EXHIBIT 5

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF INDIANA
INDIANAPOLIS DIVISION

ALL-OPTIONS, INC.; *et al.*,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	
	)	Case No. 1:21-cv-1231-JPH-MJD
ATTORNEY GENERAL OF INDIANA, in his official capacity, *et al.*,	)	
	)	
	)	
Defendants.	)	
	)	
	)	

DECLARATION OF DR. DONNA HARRISON

I, Donna Harrison, M.D., pursuant to the provisions of 28 U.S.C. § 1746, do hereby declare as follows:

1. I, Donna Harrison, M.D., am a physician licensed to practice medicine in Michigan, I am certified by the American Board of Obstetricians and Gynecologists, and I have held this certification since 1993. I graduated from the University of Michigan Medical School in 1986, and I completed residency training in Obstetrics and Gynecology in 1990 at St. Joseph Mercy Hospital (a University of Michigan affiliate hospital in Ypsilanti). I entered private obstetrical practice in 1991 in Ann Arbor. I also served as Associate Professor in the Department of Obstetrics and Gynecology at the University of Michigan until 1993 when I joined a multispecialty group in an underserved rural area of Michigan. I continued in private practice in this underserved area, including serving as a sexual abuse examiner for Cass County, Michigan,

until 2000. Further details of my training and professional background are given in my resume, attached as Exhibit A.

2. Since 1996, I have closely scrutinized the U.S. Food and Drug Administration (FDA) approval process for Mifeprex (mifepristone), and I have conducted significant research into the safety and efficacy of abortion-inducing drugs, authoring several papers on the subject. From 2000 until 2006, I was Chairman of the Subcommittee on Mifeprex for the American Association of Pro-Life Obstetricians and Gynecologists (AAPLOG). Since 2000, I have focused my professional activities on teaching, writing, and research for AAPLOG. Since 2013, I have served as AAPLOG's Executive Director and since 2021 serve now as Chief Executive Officer.

3. I spend approximately 50 hours per week reviewing the medical literature for the effects of abortion on women, teaching physicians and other health care personnel about the medical literature, and making that information known by way of scientific publication and through the AAPLOG website. I have devoted particular attention to abortions performed through the administration of drugs.

4. In the past four years, I have testified as an expert in cases in Indiana, Missouri, Arkansas, Illinois, Oklahoma, Mississippi and Tennessee in both state and federal court.[1]

5. I have been asked by the Indiana Attorney General to opine regarding *All-Options, Inc. v. Attorney General of Indiana*, No. 1:21-cv-1231 (S.D. Ind.), a legal action brought against various Indiana officials. The complaint challenges several aspects of Indiana law. I have been asked to opine regarding the provision that abortion providers are required to inform medication abortion patients that "[s]ome evidence suggests that the effects of Mifepristone may be avoided,

[1] *See, e.g.*, *Planned Parenthood Ark. and E. Okla. v. Jegley*, No. 4:15-cv-00784-KGB, 2018 WL 3816925 (E.D. Ark. 2018); *Little Rock Fam. Plan. Servs. v. Rutledge*, 397 F. Supp. 3d 1213 (W.D. Ark. 2019) (appeal pending in the 8th Cir.); *Tulsa Women's Reprod. Clinic, LLC v. Hunter*, No. CV-2019-2176 (Ok. County District Court).

ceased, or reversed if the second pill, Misoprostol, has not been taken."[2] I am being compensated, pursuant to an expert services contract, at three hundred fifty dollars ($350.00) per standard hour worked, and will be compensated four thousand dollars ($4,000.00) per day for testimony given at any deposition, hearing, or trial of the lawsuit.

6. The opinions I express in this declaration are based on my education, training, experience, and ongoing familiarity with the medical literature. These opinions are my own, and do not represent any group.

OPINIONS

7. I have reviewed the challenged Indiana law requiring doctors to inform medication abortion patients that the effects of mifepristone may be able to be reversed. I have also reviewed the Plaintiffs' complaint and medical testimony. Although there are many subjects that could be addressed within a longer time frame, I will focus this declaration on two important topics: I) the scientific basis for effective progesterone administration after mifepristone intake (i.e. "reversal"), and II) the criticisms of the Davenport and Delgado publications.

I. There is scientific support for effective progesterone administration after mifepristone, which is otherwise known as abortion reversal

8. Mifepristone (a.k.a. RU-486 or RU-38486) 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, 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 in turn eventually leads to the death of the embryo through, in essence, starvation.[3]

---

[2] P.L. 218-2021 § 4(a)(1) (2021).

[3] E.E. Baulieu & S.J. Segal, *The Antiprogestin Steroid RU486 and Human Fertility Control*, Proceedings of a Conference on the Antiprogestational Compound RU486. Oct 23-25. Bellagio Italy. Published in the series P Reproductive Biology 1984 Sheldon Segal Series Editor 1985 Plenum Press.

9. Embryonic death is not inevitable, however. Mifepristone, by itself, fails to kill the fetus in a significant percentage of cases. (The specifics of that percentage I will discuss below.) This is why women are told to administer the drug misoprostol afterward, to make the procedure more effective.

10. Indiana's House Enrolled Act No. 1577 requires abortion providers to inform women that "[s]ome evidence suggests that the effects of Mifepristone may be avoided, ceased, or reversed if the second pill, Misoprostol, has not been taken" [4] Indiana's use of the word "may" is particularly notable, as it is a measured term that calls to mind scientific possibility rather than absolute scientific proof. Notably, Plaintiffs' expert Schreiber misconstrues the wording of the statute, ignoring the word "may" and inserting instead the word "can".[5]

11. Yet Indiana does not state that the effects of mifepristone *can* be avoided, ceased, or reversed, but rather that the effect of mifepristone *may* be avoided, ceased, or reversed. And based on the known evidence, it is untenable to deny that there is at least a possibility that progesterone reversal actually works. Based on the available scientific evidence, reversal is indeed possible.

