This procedure is approved in pregnancy up to 70 days measured from the woman's last menstrual period.[2] Mifepristone is a drug that blocks the action of a natural pregnancy hormone called progesterone by binding with a woman's progesterone receptors on the nuclear membranes of cells in the uterus, ovary,

1. Food and Drug Administration. (2016). *Mifeprex Label* (attached).
2. Food and Drug Administration. (2016). *Mifeprex Label* at 2 (attached)

brain, breast, and immune system. With mifepristone blocking the connection of progesterone with progesterone receptors in the uterus of a pregnant woman, the mother's cells in the placenta stop functioning, which leads to the death of the human embryo.[3] However, only about 39% (7/18) of women who are 7 weeks or less will completely pass the pregnancy tissue with 200 mg of mifepristone alone.[4] Thus a second drug, misoprostol, is administered to induce contractions.

Misoprostol is a synthetic prostaglandin which is used to prevent gastric ulcers in patients who have a high risk of developing a gastric ulcer, or who are on drugs which induce gastric ulcers.[5] Misoprostol induces contractions of the pregnant uterus in order to expel the embryo or fetus.

Embryonic death is not inevitable, however. Mifepristone by itself fails to kill the fetus in a significant percentage of cases. This is why women are told to administer the drug misoprostol afterward, to make the procedure more effective.

## Need for thorough in-person evaluation by a physician

Prudent use of mifeprex abortion requires at least two in-person meetings between the patient and a physician, who performs a physical examination.

Mifepristone is contraindicated in a number of instances, including when ectopic pregnancy is suspected or confirmed; when there is chronic adrenal failure; when there is concurrent long-term corticosteroid therapy or anti-coagulant therapy; when the patient is allergic to mifepristone, misoprostol, or other prostaglandins; when the patient has inherited porphyria; and when the patient has an IUD in place.[6] It is the responsibility of the prescribing physician to ensure that the patient does not have any of these contraindications prior to prescribing mifepristone.

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3. Baulieu, E. E. & Segal, S. J. (Eds.) (1985) *Reproductive Biology: The Antiprogestin Steroid RU486 and Human Fertility Control. Proceedings of a Conference on the Antiprogestational Compound RU486*. Plenum Press.
4. Baulieu, E. E. & Segal, S. J. (Eds.) (1985) *Reproductive Biology: The Antiprogestin Steroid RU486 and Human Fertility Control. Proceedings of a Conference on the Antiprogestational Compound RU486*. Plenum Press. at 211.
5. Food and Drug Administration. (2009). *Cyotec (Misoprostol) Medication Guide*. https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/019268s041lbl.pdf
6. Food and Drug Administration. (2016). *Mifeprex Label* at 4-5 (attached).

These contraindications require close attention to patient history and medications as well as a thorough physical examination by a physician capable of diagnosing hemorrhagic disorders, porphyria, adrenal failure, ectopic pregnancy, etc. A pelvic examination is required to rule out undiagnosed adnexal mass and look for the presence of an IUD, as well as to check for tenderness consistent with pelvic inflammatory disease.

Failure to perform an in-person examination can have serious consequences for the patient, including death. For example, if a woman who has an ectopic pregnancy (i.e., a pregnancy implanted in the Fallopian tube) is given mifepristone, she is in significant danger of the ectopic pregnancy rupturing, which will cause massive internal bleeding. The symptoms of a rupturing ectopic pregnancy are identical to the symptoms that a woman experiences when she has a mifepristone abortion: bleeding, cramping and severe abdominal pain.[7] Delay in diagnosis due to thinking that these symptoms are a "normal" part of mifepristone abortion can result in massive intraabdominal hemorrhage and death.

In addition, prudent use of mifeprex abortion requires a follow-up in-person examination to ensure the abortion is complete, i.e., all products of conception have been removed, and to confirm the patient has not suffered serious complications.[8]

## Medication abortion complication rates

Medication abortions commonly lead to complications, and at a rate higher than surgical abortions.

