

August 2, 2023

Via Electronic Transmission

Colorado Board of Medicine
Colorado Board of Nursing
Colorado Board of Pharmacy
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**Re: 46 Colo. Reg. 157-58, Proposed Rules and Regulations Regarding
Generally Accepted Standards of Medical Practice Regarding
Pregnancy-Related Services**

To Whom It May Concern:

Together, the American College of Obstetricians and Gynecologists (“ACOG”), the Society for Maternal-Fetal Medicine (“SMFM”), and the Society for Family Planning (“SFP”) appreciate the opportunity to provide scientific and medical information related to the “Proposed Rules and Regulations Regarding Generally Accepted Standards of Medical Practice Regarding Pregnancy-Related Services” (the “Proposed Rule”)¹ published by the Colorado medical board, the state board of pharmacy, and the state board of nursing (collectively, the “Board”),

¹ 46 Colo. Reg. 157-58 (July 2023).

regarding whether “medical abortion reversal”² is a generally accepted standard of practice.³

ACOG is the nation’s leading association of physicians providing health care for women.⁴ With more than 62,000 members, ACOG advocates for quality health care for women, maintains the highest standards of clinical practice and continuing education of its members, promotes patient education, and increases awareness among its members and the public of the changing issues facing women’s health care. ACOG supports and represents members in all 50 states and U.S. territories, the three branches of the U.S. armed forces, as well as over 24 affiliates in Latin America, Central America, the Caribbean, and Canada.⁵ ACOG’s medical practice guidelines have been cited by numerous authorities, including the U.S. Supreme Court and state supreme courts, as a leading provider of authoritative scientific data regarding childbirth and abortion.⁶

² For purposes of this comment, “abortion reversal” includes “medical abortion reversal” and “abortion pill reversal.” Legislatures, state courts, organizations, and physicians have used varying language, but “abortion reversal” in this comment describes all instances in which a provider attempts to “reverse” or provides care that the provider claims can “reverse” the effects of a medication abortion, abortion pill regimen, or nonsurgical abortion. Additionally, “abortion reversal” will be used in quotations because the use of the word “reversal” does not accurately describe the treatment administered. “Reversal” implies cancellation or nullification, and there is no evidence that “abortion reversal” cancels or nullifies the effects of a medication abortion.

³ See Concerning Policies to Make Punishable Deceptive Actions Regarding Pregnancy-Related Services, Colo. Rev. Stat. Ann. §§ 6-1-105, 6-1-734, 12-30-120, 25-6-402 (2023).

⁴ *About*, ACOG, <https://www.acog.org/about> (last visited Jul. 31, 2023).

⁵ *Districts & Sections*, ACOG, <https://www.acog.org/community/districts-and-sections> (last visited Jul. 31, 2023).

⁶ See, e.g., *American Medical Association v. Stenehjem*, 412 F.Supp.3d 1134, 1142 (D. N.D. 2019) (“I find ACOG to be a reliable, well-respected, source on best practices in obstetric and gynecological care that has an obligation to support evidence-based reproductive health care.”); *June Med. Servs. LLC v. Russo*, 140 S. Ct. 2103 (2020); *Whole Woman’s Health v. Hellerstedt*, 579 U.S. 582 (2016); *Stenberg v. Carhart*, 530 U.S. 914, 932–936 (2000) (quoting ACOG extensively and referring to ACOG’s work as among the “significant medical

SMFM is the medical professional society for maternal-fetal medicine subspecialists, who are obstetricians with additional training in high-risk pregnancies. SMFM was founded in 1977, and it represents more than 6,500 members who care for high-risk pregnant people.⁷ SMFM provides education, promotes research, and engages in advocacy to advance optimal and equitable perinatal outcomes for all people who desire and experience pregnancy. All clinical guidelines by SMFM follow an established methodology, including the grading of scientific literature, suggestions from experts, and a multi-level internal peer-review process for randomized clinical trials.⁸ SMFM’s briefs also have been cited by courts in cases raising a variety of medical issues.⁹

authority” supporting the comparative safety of the abortion procedure at issue); *Hodgson v. Minnesota*, 497 U.S. 417, 454 n.38 (1990) (quoting ACOG in assessing disputed parental notification requirement); *Simopoulos v. Virginia*, 462 U.S. 506, 517 (1983) (citing ACOG in discussing “accepted medical standards” for the provision of obstetric-gynecologic services, including abortions); *Planned Parenthood S. Atl. v. State*, 882 S.E.2d 770, 787–788 (S.C. Jan 5, 2023) (citing ACOG’s practice guidance as authority in opinion considering whether an abortion ban violates the state constitution); *Hodes & Nauser, MDs, P.A. v. Schmidt*, 440 P.3d 461, 505 (Kan. 2019) (Biles, J., concurring) (citing ACOG’s practice guidance as medical authority in opinion that considered whether Kansas recognizes the state constitutional right to abortion); see also *Gonzales v. Carhart*, 550 U.S. 124, 170–71, 175–78, 180 (2007) (Ginsburg, J., dissenting) (referring to ACOG as “experts” and repeatedly citing ACOG’s brief and congressional submissions regarding abortion procedure).