12. To be precise, the available evidence, discussed more thoroughly below, shows that after mifepristone is taken, its effects can be countered and potentially minimized if a woman is given high amounts of natural progesterone,[6] as long as this progesterone is administered within 72 hours of taking mifepristone. Progesterone and mifepristone competitively bind to the same receptor in cells, but this binding is reversible.[7] If there is enough progesterone, the

---

[4] P.L. 218-2021 § 4(a)(1) (2021).
[5] ECF No. 53-6, Decl. of Courtney A. Schreiber, M.D., M.P.H. ¶ 21.
[6] American Association of Pro-Life Obstetricians and Gynecologists, P*ractice Bulletin 6: The reversal of the effects of mifepristone by progesterone* (Nov. 6, 2019), https://aaplog.org/wp-content/uploads/2020/01/FINAL-PB-6-Abortion-Pill-Reversal-1.pdf.
[7] C.H. Spilman et al., *Progestin and Antiprogestin Effects on Progesterone Receptor Transformation*, 24 J. STEROID BIOCHEMISTRY 1, 385-389 (1986).

progesterone out-competes the mifepristone at the level of the progesterone receptor, acting in the same manner as an antidote to a toxicant (i.e., a poison).

13. In attacking this "reversal" proposition, the Plaintiffs' experts focus almost entirely on undermining two publications by Dr. George Delgado, released in 2012 and 2018, respectively. I will talk about those works shortly, as they are important. But first, I want to discuss a number of other scientific points that are ignored or glossed over—points that provide scientific evidence of the logic and feasibility of progesterone reversal of a mifepristone blockade.

14. First, this proposition was not conjured out of thin air. Understanding the scientific principles underlying the use of progesterone to block mifepristone action requires defining some basic terms in biochemistry. One of those terms is substrate. "A substrate is a molecule acted upon by an enzyme. A substrate is loaded into the active site of the enzyme, or the place that allows weak bonds to be formed between the two molecules. An enzyme substrate complex is formed, and the forces exerted on the substrate by the enzyme cause it to react and become the product of the intended reaction. The bonds that form between the substrate and enzyme cause the conformational change, or shape change, in the enzyme. The resulting shape change is what applies pressure to the substrate, either forcing molecules together or tearing them apart."[8] It is understood, generally, that competitive inhibitors (like mifepristone) that replace and block out substrates (like natural progesterone) may be thwarted if there is enough substrate around. An important principle to remember is that mifepristone binding is competitive and reversible. A reversible reaction is "A chemical equation of the form A ® B represents the transformation of A into B, but it does not imply that all of the reactants will be converted into products, or that the reverse reaction B ® A cannot also occur. In general, both processes can be expected to occur,

[8] *Substrate, Biology Dictionary (Apr. 28, 2017),* https://biologydictionary.net/substrate/.

resulting in an equilibrium mixture containing all of the components of the reaction system."[9] When mifepristone is present, the mifepristone binds to the progesterone nuclear receptor in the cell's nuclear membrane. While mifepristone is bound to the progesterone receptor, progesterone cannot bind. However, mifepristone binding is reversible, and if there is sufficient progesterone present, the progesterone can outcompete mifepristone for the receptor site. This is a basic principle in biochemistry. "*The inhibitor creates a competing equilibrium to that of the substrate (S), removing a fraction of the enzyme to an inactive form. Adding more substrate will yield more of the active substrate ES form*."[10] "ES" stands for Enzyme-Substrate, which in this case is the progesterone receptor bound with progesterone. In other words, mifepristone reversal efforts are patterned after a known biological phenomenon which is a basic principle in biochemistry.

15. As such, it is not surprising when even an admittedly pro-choice abortion doctor like Dr. Harvey Kliman, the director of reproductive and placental research unit at the Yale School of Medicine, tells the New York Times that mifepristone reversal "makes biological sense" and is "totally feasible."[11] Indeed, Dr. Kliman went so far as to say that "if one of his daughters came to him and said she had somehow accidentally taken mifepristone during pregnancy, he would tell her to take 200 milligrams of progesterone three times a day for several days, just long enough for the mifepristone to leave her system: 'I bet you it would work.'"[12]

16. This basic medical principle of poison treatment after exposure to a cellular poison has been applied elsewhere in medicine. When a person has carbon monoxide poisoning, the carbon monoxide binds tightly to the oxygen carrying red blood cells and does not allow the red blood cells to carry oxygen. In fact, carbon monoxide binds more tightly to the red blood cells

---

[9] Stephen K. Lower, *Chemical Equilibrium: A Chem 1 Reference Text*, SIMON FRASER UNIVERSITY (Mar. 2013), http://www.chem1.com/acad/pdf/chemeq.pdf.
[10] John W. Pelley, ELSEVIER'S INTEGRATED REVIEW BIOCHEMISTRY 33–34 (2nd ed. 2011).
[11] Ruth Graham, *A New Front in the War Over Reproductive Rights: 'Abortion-Pill Reversal'*, N.Y. TIMES MAGAZINE (July 18, 2017).
[12] *Id.*

than does oxygen. However, the carbon monoxide can be displaced from the red blood cell when enough oxygen is administered.[13] Similarly, when the drug methotrexate is given to kill cancer cells, for example, it can also kill non-cancer cells. In order to "rescue" those non-cancer cells, the drug leucovorin (also known as the vitamin "folinic acid") is given to out-compete the inhibitor, which is methotrexate.[14]

17. Second, in addition to the basic principle of out-competing mifepristone at the receptor being sound, the reversibility of mifepristone binding is backed up by manufacturer studies as published by Baulieu,[15] (one of the developers of the drug mifepristone) as well as studies and presentation by Dr. Esther Sternberg,[16] (a researcher from the National Institutes of Health) looking at reversing the effects of another nuclear receptor which mifepristone also binds: the glucocorticoid receptor. Specifically, mifepristone also blocks natural stress hormones (glucocorticoids) by binding with glucocorticoid receptors. And using animal models, Sternberg reviewed the studies showing that the blockade of mifepristone at the glucocorticoid receptor "can be reversed" by the administration of additional glucocorticoids.[17]

18. Third, a study in 1989 (Yamabe) directly indicated that mifepristone blockage of progesterone receptors can be overcome by the administration of additional natural

---

[13] Ctrs. For Disease Control & Prevention, *Clinical Guidance for Carbon Monozide (CO) Poisoning* (Nov. 4, 2020), https://www.cdc.gov/disasters/co_guidance.html.