The most widely accepted definition for the frequency of drug complications is given by the Council for International Organizations of Medical Sciences (CIOMS), an international, non-governmental, non-profit organization established jointly by World Health Organization and UNESCO in 1949. The CIOMS training

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7. Food and Drug Administration. (2016). *Mifeprex Label* at 6 (attached).
8. Food and Drug Administration. (2016). *Mifeprex Label* at 4 (attached); American College of Obstetricians and Gynecologists. (2014). Practice bulletin no. 143: Medical management of first-trimester abortion. *Obstetrics and Gynecology*, *123*(3), 676-692. doi: 10.1097/01.AOG.0000444454.67279.7d.

manual on medicine safety states that "adverse drug reactions" are "very common" if they occur in over 10% of cases and "common (frequent)" if they occur between 1 and 10% of the time.[9]

Using the CIOMS criteria, complications from medical abortions are "common" or "frequent." An Australian study, for example, found that 3.3% of patients who used mifepristone in the first trimester required emergency hospital treatment.[10] In contrast, 2.2% of patients who underwent surgical abortions were later treated in the hospital because of emergency complications. And women receiving medical abortions were admitted to hospitals at a rate of 5.7% following the abortion, as compared with 0.4% for patients undergoing surgical abortion.

A comprehensive medical records study from Finland found that 15.6% of women experienced hemorrhage after a medical abortion, that 6.7% of women had incomplete abortions, and that 5.9% required surgery to complete the abortion.[11] This study found that the overall incidence of immediate adverse events is four-fold higher for medical abortions than for surgical abortions. In particular, this study indicated that hemorrhage and incomplete abortion are more common after medical abortions; the incidence of hemorrhage was 15.6% following medical abortions, compared to 2.1% for surgical abortions, and 6.7% of medical abortions resulted in incomplete abortion, compared with 1.6% of surgical abortions.

Medical abortion carries a risk of hemorrhage because of mifepristone's action at the cellular level, which blocks the ability of the uterus to control bleeding.[12] The risk of infection is also significant, since both

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9. World Health Organization. (n. d.) *Medication Safety Training Course* at 10, https://www.who.int/medicines/areas/quality_safety/safety_efficacy/trainingcourses/definitions.pdf
10. Mulligan, E. & Messenger, H. (2011). Mifepristone in South Australia -- the first 1343 tablets. *Australian Family Physician*, *40*(5), 342-345.
11. Niinimäki, M., Pouta, A., Bloigu, A., Gissler, M., Hemminki, E., Suhonen, S., & Heikinheimo, O. (2009). Immediate Complications After Medical Compared With Surgical Termination of Pregnancy. *Obstetrics & Gynecology*, *114*(4), 795-804. doi: 10.1097/aog.0b013e3181b5ccf9
12. Miech, R. P. (2007). Pathopharmacology of excessive hemorrhage in mifepristone abortions. *The Annals of Pharmacotherapy*, *41*(12), 2002-2007. doi: 10.1345/aph.1K351

mifepristone[13] and misoprostol[14] may depress a woman's immune response to infection, which can allow simple infections to become overwhelming and lead to fatal sepsis. In fact, this concern about serious infections led Planned Parenthood to abandon the off-label use of misoprostol in the vagina and substitute instead the off-label use of misoprostol in the cheek (buccal administration).[15]

Similarly, a 2015 meta-analysis published by Chen, *et al.* examined all of the existing publications on mifepristone abortion using buccal administration of the second drug, misoprostol, a total of 20 studies, stretching from November 2005 through January 2015. Just as in all mifepristone abortion regimens, the failure rate increases as the gestational age increases, especially at gestational ages greater than the 49-day limit originally set by the FDA. (See Table 1 from the Chen study copied below). [16]