⁷ *What is the Society for Maternal-Fetal Medicine?* SMFM, <https://www.smfm.org/what-is-the-society> (last visited Aug. 1, 2023).

⁸ SMFM, *SMFM Clinical Practice Guidelines Development Process*, https://s3.amazonaws.com/cdn.smfm.org/media/2569/Guidelines_Dev_Process_Public_for_website2.pdf (last visited Aug. 1, 2023).

⁹ See, e.g., *Mayor of Baltimore v. Azar*, 973 F.3d 258, 285 & n.19 (4th Cir. 2020) (quoting amicus brief by ACOG, SMFM and other medical organizations supporting challenge to federal rule prohibiting physicians and other clinicians in Title X programs from referring patients for abortion, and noting that ACOG and SMFM are “reputable and nonpartisan medical organizations”).

The SFP vision is just and equitable abortion and contraception informed by science.¹⁰ SFP represents more than 1,500 top-of-their-field clinicians, scholars, and partners united by a shared interest in advancing the science and clinical care of family planning. The pillars of SFP’s strategic plan are: 1) convening a diverse, equitable, inclusive, and multidisciplinary community of all engaged in the science and medicine of abortion and contraception; 2) supporting the production and resourcing of research primed for impact; 3) organizing and leveraging research primed for impact; 4) ensuring clinical care is evidence-informed and person-centered through guidance, medical education, and other activities; 5) developing and supporting leaders in abortion and contraception to transform healthcare systems; and 6) aligning the organization’s governance, operations, and overall resources to be in service of the strategies designed to bring our collective vision to life.¹¹

We take seriously our responsibility to represent physicians involved in critical medical care for pregnant individuals. ACOG, SMFM, and SFP recognize the deep expertise of clinicians practicing in these care settings. However, when a very small minority of clinicians rely on misinformation and unsupported claims to guide their medical care, it is our responsibility to emphasize the generally accepted standard of medical practice based on evidence and research.

We are pleased to see that the Proposed Rule emphasizes the importance of “practic[ing] evidence-based medicine” and requires licensees to “exercise the same degree of knowledge, skill, and care” as others in the same field of medicine.¹² We further support the Board’s focus on “the tenets of the school of practice to which

¹⁰ *About*, Society for Family Planning, <https://societyfp.org/about/> (last visited Aug. 2, 2023).

¹¹ *Strategic Plan*, Society for Family Planning, <https://societyfp.org/about/strategic-plan/> (last visited Aug. 2, 2023).

¹² 46 Colo. Reg. 157-58 (July 2023).

the licensee professes to follow.” In addition, we support the Proposed Rule’s focus on protecting patients from deceptive and dangerous practices masquerading as medical care and acknowledging that “fully informed consent” is a critical component to medical care.

However, based on our significant expertise in obstetrics, gynecology, high-risk pregnancies, and medical research, it is our view that “abortion reversal” is not a generally accepted standard of practice based on the current evidence base. ACOG guidance states that “[c]laims regarding abortion ‘reversal’ treatment are not based on science and do not meet clinical standards.”¹³ Making a determination that the conduct is not a generally accepted standard of practice will help protect patients in Colorado from this misleading and harmful practice.

This comment will first show that “abortion reversal” is unsupported by scientific evidence. It will then explain that what evidence exists suggests the opposite; “abortion reversal” can in fact increase the risk of physical and mental harm to patients. It will then discuss how the promotion of “abortion reversal” is misleading and in violation of medical ethics guidelines.

¹³ *Facts Are Important: Medication Abortion “Reversal” Is Not Supported by Science*, ACOG, <https://www.acog.org/advocacy/facts-are-important/medication-abortion-reversal-is-not-supported-by-science> (last visited Jul. 10, 2023) [hereinafter “*Facts Are Important*”].

I. Background

A. Medication Abortion

Medication abortion is currently the most common method of abortion in the United States.¹⁴ Medication abortion is a two-medication regimen consisting of mifepristone and misoprostol.¹⁵ Mifepristone blocks progesterone, which is needed for the continuation of a pregnancy.¹⁶ Misoprostol then causes uterine contractions to expel the pregnancy tissue and is taken within six to 48 hours of ingesting mifepristone.¹⁷ The two-step regimen is 97% effective for patients up to 10 weeks' gestational age, and serious complications occur in less than one percent of patients.¹⁸

While the anti-abortion movement has advanced the notion that individuals often regret their abortions, studies show the opposite.¹⁹ Patients are most likely to experience relief after an abortion, rather than regret or other negative emotions;

¹⁴ Sara K. Redd et al., *Medication Abortion “Reversal” Laws: How Unsound Science Paved the Way to Dangerous Abortion Policy*, 113 Am. J. Pub. Health 202, 202 (2023) (noting that medication abortions account for 54% of all nonhospital abortions as of 2020).