[14] *Drug Info: Folinic Acid*, Chemocare, http://chemocare.com/chemotherapy/drug-info/folinic-acid.aspx.

[15] E.E. Baulieu & S.J. Segal, *The Antiprogestin Steroid RU486 and Human Fertility Control*, Proceedings of a Conference on the Antiprogestational Compound RU486. Oct 23-25. Bellagio Italy. Published in the series P Reproductive Biology 1984 Sheldon Segal Series Editor 1985 Plenum Press.

[16] J. L. Webster & E.M. Sternberg, *Role of the Hypothalamic-Pituitary-Adrenal Axis, Glucocorticoids and Glucocorticoid Receptors in Toxic Sequelae of Exposure to Bacterial and Viral Products*, 181 Journal of Endocrinology 207-221 (2004); *See also Emerging Clostridial Disease Workshop*, Food & Drug Administration , 23 (June 22, 2006).

[17] Jeanette I. Webster & E.M. Sternberg, *Role of the Hypothalamic-Pituitary-Adrenal Axis, Glucocorticoids and Glucocorticoid Receptors in Toxic Sequelae of Exposure to Bacterial and Viral Products*, 181 J. ENDOCRINOLOGY 207–221 (2004).

progesterone.[18] That study separated pregnant rats into three groups. The first group received no drugs, the second group was given mifepristone, and the third group was given mifepristone followed by natural progesterone. Every member of the no-drug group delivered live offspring. Only 33.3% of the mifepristone-only group delivered live offspring. In the third group, which was given mifepristone and then progesterone, 100% delivered live offspring.[19] The Plaintiffs' doctors do not address this scientific study, which indicates that the blockage of progesterone receptors by mifepristone is not permanent but rather reversible.

19. Fourth, Plaintiffs' doctors are also seemingly unaware of a peer-reviewed case series out of Australia (Garratt),[20] that was published in 2017 in the European Journal of Contraceptive and Reproductive Health Care. Though small, that case series documented similar results to Dr. Delgado's first case series, with two out of three women who attempted reversal with progesterone achieving success with live, healthy births.

20. Fifth, the scientific literature surrounding the development of mifepristone is summarized by the developer (Baulieu)[21]. Baulieu (at Figure 3 pg. 91) showed in a graph the rate at which RU486 could be removed from the progesterone receptor, in the presence of high concentrations of progesterone. This pharmacokinetic study clearly shows that mifepristone's blockade of progesterone receptors is reversible—not permanent—and that high concentrations of progesterone will reverse the binding of mifepristone at the progesterone receptor.

---

[18] S. Yamabe et al., *The Effect of RU486 and Progesterone on Luteal Function During Pregnancy*, 65 Nihon Naibunpi Gakkai Zasshi 497 (1989), https://www.jstage.jst.go.jp/article/endocrine1927/65/5/65_497/_article/-char/ja/..

[19] *Id.*

[20] Deborah Garratt & Joseph V. Turner, *Progesterone for preventing pregnancy termination after initiation of medical abortion with mifepristone*, 22 EUR. J. CONTRACEPTIVE & REPROD. HEALTH CARE 6472-475 (Dec. 2017).

[21] E.E. Baulieu & S.J. Segal, *The Antiprogestin Steroid RU486 and Human Fertility Control*, Proceedings of a Conference on the Antiprogestational Compound RU486. Oct 23-25. Bellagio Italy. Published in the series P Reproductive Biology 1984 Sheldon Segal Series Editor 1985 Plenum Press.

21. In the end, it is not my contention that each of these scientific points by themselves prove reversibility is effective. Rather, my opinion is that, even apart from Dr. Delgado's publications, they demonstrate that reversibility is scientifically feasible, as it is based on scientific principles, facts, studies, and experience.

22. Dr. Delgado's publications document the repeated success of mifepristone reversal attempts in large numbers of women. Dr. Delgado published two case series—a small one in 2012[22] and a much larger one in 2018.[23] Both indicate that having a woman take progesterone shortly after she ingested mifepristone may improve the chances of embryo survival.

23. The 2012 case series was small in size, reporting on a total of six women who had used progesterone after mifepristone. Four of those women went on to complete delivery of live born infants. No malformations were observed in the children.

24. The 2018 case series was much larger and more substantial. In it, Dr. Delgado and his co-authors analyzed the records of 547 women who took progesterone after mifepristone in an attempt to reverse the mifepristone effects. Of those 547 women, they found an overall embryo survival rate, at 20 weeks gestation of 48%. The authors then analyzed the survival rates based on how and in what doses the progesterone was given, and they found a remarkable 68% survival rate if the progesterone was taken by mouth or by intramuscular injection.

25. Dr. Delgado and his co-authors used a historical control to determine if the 68% success rate was any different from what would have happened to women if they had not taken progesterone. That historical control was derived from the systematic review by Davenport in

[22] George Delgado & Mary L. Davenport, *Progesterone Used to Reverse the Effects of Mifepristone*. 46 ANNALS PHARMACOTHERAPY 12, 12 (Dec. 2012).
[23] George Delgado, et.al., *A Case Series Detailing the Successful Reversal of the Effects of Mifepristone Using Progesterone*, 33 ISSUES IN L. & MED. 21-31 (2018).

2017.[24] In short, Davenport reviewed all the studies ever published on the outcomes of women who had taken mifepristone alone, but not misoprostol. She found fetus survival rates using total doses of 200–300 mg of mifepristone ranged from 10% to 23.3%. (The current FDA-approved dosage is 200 mg.) In other words, if a woman decides not to take the second pill, and leaves it at that, there is a 10% to 23% chance the baby will survive, according to the published peer reviewed literature. In contrast, Dr. Schreiber cites only one study, Zheng,[25] for her claim that the survival rate "may be as high as forty-six percent."[26] In the Zheng study, the authors did not perform an ultrasound after taking mifepristone to determine whether or not the fetus survived the mifepristone. The study thus cannot tell the difference between a living fetus after mifepristone and retained pregnancy tissue after mifepristone. Thus, it is scientifically invalid to use the Zheng study as an estimate of the survival of living fetuses after ingestion of mifepristone.