**Table 1.** Efficacy and Ongoing Pregnancy Rates With Mifepristone and Buccal Misoprostol for Medical Abortion Through 70 Days of Gestation

| | Successful Abortion | | | Ongoing Pregnancy | | |
|---|---|---|---|---|---|---|
| | No. in Analysis | No. Successful | % (95% CI) | No. in Analysis | No. of Ongoing Pregnancies | % (95% CI) |
| Overall | | | | | | |
| Through 63 d of gestation | 33,514 | 32,394 | 96.7 (96.5–96.8) | 32,479 | 252 | 0.8 (0.7–0.9) |
| Through 70 d of gestation | 33,846 | 32,703 | 96.6 (96.4–96.8) | 32,785 | 261 | 0.8 (0.7–0.9) |
| By gestational age (d)* | | | | | | |
| 49 or less | 12,555 | 12,318 | 98.1 (97.9–98.3) | 10,781 | 40 | 0.4 (0.3–0.5) |
| 50–56 | 4,161 | 4,024 | 96.7 (96.1–97.2) | 4,008 | 34 | 0.8 (0.6–1.2) |
| 57–63 | 2,202 | 2,096 | 95.2 (94.2–96.0) | 2,119 | 39 | 1.8 (1.3–2.5) |
| 64–70 | 332 | 309 | 93.1 (89.6–95.5) | 306 | 9 | 2.9 (1.4–5.7) |

CI, confidence interval.
All outcomes are based on patients for whom outcome was determined (patients without follow-up are not included).
* Not all studies reported outcome within each specific gestational age range; outcomes are calculated using only those studies with outcome data presented by gestational age.

13. Webster, J. I. & Sternberg, E. M. (2004). Role of the hypothalamic-pituitary-adrenal axis, glucocorticoids and glucocorticoid receptors in toxic sequelae of exposure to bacterial and viral products. *The Journal of Endocrinology*, *181*(2), 207-221. doi: 10.1677/joe.0.1810207; Miech, R. P. (2005). Pathophysiology of mifepristone-induced septic shock due to Clostridium sordellii. *The Annals of Pharmacotherapy*, *39*(9), 1483-1488. doi: 10.1345/aph.1G189
14. Aronoff, D. M., Hao, Y., Chung, J., Coleman, N., Lewis, C., Peres, C. M., Serezani, C. H., Chen, G. H., Flamand, N., Brock, T. G., Peters-Golden, M. (2008). Misoprostol impairs female reproductive tract innate immunity against Clostridium sordellii. *Journal of Immunology*, *180*(12), 8222-8230. doi: 10.4049/jimmunol.180.12.8222
15. Fjerstad, M., Trussell, J., Sivin, I., Lichtenberg, S., & Cullins, V. (2009). Rates of serious infection after changes in regimens for medical abortion. *The New England Journal of Medicine*, *361*, 145-151. doi: 10.1056/NEJMoa0809146
16. Chen, M. J., & Creinin, M. D. (2015). Mifepristone With Buccal Misoprostol for Medical Abortion. *Obstetrics & Gynecology*, *126*(1), 12–21. doi: 10.1097/aog.0000000000000897

The 2016 FDA label for mifepristone acknowledges this fact. Table 4 on page 13 of the FDA label shows mifepristone failure rate more than triples when comparing successful mifepristone abortions at 49 days (98.1%) to successful mifepristone abortions at 63 days (92.7%). So, by 63 days gestation, nearly one out of 13 women fail their Mifeprex abortion and require surgical completion. Table 4 also documents a nearly 10-fold increase in ongoing pregnancies when comparing Mifeprex abortions at 49 days with Mifeprex abortions at 63 days.