¹⁵ Sandee LaMotte, *How a Medication Abortion, Also Known as an “Abortion Pill,” Works*, CNN Health (May, 11 2023, 4:57 AM), <https://www.cnn.com/2023/01/06/health/medication-abortion-process-wellness/index.html>.

¹⁶ *Id.*

¹⁷ *Id.*

¹⁸ Rebecca H. Cohan & Stephanie B. Teal, *Medication Abortion*, 328 *Jama Network* 1779, 1779 (2022), <https://jamanetwork.com/journals/jama/fullarticle/2795652>; Daniel Grossman, et al., *Continuing Pregnancy After Mifepristone and “Reversal” of First-Trimester Medical Abortion: A Systematic Review*, 92 *Contraception* 206 (2015).

¹⁹ See Laura Kurtzman, *Five Years After Abortion, Nearly All Women Say It Was the Right Decision, Study Finds*, U.C.S.F. (Jan. 13, 2020), <https://www.ucsf.edu/news/2020/01/416421/five-years-after-abortion-nearly-all-women-say-it-was-right-decision-study> (referring to the overview and other physician commentary on the study).

this remains true at every point throughout a five-year period after the abortion.²⁰ Clinicians counsel patients regarding all options and confirm that a patient is sure in their decision before moving forward with the abortion process.²¹ In addition, once an individual begins the medication abortion process—i.e., taking mifepristone—less than 0.005% change their mind and wish to continue their pregnancy. For those individuals, the current general standard of medical care is expectant management.²²

B. “Abortion Reversal.”

Certain anti-abortion physicians and organizations have promoted a regimen that they claim negates the effects of mifepristone. “Abortion reversal” is an unsupported practice that purports to “reverse” a medication abortion, following the administration of mifepristone, with doses of progesterone. This practice also involves a patient not taking misoprostol, the second medication in the two-step regimen of medication abortion. There is no reliable evidence to support this

²⁰ Corrine H. Rocca, et al., *Emotions and Decision Rightness Over Five Years Following an Abortion: An Examination of Decision Difficulty and Abortion Stigma*, 248 Soc. Sci. & Med., Mar. 2020, at 1.

²¹ ACOG, *Informed Consent and Shared Decision Making in Obstetrics and Gynecology* (Feb. 2021) <https://www.acog.org/-/media/project/acog/acogorg/clinical/files/committee-opinion/articles/2021/02/informed-consent-and-shared-decision-making-in-obstetrics-and-gynecology.pdf> (explaining that physicians are ethically obligated to provide patients with “adequate, accurate, and understandable information,” give patients “the ability to understand and reason through this information” and to “ask questions and to make an intentional and voluntary choice, which may include refusal of care or treatment”).

²² LaMotte, *supra* note 15; see also ACOG, *Medication abortion up to 70 days of gestation* (Oct. 2020), <https://www.acog.org/clinical/clinical-guidance/practice-bulletin/articles/2020/10/medication-abortion-up-to-70-days-of-gestation>. Expectant management is the practice of “letting tissue pass on its own.” Dr. Rebecca Cohen, *What Happens After a Miscarriage? An Ob-Gyn Discusses the Options*, ACOG, <https://www.acog.org/womens-health/experts-and-stories/the-latest/what-happens-after-a-miscarriage-an-ob-gyn-discusses-the-options> (last visited Aug. 2, 2023).

practice; it is not proven to be safe or effective, is often presented to patients in a way that is misleading, and is potentially dangerous.

II. “Abortion Reversal” Is Unsupported by Scientific Evidence.

Since the concept of “abortion reversal” was developed, it has been an experimental process with no quality scientific evidence supporting its safety or efficacy. Existing evidence indicates that “abortion reversal” can harm the physical and mental health of patients. Claims supporting the practice of “abortion reversal” treatment are not based on science and do not meet clinical standards.²³

ACOG, SMFM, and SFP take seriously a clinician’s obligation to uphold a high standard of care in providing medical services to patients. ACOG issues evidence-based clinical practice guidelines and has developed evidence-based statements of policy on reproductive health care through a thorough, deliberative, and collaborative process among leading experts in the field of women’s health. Similarly, SMFM’s guideline development process includes a rigorous review and grading of the evidence in the relevant scientific literature, input of a committee of expert members, and a multilayered peer review approval process.²⁴ SFP also develops “methodologically rigorous, evidence-based clinical guidance based on existing medical literature and best practice.”²⁵ In addition, ACOG’s ethical