26. Wisely, Dr. Delgado and his co-authors chose to use a historical control comparator number (25% survival) which was higher than Davenport's highest number (23.3%). Even with this higher estimate, there was a notable difference between the outcome of women who did not receive progesterone in the historical control (25%) and the outcome of women who received progesterone by the best protocols (68%).

27. Dr. Delgado and his co-authors also analyzed their results by gestational age at the time of reversal attempt and found that the success rate increased with increasing gestational age.

28. In addition, Dr. Delgado and his co-authors analyzed the interval of time between mifepristone injection and progesterone administration and found that success rates were the

---

[24] Mary L. Davenport et al., *Embryo Survival After Mifepristone: A Systematic Review of the Literature*, 32 ISSUES IN L. & MED. 1, 3–18 (2017).
[25] S.R. Zheng, *RU 486 (mifepristone): Clinical Trials in China*. 68 ACTA OBSTETRICIA GYNECOLOGICA SCANDINAVICA 149, 19–23 (1989).
[26] ECF No. 53-6, Schreiber Decl. ¶ 17.

same, as long as the progesterone was given within 72 hours of the use of mifepristone. This is consistent with what we know about mifepristone, which is that it takes several days to act and thus does not kill the embryo immediately. This finding is also consistent with the Yamabe study,[27] which found that in the rats given mifepristone alone, the level of progesterone in the blood began to decrease at 48 hours and continued to decrease at 72 hours. In contrast, where mifepristone was followed by progesterone, the progesterone levels were the same at 72 hours as the group which had not received anything. Notably, Yamabe's findings contradict Dr. Schreiber, who speculates , without support, that embryos with cardiac activity within the first 72 hours after mifepristone ingestion have "already withstood the initial effects of mifepristone."[28] This is not necessarily the case.

29. Dr. Delgado and his co-authors also analyzed safety. For example, they looked at the birth defect rate among the 257 women who had reversals and followed up after their delivery. They found no increase of birth defects when compared to the general population of births, which is consistent with other studies which have found no increase in malformation rate over the general population in infants who are born after exposure to mifepristone in utero.[29,30] This contradicts the speculative claims by Schreiber that birth defects might result from reversal attempts.[31] Similarly, Dr. Delgado found that the preterm delivery rate was 2.7%, a number much lower than the rate of preterm births in the general population.

30. Natural progesterone has routinely been given to women during pregnancy for over 50 years. For instance, progesterone administered by various routes is the standard of care

---

[27] S. Yamabe et al., *The Effect of RU486 and Progesterone on Luteal Function During Pregnancy*, 65 Nihon Naibunpi Gakkai Zasshi 497 (1989), https://www.jstage.jst.go.jp/article/endocrine1927/65/5/65_497/_article/-char/ja/.

[28] ECF No. 53-6, Schreiber Decl. ¶ 31.

[29] N. Bernard, et al., *Continuation of Pregnancy After First-Trimester Exposure to Mifepristone: An Observational Prospective Study*, 120(5) BJOG, 568, 568-74 (2013).

[30] R. Sitruk-Ware, et al., *Fetal Malformation and Failed Medical Termination of Pregnancy*, 352 LANCET 323 (1988).

[31] ECF No. 53-6, Schreiber Decl. ¶ 49.

for women who become pregnant by in-vitro fertilization (IVF). As such, the IVF industry has looked carefully to see if there are any indications of an increased risk from natural progesterone and have found none.[32] In addition, in women who have progesterone deficiencies in early pregnancy for various reasons, it is common to use natural progesterone to supplement the deficiency.[33]

31. Dr. Schreiber cites a 2019 study taken from the PRISM database whose conclusions state: "Among women with bleeding in early pregnancy, progesterone therapy administered during the first trimester did not result in a significantly higher incidence of live births than placebo."[34] However, the final full analysis of that PRISM database, by the same authors, published in 2020, states: "Progesterone therapy in the first trimester of pregnancy did not result in a **significantly** higher rate of live births among women with threatened miscarriage **overall**. However, an increase in live births was observed in the subgroup of women with early pregnancy bleeding and a history of previous miscarriages" (emphasis added).[35]

32. The key to understanding the results of this important PRISM study lies in the word "significantly higher." The actual final results of the PRISM study state: "The live birth rate was 75% (1513 out of 2025 participants) in the progesterone group compared with 72% (1459 out of 2013 participants) in the placebo group (relative rate 1.03, 95% confidence interval 1.00 to 1.07; p = 0.08)."

33. While it is true that the overall higher survival with progesterone did not meet statistical significance, nonetheless, the study did show a higher survival with progesterone, and

---

[32] Progesterone: Risks and Benefits, Society for Assisted Reproductive Technology, https://www.sart.org/patients/a-pafients-guide-to-assisted-reproductive-technology/stimulation/progesterone/

[33] Prac. Comm. of the Am. Soc. for Reprod. Med., *Progesterone Supplementation During the Luteal Phase and in Early Pregnancy in the Treatment of Infertility: An Educational Bulletin*, Fert. Steril. 789 (2008).

[34] ECF No. 53-6, Schreiber Decl. ¶ 28.

[35] Arri Coomarasamy, et al., *Progesterone to prevent miscarriage in women with early pregnancy bleeding: the PRISM RCT*, 24 Health Technol Assess. 1-70 (2020).

in fact identified a subgroup of women with recurrent miscarriages in which progesterone supplementation demonstrating increasing efficacy toward survival:

> A significant subgroup effect (interaction test p = 0.007) was identified for prespecified subgroups by the number of previous miscarriages: none (74% progesterone vs. 75% placebo; relative rate 0.99, 95% confidence interval 0.95 to 1.04; p = 0.72); one or two (76% progesterone vs. 72% placebo; relative rate 1.05, 95% confidence interval 1.00 to 1.12; p = 0.07); and **three or more (72% progesterone vs. 57% placebo; relative rate 1.28, 95% confidence interval 1.08 to 1.51; p = 0.004**), thus demonstrating a biological gradient by the increasing number of previous miscarriages. [36]

34. In addition, the study found that for later pregnancies:

> [T]here was evidence that progesterone may increase the rate of ongoing pregnancy at 12 weeks (83% in the progesterone group vs. 80% in the placebo group; relative rate 1.04, 95% confidence interval 1.01 to 1.07; p = 0.01). [37]

35. And finally, but importantly, the study states: "There was no evidence of a difference in the safety outcomes,"[38] which means that there was no evidence of any safety concerns with the administration of progesterone in early pregnancy.