An ACOG Practice Bulletin also acknowledges that "[c]ompared with surgical abortion, medical abortion takes longer to complete, requires more active patient participation, and is associated with higher reported rates of bleeding and cramping."[17]

Both the FDA and drug manufacturers have acknowledged that the use of mifepristone/misoprostol regimens to induce an abortion poses health risks for pregnant women. The final printed labeling (FPL) shaped and approved by the FDA warns that "About 85% of patients report at least one adverse reaction following administration of MIFEPREX and misoprostol, and many can be expected to report more than one such reaction."[18] These reactions include, but are not limited to, vomiting, headache, uterine hemorrhage, viral infections, and pelvic inflammatory disease.[19]

The FDA considers Mifeprex complications serious and frequent enough to issue a black box warning to prescribers titled **"WARNING: SERIOUS AND SOMETIMES FATAL INFECTIONS OR BLEEDING."**[20] In addition, the FDA has instituted a Risk Evaluation and Mitigation Strategy (REMS) for Mifeprex.[21] According to the FDA, REMS "is a drug safety program" that the FDA "can require for certain medications

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17. American College of Obstetricians and Gynecologists. (2014). Practice bulletin no. 143: Medical management of first-trimester abortion. *Obstetrics and Gynecology*, *123*(3), 676-692. doi: 10.1097/01.AOG.0000444454.67279.7d
18. Food and Drug Administration. (2016). *Mifeprex Label* at 7 (attached).
19. Food and Drug Administration. (2016). *Mifeprex Label* at 7–8 (attached).
20. Food and Drug Administration. (2016). *Mifeprex Label* at 1–2 (attached).
21. Food and Drug Administration. (2019). Risk evaluation and mitigation strategy (REMS) single shared system for mifepristone 200mg. https://www.accessdata.fda.gov/drugsatfda_docs/rems/Mifepristone_2019_04_11_REMS_Document.pdf.

with *serious safety concerns*."[22] The FDA goes on to emphasize that "[w]hile all medications have labeling that informs health care stakeholders about medication risks, *only a few medications require a REMS*."[23] Moreover, the FDA reports that, as of December 31, 2018, over 4000 women in the United States have experienced "adverse events" after using mifepristone for the termination of pregnancy.[24] Among those adverse events were 24 deaths, 1,042 hospitalizations, 599 blood transfusions, and 412 infections. [25] This last figure includes 69 severe infections, which the FDA says "generally result in death or hospitalization for at least 2-3 days, require intravenous antibiotics for at least 24 hours and total antibiotic usage for at least 3 days[.]" The same report indicates that there have been "11 additional reported deaths in women in foreign countries who used mifepristone for medical termination of pregnancy."[26] According to FDA records, many of the first 600 severe adverse event reports in the first four years after mifepristone approval in 2000 would have been fatalities except for prompt access to emergency intervention and adequate hospital access.[27]

In summary, the requirements of Senate Bill 456 are medically reasonable to ensure the safety of women in Georgia who are undergoing a mifeprex abortion.

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22. Food and Drug Administration. (2019). *Risk Evaluation and Mitigation Strategies* (*REMS*). https://www.fda.gov/drugs/drug-safety-and-availability/risk-evaluation-and-mitigation-strategies-rems
23. Food and Drug Administration. (2019). *Risk Evaluation and Mitigation Strategies* (*REMS*). https://www.fda.gov/drugs/drug-safety-and-availability/risk-evaluation-and-mitigation-strategies-rems
24. Food and Drug Administration. (2018). *Mifepristone U.S. Postmarketing Adverse Events Summary Through 12/31/2018*. https://www.fda.gov/media/112118/download
25. Food and Drug Administration. (2018). *Mifepristone U.S. Postmarketing Adverse Events Summary Through 12/31/2018*. https://www.fda.gov/media/112118/download
26. Food and Drug Administration. (2018). *Mifepristone U.S. Postmarketing Adverse Events Summary Through 12/31/2018*. https://www.fda.gov/media/112118/download
27. Gary, M. M., & Harrison, D. J. (2006). Analysis of severe adverse events related to the use of mifepristone as an abortifacient. *The Annals of Pharmacotherapy*, *40*(2), 191-197. doi: 10.1345/aph.1G481

Respectfully submitted,

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