²³ *Medication abortion up to 70 days of gestation supra note 22; Facts are Important, supra note 13.*

²⁴ *What is the Society for Maternal-Fetal Medicine?, supra note 7.*

²⁵ *Clinical Guidance, Society for Family Planning, <https://societyfp.org/clinical-guidance/> (last visited Aug. 2, 2023).*

guidelines require of all practicing physicians “maintenance of medical competence through study, application, and enhancement of medical knowledge and skills.”²⁶

It is ACOG’s assessment that the process referred to as “abortion reversal” is not aligned with evidence-based clinical practice.²⁷ There is a significant lack of evidence as to the “abortion reversal” process’s safety and efficacy.²⁸ ACOG “ranks its recommendations on the strength of the evidence and does not support prescribing progesterone to stop a medication abortion.”²⁹ And as the American Medical Association has concluded, “[t]he fact that there are physicians experimenting with using progesterone to counteract mifepristone does not constitute credible, medically accepted evidence that the experimental practice is effective or safe.”³⁰

In response to the scientific evidence and clinical guidelines that demonstrate the risks associated with “abortion reversal,” those in support of the process point to their own research to argue that the practice is supported by science. This is not the case. As organizations representing clinicians and researchers that uphold the highest standards with respect to research and medical care, it is important for ACOG, SMFM, and SFP to thoroughly address why studies that support the practice of “abortion reversal” are fundamentally flawed and misleading.

²⁶ *Code of Professional Ethics*, ACOG 1 (2018), <https://www.acog.org/-/media/project/acog/acogorg/files/pdfs/acog-policies/code-of-professional-ethics-of-the-american-college-of-obstetricians-and-gynecologists.pdf>.

²⁷ *Medication abortion up to 70 days of gestation supra note 22; Facts are Important, supra note 13.*

²⁸ *Medication abortion up to 70 days of gestation supra note 22; Facts are Important, supra note 13.*

²⁹ *Facts are Important, supra note 13.*

³⁰ Complaint ¶ 58, *American Medical Association v. Stenehjem*, 412 F.Supp.3d 1134 (No. 19-cv-00125).

The development of the concept of “abortion reversal,” and almost all the “studies” in support of the process, can be tied to a single clinician, Dr. George Delgado (“Delgado”). The theory of “abortion reversal” is largely based on Delgado’s theory of “biologic logic,” and two papers co-authored by Delgado.³¹ None of this evidence withstands scientific scrutiny.

Delgado’s “biologic logic,” the conceptual underpinning for why “abortion reversal” might be expected to work, contends that increasing levels of progesterone during pregnancy allow progesterone molecules to “outcompete” the mifepristone molecules.³² Health care professionals and researchers have strongly questioned this theory of “abortion reversal,” arguing that “reversal theory does not make biological sense because mifepristone binds more strongly to the progesterone receptor than progesterone, and there is no evidence that the progesterone molecules will cause mifepristone to detach, or that it will ‘outcompete’ mifepristone.”³³

Delgado has published two case studies attempting to support this theory. Each has been found to be flawed and lacking scientific rigor. As one analysis

³¹ See Redd et al., *supra* note 14 (explaining how anti-abortion organizations and policymakers have heavily relied on Dr. Delgado’s initial descriptions of “abortion reversal” and his two case series). See also Nina Liss-Schultz, *This Doctor Says He Can “Reverse” Abortions*, Mother Jones (June 9, 2017), <https://www.motherjones.com/politics/2017/06/medication-abortion-pill-reversal-science-christian/>. Delgado also points to a 1998 Japanese study using rats as subjects to support the theory of “abortion reversal,” though he himself has admitted “neither biologic logic nor animal studies are sufficient to prove the safety and efficacy of his progesterone therapy on humans.” *Planned Parenthood of Tennessee v. Slatery*, 523 F.Supp.3d. 985, 992 (M.D. Tenn. 2021).

³² *Slatery*, 523 F.Supp.3d. at 992.

³³ *Id.* at 996; see also *All-Options, Inc. v. Att’y Gen. of Ind.*, 546 F.Supp.3d 754, 768 (S.D. Ind. 2021) (“[R]egardless of mifepristone’s effectiveness, adding progesterone is ‘entirely unlikely’ to prevent an abortion.”).

concluded, “[n]umerous ethical and scientific problems highlight the poor quality of these case series.”³⁴

The first “abortion reversal” paper co-authored by Delgado is a 2012 case series documenting the experiences of six women who he claims were administered progesterone after taking mifepristone.³⁵ The paper suggested that “progesterone therapy” could “reverse” the effects of mifepristone because, according to Delgado, four of the six women given progesterone after ingesting mifepristone delivered to term.³⁶ However, physicians have taken issue with how few pregnancies were reviewed in this case study, and an analysis of the case report found that “evidence is insufficient to determine whether treatment with progesterone after mifepristone results in a higher proportion of continuing pregnancies compared to expectant management.”³⁷

The second case series, which is the primary source cited by supporters of “abortion reversal,” is flawed in numerous ways. The 2018 case series is a retrospective analysis of data from 754 patients who underwent “progesterone therapy” after taking mifepristone.³⁸ Supporters of “abortion reversal” point to high

³⁴ Redd et al., *supra* note 14, at 203.