Further, page three of the 2020 publication of the PRISM study also included a review of the six previous studies of progesterone supplementation in threatened miscarriage, all of which demonstrated that progesterone supplementation increased survival rate.[39] Further, the 2020 PRISM study goes on to note:

> More recently, a Cochrane review on this question summarized evidence from seven studies (see Table 1). The review found that the studies were small with methodological weaknesses (the largest study had a sample size of 191) but the pooled analysis found a significantly lower risk of miscarriages among women who received progesterone than among those who received placebo or no treatment (risk ratio 0.64, 95% CI 0.47 to 0.87).[40]

---

[36] *Id.*
[37] *Id.*
[38] *Id.*
[39] *Id.*
[40] *Id.*

36. Thus, the 2019 study cited by Schreiber, in its final analysis does not provide any evidence that progesterone use after mifepristone is ineffective, and in fact, the 2020 final analysis of that database suggests the opposite.

37. My point is confirmed by an additional publication in 2020 by the PRISM study authors in which they comment on the discrepancy between the conclusions of the 2019 NEJM article cited by Schreiber, and their final analysis:

> The *New England Journal of Medicine* article on the PRISM trial noted a 3% increase in live birth rate with vaginal micronized progesterone, but suggested it was a negative result, as the *P* value associated with this finding was .08.[10] However, our interpretation of the PRISM trial in this review takes into account the totality of available evidence, suggesting a potential role for progesterone for women at high risk of a miscarriage. We propose the apparent discordance between the published *New England Journal of Medicine* manuscript[10] and our interpretation relates to the issue of statistical inference vs scientific inference. Statistical inference focuses on hypothesis testing. Scientific inference, in contrast, not only considers any statistical uncertainty in the findings but in addition takes into account the full extent of all other evidence, to make a considered judgement. The American Statistical Association (ASA) has issued a series of 44 instructive articles on drawing scientific inferences from studies.[11] Appreciation of the key messages from these ASA articles is essential for making clinical sense of the PROMISE and PRISM trials.
>
> The ASA's statements recommend that "scientific conclusions or policy decisions should not be based on only whether a *P*-value passes a specific threshold" and "no single index should substitute for scientific reasoning."[11] Further, the ASA states that "practices that reduce data analysis or scientific inference to mechanical 'bright-line' rules (such as $P<.05$, or equivalent confidence intervals) for justifying scientific claims or conclusions can lead to erroneous beliefs and poor decision making."[11] The ASA notes "a conclusion doesn't immediately become 'true' on one side of the divide ($P<.05$) and 'false' on the other," and the ASA recommends that phrases such as "statistically significant" and "statistically nonsignificant" are no longer used. Instead, the ASA recommends that researchers bring many contextual factors into play to derive scientific inferences, including the design of the study, replicability, and other external evidence.[41]

[41] Arri Coomarasamy, et al., *Micronized vaginal progesterone to prevent miscarriage: A Critical Evaluation of Randomized Evidence*, 223 AM. J. OBSTETRICIANS GYNECOLOGISTS 167-76 (2020).

38. Schreiber cites a 2015 review of mifepristone research.[42] However, this review was published prior to the 2018 chart review by Delgado and in fact does not support the claim that progesterone use after mifepristone is ineffective. Rather, it states that there is insufficient evidence in 2015. Similarly, the 2018 article cited by Schreiber does not support the claim that progesterone is not effective, but rather confuses statistical and scientific inferences, as I addressed above in the quotation from the authors of the PRISM study.

39. Schreiber quotes a 2020 publication from ACOG which states: "[t]here is no evidence that treatment with progesterone after taking mifepristone increases the likelihood of the pregnancy continuing."[43] However, in that same document,[44] ACOG contradicts itself by citing studies which provide evidence that supplementation with the synthetic progestin depo-provera does in fact lead to an increase in ongoing pregnancies:

> Concern has been raised that the immediate use of hormonal contraception that contains progestins could theoretically interfere with medication abortion efficacy. Etonogestrel implant use does not affect medication abortion outcomes (121, 122). However, DMPA injection at the time of mifepristone administration may slightly increase the risk of an ongoing pregnancy (119). In a randomized trial that evaluated the effects of DMPA injection timing on medication abortion outcomes, ongoing pregnancy was more common among those randomized to receive DMPA injection on the day of mifepristone administration compared with those who received DMPA at a follow-up visit (3.6% versus 0.9%; 90% CI, 2.7 [0.4–5.6]).[45]

So, in fact, ACOG, in the same practice bulletin, is acknowledging the fact that the progestin compound, depo-provera, increases the rate of ongoing pregnancies after mifeprex while providing evidence that use of progesterone-like compounds shortly after mifeprex can lead to an increase in ongoing pregnancies.

---

[42] ECF 53-6, Schreiber Decl. ¶ 43.
[43] *Id.* ¶ 46.
[44] Am. Coll. of Obstetricians & Gynecologists and Soc'y of Family Planning, *Practice Bulletin No. 225: Medication Abortion up to 70 Days of Gestation*, 136 OBSTETRICS & GYNECOLOGY 1, 3 (2020).
[45] *Id.*

40. An additional study, quoted by Schreiber, actually demonstrates the effectiveness of progesterone to reverse the effects of mifepristone.[46] The study by Creinin involved, at the end, a total of ten patients. Five of these ten patients received mifeprex and placebo. The other five received mifeprex and natural progesterone. The study results state:

> Among the remaining 10 patients (five per group), gestational cardiac activity continued for 2 weeks in four in the progesterone group and two in the placebo group.[47]

That means that four out of the five patients in the progesterone group, i.e., 80%, had a living fetus at two weeks after progesterone.