³⁵ George Delgado & Mary Davenport, *Progesterone Use to Reverse the Effects of Mifepristone*, 46 *Annals Pharmacotherapy*, Dec. 2012, <https://citeseerx.ist.psu.edu/document?repid=rep1&type=pdf&doi=406aec089e809942f4b58b6b16f0b0b4f038256b>.

³⁶ *Id.* at 2-3.

³⁷ Grossman et al., *supra* note 18, at 206.

³⁸ George Delgado, et al., *A Case Series Detailing the Successful Reversal of the Effects of Mifepristone Using Progesterone*, 33 *Issues L. & Med.* 21 (2018). *See also* Sophia Resnick, *‘Issues in Law and Medicine’: A One-Stop Journal for Anti-Vaccine, Anti-Abortion Pseudoscience*, *Rewire News Grp.* (Mar. 23, 2017, 10:59 A.M.), <https://rewirenewsgroup.com/2017/03/23/issues-law-medicine-one-stop-journal-anti-vaccine-anti-abortion-pseudoscience/> (detailing the publishing journal’s ties to fringe pseudoscience movements).

rates of continuing pregnancy to support claims that “abortion reversal” is effective.³⁹ However, “two significant limitations make [this study] unreliable.”⁴⁰ First, the study’s data was compromised. For example, of the 754 patients who had initiated “progesterone therapy,” Delgado selectively included only 547 patients based on questionable criteria that could have biased the results.⁴¹ Delgado also assumed unjustifiably that any participants who dropped out of the study following 20 weeks gestation were assumed to have completed a successful “abortion reversal,” despite having no confirmation of that occurrence.⁴² The case series also failed to consider the amount of mifepristone ingested by each patient; did not follow the same procedure for progesterone administration, including the milligrams administered, frequency and duration of the treatment, or method of treatment, such as oral or intramuscular; and made no effort to record patients’ demographic information, including their age, underlying health conditions, race, or socioeconomic status.⁴³

³⁹ See Delgado et al., *A Case Series Detailing the Successful Reversal of the Effects of Mifepristone Using Progesterone*, *supra* note 38, at 22 (concluding that “abortion reversal” is safe and effective because continuous progesterone injections and high dose oral progesterone had “reversal” rates of 64% and 68%, respectively).

⁴⁰ *All-Options, Inc.*, 546 F.Supp.3d at 766.

⁴¹ Daniel Grossman & Kari White, *Abortion “Reversal” – Legislating Without Evidence*, 379 *New Eng. J. Med.* 1491, 1492 (2018) (highlighting that the study excluded any individuals for whom an ultrasound confirmed that mifepristone had already taken effect).

⁴² Delgado et al., *A Case Series Detailing the Successful Reversal of the Effects of Mifepristone Using Progesterone*, *supra* note 38, at 25 (according to Dr. Delgado, patients experiencing miscarriage after 20 weeks gestation were considered “reversals” for the analysis because “any pregnancy loss after 20 weeks would be unlikely to be attributable to the early mifepristone exposure”).

⁴³ *Id.*

The study also did not use a legitimate control group to compare outcomes.⁴⁴ Delgado established a “historical” control group of 30 patients—a much smaller number of individuals, and ones who did not share characteristics with the patients in the case study.⁴⁵ For example, patients in the case series included those with a higher gestational age than those in the control group.⁴⁶ These gestational age differences could contribute to different levels of effectiveness of mifepristone.⁴⁷ Further, some of the patients in the case series received a lower dose of mifepristone than the patients in the control group.⁴⁸ And finally, the small number of patients in the control group could impact its reliability as a legitimate comparator.

Following the publication of this study, the University of San Diego (USD) (with whom Dr. Delgado was affiliated at the time as a volunteer professor) investigated concerns related to the article and asked him and his co-authors to

⁴⁴ Grossman & White, *supra* note 41, at 1491.

⁴⁵ *Id* (noting that the historical control group consisted of patients from studies on mifepristone in the 1980s and that Dr. Delgado’s paper provided little information why those patients were selected for the “control” group, given the relevant differences between the control group and treatment group).

⁴⁶ Delgado et al., *A Case Series Detailing the Successful Reversal Of The Effects Of Mifepristone Using Progesterone*, *supra* note 38, at 23, 25.