41. In contrast, two out of the five patients who did not receive progesterone, i.e., 40%, had a living fetus at two weeks after progesterone. So, progesterone supplementation doubled the rate of survival in this small trial.

42. What is even more interesting is the examination of those women who had hemorrhage. The results state:

> Severe hemorrhage requiring ambulance transport to hospital occurred in three patients; one received progesterone (complete expulsion, no aspiration) and two received placebo (aspiration for both, one required transfusion).[48]

So, in the group of five women who received progesterone, one woman went to the ER with hemorrhage; her hemorrhage, however, had stopped by the time she reached the ER, and she received no treatment.

43. In contrast, out of the group of five women who did not receive progesterone, two women ended up in the ER. Both had to have emergency D&Cs to stop the bleeding and one of them ended up with a transfusion. The study was stopped for safety considerations due to

---

[46] ECF No. 53-6, Schreiber Decl. ¶ 50.
[47] Creinin , M.Y. Hou , L. Dalton , R. Steward , M.J. Chen , *Mifepristone Antagonization With Progesterone to Prevent Medical Abortion: A Randomized Controlled Trial,* Obstetricians Gynecology, (Jan. 2020) .
[48] *Id.*

hemorrhage in the group that did not receive progesterone. The authors, in an amazing feat of gymnastics, speculated that the cause of the hemorrhage was a lack of the second drug, misoprostol. But that conclusion is incoherent and unsupported by their data, as the group which received progesterone and did not receive misoprostol, had a lower hemorrhage rate and no need for surgical intervention.

44. In fact, the speculation that a lack of misoprostol is the reason for hemorrhage is not supported by a recent analysis of all adverse events submitted to the FDA after the use of mifepristone as an abortifacient.[49] In that review, the rate of hemorrhage for women who received both mifepristone and misoprostol was higher than the rate of hemorrhage for women who received misoprostol alone.[50] The results state: "Hemorrhage occurred more often in those who took mifepristone and misoprostol (51.44%) than in those who took mifepristone alone (22.41%)."

45. The extensive usage of progesterone in the IVF industry has allowed us to know, for decades now, that using natural progesterone in pregnancy is safe. Nevertheless, Plaintiffs' doctors errantly speculate, without scientific support, that patients are at increased risk of stillbirth or birth defects in their pregnancies when they are exposed to natural progesterone.[51]

46. Dr. Schreiber further states that: "[i]nvestigators also have reported associations with hypospadias, a defect in the male infant's genitalia, occurring in the male infants born to women who used progestins (synthetic or pharmacologic progesterones) during pregnancy."[52] Both of these claims are misleading because the studies cited do not use natural progesterone, but rather used progestins — synthetic chemicals similar to progesterone in some ways, but

---

[49] Aultman K, et al., *Deaths and Severe Adverse Events after the use of Mifepristone as an Abortifacient from September 2000 to February 2019*, 36 ISSUES L. MED. 3-26 (2021).
[50] *Id.*
[51] ECF 53-6, Schreiber Decl. ¶ 49.
[52] *Id.*

which contain actions and side effects which progesterone does not have[53] In the end, there is simply no evidence that natural progesterone has ever, after decades of its widespread use in pregnancy, been shown to increase the risk of birth defects.

47. Given the long history of progesterone use in pregnancy, the established safety of progesterone use in early pregnancy for both the mother and her fetus in IVF pregnancies, the known ability of progesterone to counteract the abortive effects of mifepristone in animal models, and the actual evidence of progesterone allowing numerous women to save their babies, it is scientifically proper to use this medication in those women who are desperate to save their pregnancies after regretting the start of their mifepristone abortion attempt..[54]

48. In summary, using natural progesterone to counter the effects of ingested mifepristone is logical, medically speaking, and founded on basic principles of biochemistry, animal studies, and analysis of human experience.

II. Plaintiffs' doctors are wrong to disregard the Delgado and Davenport publications

49. Plaintiffs' doctors argue that Dr. Delgado's publications are worthless as scientific evidence. Although they are not perfect, Dr. Delgado's efforts, and the many women included therein, cannot just be ignored, especially given that no scientific studies to date have been performed that point in the opposite direction.

50. Dr. Schreiber opines at great length about Institutional Review Board (IRB) approval in the 2018 Delgado paper. Similarly, Dr. Schreiber states, without evidence, that the 2018 Delgado paper was withdrawn.[55] Both are incorrect. The 2018 Delgado paper was temporarily removed, but not withdrawn, and it is now restored, published, and available online.

---

[53] Soc. for Assisted Reprod. Tech., *Progesterone: Risks and Benefits*, https://www.sart.org/patients/a-patients-guide-to-assissted-reproductive-technology/stimulation/progesterone/.
[54] Am. Assoc. of Pro-Life Obstet. and Gynecol., *Practice Bulletin 6: The Reversal of the Effects of Mifepristone by Progesterone 2019*, https://aaplog.org/wp-conten/uploads/2020/01/FINAL-PB-6-Abortion-Pill-Reversal-1.pdf
[55] ECF 53-6, Schreiber, Decl. ¶ 36.

The final 2018 Delgado paper states clearly: "The study was reviewed and approved by an institutional review board." These complaints are spurious.

51. Dr. Schreiber implies there was no control group in the 2018 Delgado retrospective chart review.[56] This is erroneous. As explained above, there was a historical control group previously published in the Davenport paper, which gives the rate of embryo survival after the use of mifepristone at 10-23%. Dr. Delgado and his co-authors assumed a survival rate above that figure (25%).