⁴⁷ Grossman & White, *supra* note 41, at 1492; see also Grossman et. al., *supra* note 18. (“The proportion of pregnancies continuing 1–2 weeks after mifepristone alone varied from 8% to 46%. Continuing pregnancy was more common with lower mifepristone doses and advanced gestational age.”) (cleaned up).

⁴⁸ Delgado et al., *A Case Series Detailing The Successful Reversal Of The Effects Of Mifepristone Using Progesterone*, *supra* note 38, at 24 (comparing a “historical control group” of patients that were administered anywhere between a single dose of 600 mg to reoccurring doses of 100 mg of mifepristone to a treatment group of patients who ingested only a single dose of mifepristone at 200 mg).

withdraw and correct the paper.⁴⁹ Dr. Delgado has never offered a corrected version.

Moreover, neither case series was approved or overseen by an Institutional Review Board (IRB), which raises serious questions about both studies. IRBs are critical to ensuring the legitimacy of research studies and the safety of research participants. An IRB is a body that has been formally designated to protect the “rights and welfare of humans participating as subjects in the research.”⁵⁰ Such bodies are necessary following the “tragic outcomes of unregulated, unethical research conducted worldwide.”⁵¹ In the United States, for example, the “deceptive and unethical” U.S. Public Health Services’ Tuskegee Syphilis Study “denied treatment to infected individuals even after the commercial availability of penicillin—a known and accepted treatment for syphilis.”⁵² Following the publicity of the study, the U.S. passed significant protections for research subjects, including rules requiring the use of an IRB in conjunction with any federally funded human subject research.

ACOG clinical guidance states that “appropriate and adequately informed consent” and “an independent review of the risks and benefits of research” by an IRB “are fundamental to the formulation of any research protocol.”⁵³ Neither of

⁴⁹ Ruth Graham, *The Dubious Research on Abortion-Pill “Reversal”*, Slate (Jul. 19, 2018, 1:31 P.M.), <https://slate.com/human-interest/2018/07/why-an-abortion-pill-reversal-study-has-been-temporarily-withdrawn-by-the-pro-life-journal-that-published-it.html>.

⁵⁰ Felix Khin-Maung-Gyi, *The History and Role of Institutional Review Boards: Local and Central IRBs, A Single Mission*, 11 Am. Med. Ass’n J. Ethics 311, 314 (2009).

⁵¹ *Id.* at 317.

⁵² *Id.*

⁵³ *Ethical Considerations for Including Women as Research Participants*, ACOG, <https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2015/11/ethical-considerations-for-including-women-as-research-participants> (last visited Aug. 1, 2023) (SMFM endorsed this clinical Committee Opinion published by ACOG); *see also Joint Statement: Collective Action Addressing Racism*, ACOG, SMFM, & SFP (Aug. 2020)

Delgado's case series were supervised by an IRB nor an independent ethical review committee.⁵⁴ One expert found the informed consent forms associated with the larger case study to be inadequate.⁵⁵ As ACOG has previously explained, Delgado's refusal to allow his research to be "supervised by an institutional review board (IRB) or an ethical review committee, required to protect human research subjects, [raises] serious questions regarding the ethics and scientific validity of the results."⁵⁶

In addition, these studies failed to consider a variety of factors, leading to severely flawed results. Dr. Kathryn Eggleston, a medical director of a reproductive health-care clinic in North Dakota, concluded that the "papers are flawed and do not represent ethical, evidence-based medicine."⁵⁷ Conclusions from both papers are fundamentally weak, as "case series with no control groups are among the weakest forms of medical evidence."⁵⁸ Dr. Daniel Grossman, an expert in reproductive health, conducted a systematic review of each of Delgado's case series and found there was insufficient evidence to conclude that "progesterone therapy" is safe and

(describing our nation's history of conducting nonconsensual medical experiments on enslaved women).

⁵⁴ Delgado et al., *A Case Series Detailing The Successful Reversal Of The Effects Of Mifepristone Using Progesterone*, *supra* note 38, at 24.

⁵⁵ Graham, *supra* note 49.

⁵⁶ *Facts are Important*, *supra* note 13.

⁵⁷ *Stenehjem*, 412 F.Supp.3d 1134 at 1141 ("The flaws in these papers include: lack of a control group, meaning it is very possible that the studied pregnancies would have continued regardless of the administration of progesterone; flawed statistical analysis because the authors excluded from their calculations patients whose ultrasounds confirmed embryonic death; failure to separate patients based on gestational age, which affects the success of mifepristone; and lack of proof that the authors complied with standards for clinical research and rather instead were experimenting on patients with treatments that are not evidence-based.").

⁵⁸ *Facts are Important*, *supra* note 13.

effective.⁵⁹ Dr. Grossman’s review has been found to be credible by ACOG,⁶⁰ the Louisiana Department of Health,⁶¹ and experts who have been credited by multiple federal courts.⁶²

Delgado himself has acknowledged the weakness of his studies and their failure to support “abortion reversal.” Delgado admitted that with “regard to his three bases of support for progesterone therapy, neither biologic logic nor animal studies are sufficient to prove the safety and efficacy of his progesterone therapy on humans,” and that case series “cannot prove causation” and have “a greater possibility of bias . . . than with a controlled trial.”⁶³

Expert clinicians, as well as courts, have come to the same conclusion.⁶⁴ As one obstetrician-gynecologist stated on the record in a North Dakota court case:

[B]ecause there is no credible medical evidence behind it, I consider administering progesterone to try to “reverse” an abortion to be unethical experimentation on patients.

⁵⁹ Grossman & White, *Abortion “Reversal,”* *supra* note 41, at 1492 (“The safety data presented by Delgado et al. are minimal.”); Grossman, et al., *Continuing Pregnancy After Mifepristone,* *supra* note 18, at 206 (“In the rare case that a woman changes her mind after starting medical abortion, evidence is insufficient to determine whether treatment with progesterone after mifepristone results in higher proportion of continuing pregnancies compared to expectant management.”).

⁶⁰ *Facts are Important,* *supra* note 13.

⁶¹ Off. of Public Health, *Legislative Report on 2016 House Concurrent Resolution 87: Study Related to Whether the Effects of an Abortion Induced with Drugs or Chemicals Can Be Reversed,* 2016 Reg. Sess., at 4 (La. 2017) (“Dr. Grossman and his colleagues noted a number of significant flaws in the case series conducted by Dr. Delgado.”).

⁶² *All-Options, Inc.,* 546 F.Supp.3d 754 at 762; *Slatery,* 523 F.Supp.3d 985 at 995 n. 10.

⁶³ *Slatery,* 523 F.Supp.3d at 993.

⁶⁴ *Stenehjem,* 412 F.Supp.3d 1134 at 1139-45, 1150; Grossman & White, *supra* note 41, at 1491 (equating the promotion of “abortion reversal” to encouraging patients to “participate in an unmonitored research experiment”).

There is no dose and method of administering progesterone that has been shown to be both safe and effective to “reverse” a medication abortion. So giving a patient progesterone for that purpose is pure experimentation. It would be unethical for me, as a physician, to experiment on my patients outside the context of controlled research monitored and approved by an institutional review board.

American Medical Association v. Stenehjem, 412 F.Supp.3d 1134, 1140 (D. N.D. 2019).

Courts and state agencies have consistently determined that the use of “abortion reversal” falls below the generally accepted standard of care. One court called “abortion reversal” “devoid of scientific support,” “an unproven medical and scientific theory,” and “a very controversial and medically-uncertain procedure.”⁶⁵ Another concluded that evidence regarding “abortion reversal” was not “medically sound.”⁶⁶ And a panel of experts specializing in obstetrics, gynecology, and pharmacology conducted an investigation on behalf of the Louisiana Department of Health and unanimously concluded “there is insufficient evidence to suggest that there is a sound method to reverse a medication-induced abortion.”⁶⁷ Further, as one doctor testified, physicians are guided by science and evidence; they do not “presume a theoretical medical treatment works unless it is proven to be impossible” or “unsafe.”⁶⁸ Even supporters of “abortion reversal” have admitted that

⁶⁵ *Stenehjem*, 412 F.Supp.3d 1150-51.

⁶⁶ *Planned Parenthood of Mont. v. State ex rel. Knudsen*, 515 P.3d 301, 315 (Mont. 2022).

⁶⁷ Off. of Pub. Health, *Legislative Report on 2016 House Concurrent Resolution 87*, *supra* note 61.

⁶⁸ Pls.’ Br. at 7, *Slatery*, 523 F.Supp.3d 985, ECF No. 31.

the treatment is “experimental’ in nature” and that “abortion reversal” is not “widely accepted by the medical community.”⁶⁹

“Abortion reversal” is not based in science or evidence, and it should not be considered a generally accepted standard of care. A robust informed consent process, as required by the Proposed Rule, is unable to elevate this practice to become an accepted standard of care, because there is no evidence or science on which to base an informed consent and accurately disclose potential risks and harms. Thus, the Proposed Rule should make clear that the use of “abortion reversal” is not a generally accepted standard of care.

III. “Abortion Reversal” Poses a Threat to the Physical and Mental Health of Patients.

Administering progesterone to “reverse” a medication abortion is not only not based in science; it can also pose a serious risk of physical harm. “Abortion reversal” involves the practice of administering high and continuous levels of progesterone, which can introduce risk to the patient.⁷⁰ As the American Medical Association has stated, “although progesterone is considered a low-risk medication, it does carry risks.”⁷¹ Progesterone medication or treatment “has been associated with maternal complications such as depression, cholestatic jaundice, and hypertension. And while

⁶⁹ *State ex rel. Knudsen*, 515 P.3d at 315.