52. Nevertheless, Dr. Schreiber implies that no valid scientific conclusions can be drawn from the 2018 Delgado paper since the underlying data did not include a concurrent placebo control group.[57] This is ironic, and rather amazing given that the FDA's original approval of mifepristone as an abortifacient was based on non-blinded, non-randomized studies (Spitz[58] and French manufacturer data) that also had no concurrent placebo control group. Indeed, the FDA statistical review of the application for mifepristone approval for abortion states: "In the absence of concurrent control group in each of these studies, it is a matter of clinical judgment whether or not the sponsor's proposed therapeutic regimen is a viable alternative to uterine aspiration for the termination of pregnancy."[59]

53. In my experience reviewing clinical trials of mifepristone abortions around the world since 1998, I have never seen a clinical trial of mifepristone abortions which has a concurrent placebo control group. Study design for these trials is either historical control, as in the Spitz study, or a dose comparison study. Placebo control, in the context of medical abortion, has been considered unethical because it would require women who choose an abortion to be given a

[56] ECF 53-6, Schreiber, Decl. ¶ 25.
[57] ECF 53-6, Schreiber, Decl. ¶ 24-26.
[58] I.M. Spitz et al., *Early Pregnancy Termination with Mifepristone and Misoprostol in the United States*, 338 NEJM, 1241, 1241-1247 (1998).
[59] B.C. Calhoun & D.J. Harrison, *Challenges to the FDA Approval of Mifepristone*, 38 ANN PHARMACOTHER, 163, 163-68 (2004).

placebo rather than a chance at the abortion. The same ethical concerns would obviously apply here, where a true control would require giving women seeking reversal a placebo, thus, increasing her chances of losing her baby. Dr. Schreiber never acknowledges this seeming double standard, or the obvious problem it creates with her current position regarding Dr. Delgado's publications.

54. Dr. Schreiber also claims that the 2018 Delgado paper potentially overestimates survival and reversal success rates because an ultrasound was done to determine whether or not the child was still alive prior to administering progesterone.[60] This is ludicrous. The whole point of the 2018 Delgado case series was to determine whether progesterone could keep a human embryo alive after exposure to mifepristone. An already dead fetus would have no relevance to this question, and it would be absurd and scientifically invalid to administer progesterone in the case of a known fetal death or to include those patients in the analysis.

55. Dr. Schreiber claims that the design of the 2018 Delgado paper does not conform to the expectations of a prospective randomized trial.[61] But the 2018 Delgado study is not a prospective randomized trial; rather, it is explicitly a retrospective case series based on a chart review. Dr. Schrieber even admits this.[62] Yet, despite acknowledging that the paper is a retrospective chart review at 41, Schreiber errantly claims [at para 36] that the paper was a prospective analysis,[63] and then opines at length how the paper does not fit a prospective analysis. This complaint is spurious.

56. In addition to all of the other evidence discussed above, the 2018 Delgado case series, combined with the Davenport historical control, suggests that progesterone treatment can increase her baby's chance of survival from approximately 25% to approximately 68%. Women should be informed of this potentially life-saving treatment, especially given the fact that a reversal

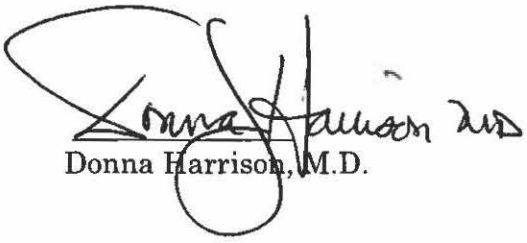
[60] ECF 53-6, Schreiber, Decl. ¶ 31, 40.
[61] ECF 53-6, Schreiber, Decl. ¶ 41-45.
[62] ECF No. 53-6, Schreiber Decl. ¶ 41.
[63] ECF 53-6, Schrieber Decl. ¶ 36.

attempt only involves the administration of a known natural hormone that has been safely used in the infertility industry for over 50 years. Contrary to Plaintiffs' doctors' insinuations, women are perfectly capable of understanding nuance and the difference between a proven remedy and a potential remedy.

57. Women who are truly sure of their decision to abort will not be harmed by information about the efficacy of medical abortions and the availability of potential remedies. Requiring informed consent to include the possibility of reversal will give women who are unsure, or who change their minds, enhanced reproductive options. These women exist, and they deserve to know their medical options.

I declare under penalty of perjury that the foregoing is true and correct to the best of my knowledge.

This declaration was executed on June 14, 2021.



Donna Harrison, M.D.

DONNA HARRISON M.D.

EXECUTIVE DIRECTOR
AMERICAN ASSOCIATION OF PRO-LIFE OBSTETRICIANS AND GYNECOLOGISTS

CONTACT

PHONE:
202 230-0997

WEBSITE:
www.aaplog.org

EMAIL:

donna@aaplog.org

Dr. Donna Harrison is a physician, board-certified in obstetrics and gynecology. She is currently serving as Executive Director of the American Association of Pro-Life Obstetricians and Gynecologists, the largest non-sectarian pro-life physician organization in the world, with over 4000 members across the United States, and associate members on every continent. Under her leadership, AAPLOG has doubled membership, launched the annual Matthew Bulfin Educational Conference, developed an up to date website and social media presence, and launched systematic outreaches to the medical, legal and policy communities to discuss the effects of abortion on women.

Dr. Harrison's research interests include Selective Progesterone Receptor Modulators, Endometrial Contraception, Maternal mortality, and Abortion Mortality and Morbidity. She has authored peer reviewed papers on the approval of RU-486 and on Ulipristal (Ella) as well as on the embryocidal potential of hormonal contraception. Dr. Harrison is a Continuing Medical Education Speaker in the United States and internationally on topics of Medical Abortion with Mifepristone and Misoprostol, Adverse Events associated with Mifepristone and Misoprostol, Emergency Contraception with Ulipristal, Maternal Mortality, and Abortion Morbidity.

She is an Adjunct Professor at Trinity International University in Deerfield, IL, teaching post graduate seminars at the annual Center for Bio Ethics and Human Dignity summer workshops. She is Associate Editor of the peer reviewed medical journal "Issues in Law and Medicine".

Dr. Harrison is married to Dr. Mark Harrison M.D, and is the mother of 5 children and 5 grandchildren.

Donna J. Harrison M.D. dip. A.B.O.G. Professional Credentials

PROFESSIONAL CERTIFICATION AND LICENSURE

- **1993-current. Diplomat of the American Board of Obstetrics and Gynecology (ABOG)**
- **1986-current. State of Michigan Board of Physician Licensing Unrestricted Medical License**
- **1997-1999. American Institute of Ultrasound in Medicine (AIUM)** (voluntary non-renewal)

EDUCATION

Medical Education:

- **1986-1990 Residency in Obstetrics and Gynecology St. Joseph Mercy Hospital, Ypsilanti, MI (affiliate of University of Michigan)**
- **1982-1986 University of Michigan Medical School, Ann Arbor, MI (top 10% of graduating class)**
- **1984 (summer) University of Arizona School of Medicine Tucson, AZ International Health Intensive**

Undergraduate Education:

- **1978-1982 Michigan State University, E. Lansing, MI. Honors Biochemistry B.S. + Chemistry B.A.**
- **1978 University of Iowa Summer Science Intensive Rocky Mountain and Boundary Waters**
- **1977 Michigan State University Summer Science Research Program Soil Science Division**

PROFESSIONAL EXPERIENCE

- **2000 – current. American Association of Pro-Life Obstetricians and Gynecologists**
  - 2013 - current. Executive Director
  - 2011 - 2013. Director of Research and Public Policy
  - 2008 - 2011 President
  - 2006 – 2008 President-Elect
  - 2000 – 2006 Chairman, Subcommittee on Mifepristone (RU-486)

- **Lakeland Regional Health System Affiliate Hospitals**

  - **1993-2000 Obstetrician/Gynecologist Private Practice Southwestern Medical Clinic, P.C**
    1995-1998 Chairman, Department of Obstetrics and Gynecology
    Lakeland Regional Health Systems, Berrien Center, MI
    1996-1999 Chairman, Quality Improvement Committee

- **University of Michigan and Affiliate Hospitals**

  - **1991-1993 Clinical Associate Professor Obstetrics and Gynecology**
    University of Michigan Medical Center 1500 E. Medical Center Dr. Ann Arbor, MI 48109

  - **1991-1993 Obstetrician/Gynecologist Private Practice Leland, Fleming, Dindoffer and Associates** R2106 Reichert Health Bldg. 5333 McAuley Dr. Ypsilanti, MI 48197

INTERNATIONAL AND DOMESTIC MEDICAL SERVICE

Visiting Lecturer Mt. Hope Nursing Schools (Bamenda and Buea Cameroon) 2014, 2017

Consultant physician, Tet Kole Nan Kris Clinic, Montrois, Haiti. 1989-1994 Trained community health workers and ran indigenous medical clinic.

Volunteer Physician, Hope Clinic, Ypsilanti, MI. 1986-1990 Provided medical care at free clinic for low income patients.

Visiting Physician, Tiruvalla Medical Mission, Kerala, India. July-Aug, 1988 provided medical and surgical care. July 1988.

Volunteer Medical Student, Hospital le Bon Samaritan, Limbe, Haiti. June-Aug, l986 provided medical care at one of the largest hospitals in Northern Haiti.

ACADEMIC HONORS

American Business Womens Scholarship recipient 1978

National Merit Scholar 1978-82

Harry S. Truman Public Policy Scholar 1980-1984

Rhodes Scholarship Competition Semi-Finalist for Ohio 1981

SELECTED PUBLICATIONS

Doctors Who Perform Abortions: Their Characteristics and Patterns of Holding and Using Hospital Privileges.
Studnicki J, Longbons T, Fisher JW, Harrison DJ, Skop I, MacKinnon SJ.
Health Serv Res Manag Epidemiol. 2019 Apr 15;6:2333392819841211. doi: 10.1177/2333392819841211. eCollection 2019 Jan-Dec. PMID: 31020009

Danish-like Regulations May Improve Postabortion Mental Health Risk. Sullins DP, Harrison D.
JAMA Psychiatry. 2019 Jan 1;76(1):99-100. doi: 10.1001/jamapsychiatry.2018.2602. No abstract available. PMID:30422159

Treatment of an Ectopic Pregnancy: An Ethical Reanalysis. Condic ML, Harrison D.
Linacre Q. 2018 Aug;85(3):241-251. doi: 10.1177/0024363918782417. Epub 2018 Jun 18.PMID:30275609

A second opinion: response to 100 professors. Wechter D, Harrison D, Adams R Sr, Beard S, Blaskiewicz R, Bush F, Calhoun B, Cirucci CA, Christiansen S, Cook C, Davenport M, DeCook J, Delgado G, Dood JJ, Dotto M, Dumpe K, Friedman WH, Glass T, Gray TL, Gray JP, Hale KA, Hersh C, Hines J, Jackson A, Johannson J, Keenan JA, Linn J, Long JD, Marshall JF, McDonald DP, McCloskey L, Mickelson J, Pestoff MR, Parker EW Jr, Sawyer AT, Schwering C, Seale F, Schoutko W, Showalter A, Skakalski T, Skop I, Smith LF, Stalter W, Steele A, Thiele SA, Varasteh N, Ward DG, Wittingen JA. Issues Law Med. 2014 Spring;29(1):147-64.PMID:25189014

No Prenatal Diagnosis = Saved Lives.
Rodriguez E, Harrison DJ. Linacre Q. 2012 Feb;79(1):7-8. doi: 10.1179/002436312803571492. Epub 2012 Feb 1. No abstract available. PMID:30082954

Introduction to the International Working Group for Global Women's Health Research 2010 Symposium Proceedings.
Harrison DJ. Linacre Q. 2011 May;78(2):190-191. doi: 10.1179/002436311803888429. Epub 2011 May 1. No abstract available. PMID:30082942

Defining reality: the potential role of pharmacists in assessing the impact of progesterone receptor modulators and misoprostol in reproductive health. Harrison DJ, Mitroka JG. Ann Pharmacother. 2011 Jan;45(1):115-9. doi: 10.1345/aph.1P608. Epub 2010 Dec 21. PMID: 21177418

Analysis of severe adverse events related to the use of mifepristone as an abortifacient. Gary MM, Harrison DJ. Ann Pharmacother. 2006 Feb;40(2):191-7. Epub 2005 Dec 27. PMID: 16380436

Challenges to the FDA approval of mifepristone. Calhoun BC, Harrison DJ.Ann Pharmacother. 2004 Jan;38(1):163-8. No abstract available. PMID:14742814