⁷⁰ For example, one patient in the first case series published by Dr. Delgado was regularly administered 100-200 mg of progesterone intramuscularly up to twice a week until almost 30 weeks gestational age. Another patient received 200 mg of progesterone intramuscularly twice a week through 27 weeks gestational age. *See Delgado & Davenport, Progesterone Use to Reverse the Effects of Mifepristone*, *supra* note 35, at 2. The 2018 case series recommended patients continue to take 400 mg of progesterone orally through the end of their first trimester. *See Delgado et al., A Case Series Detailing the Successful Reversal of the Effects of Mifepristone Using Progesterone*, *supra* note 38, at 29.

⁷¹ Compl. ¶ 56, *Stenehjem*, 412 F.Supp.3d 1134.

some data support the general safety of progesterone in pregnancy, other studies have raised concerns about possible association[s] with second trimester miscarriage, stillbirth and certain birth defects.”⁷²

In addition, use of “abortion reversal” disrupts the safe medication abortion process. As described above, medication abortion that follows the standard two-medication regimen is highly effective and results in serious complications in less than one percent of patients.⁷³ The process of “abortion reversal” disrupts that safe regimen, stopping the patient from taking the second medication, and can result in risk to the patient.

In 2020, a double-blind, randomized clinical trial under the supervision of an IRB attempted to measure the efficacy of progesterone on patients who induced a medication abortion with mifepristone and did not complete the two-step regimen with misoprostol.⁷⁴ The clinical trial intended to administer progesterone to 20 patients in the treatment group and a placebo to 20 patients in the control group.⁷⁵ However, after enrolling only twelve people, the trial prematurely ended when three

⁷² *Id.* at 1143, citing Suzan L. Carmichael et al., *Maternal Progestin Intake and Risk of Hypospadias*, 159 *Archives Pediatric & Adolescent Med.* 957 (2005); Paul J. Meiss et al., *Prevention of Recurrent Preterm Delivery by 17 Alpha-Hydroxyprogesterone Caproate*, 348 *N. Eng. J. Med.* 2379, 2382 (2003).

⁷³ Katymay Malone, *Consumer Health Info: Abortion with Pills*, Nat’l Women’s Health Network, https://nwhn.org/health-facts-abortion-with-pills/?gclid=Cj0KCQjwzdO1BhCNARIsAPMwjbzn6URtwpN2L9gSOal2vP1-QewDFJJIpeokxhD_je9_rkgjhJnFz-kaAgAcEALw_wcB, (expand section “How Safe is Medication Abortion”) (last updated Jul. 23, 2023).

⁷⁴ Claire Lampen, *Researchers Tried to Test “Abortion Reversal.” 3 Women Wound up in the Hospital*, *The Cut* (Dec. 16, 2019), <https://www.thecut.com/2019/12/abortion-reversal-study-stopped-after-women-hospitalized.html>.

⁷⁵ *Id.*; Mitchell Creinin et al., *Mifepristone Antagonization With Progesterone to Prevent Medical Abortion: A Randomized Controlled Trial*, 135 *Obstetrics & Gynecology* 158 (2020) https://journals.lww.com/greenjournal/Abstract/2020/01000/Mifepristone_Antagonization_With_Progesterone_to.21.aspx.

participants—one from the treatment group and two from the control group—severely hemorrhaged.⁷⁶ While the results regarding progesterone’s efficacy on “reversing” a medication abortion were inconclusive, the clinicians concluded that “patients in early pregnancy who use only mifepristone may be at high risk of significant hemorrhage.”⁷⁷ The study’s lead researcher warned, “[w]omen who use mifepristone for a medical abortion should be advised that not following up with misoprostol could result in severe hemorrhage.”⁷⁸ Deviation from the evidence-based and safe medication abortion regimen may lead to potentially serious complications.⁷⁹

Clinicians who encourage patients to engage in “abortion reversal” do precisely the opposite while ignoring the results of this study and introducing risk to individuals undergoing an otherwise safe medication abortion. In fact, the current medical advice for patients who take mifepristone but do not want to take misoprostol is to notify their physician and follow up with expectant management.⁸⁰ There is no evidence that “abortion reversal” is more effective at continuing a pregnancy than expectant management.⁸¹

The promotion of “abortion reversal” can also pose a significant risk to patients’ mental health. A 2023 study published in the *American Journal of Public Health* concluded that laws requiring physicians to discuss with patients the

⁷⁶ Lampen, *supra* note 74.

⁷⁷ Creinin et al., *supra* note 75.

⁷⁸ Hayley Farless, “*Abortion Reversal*” is Not Only B.S. but is Dangerous Too, Rewire News Group (Dec. 6, 2019, 4:55 P.M.), <https://rewirenewsgroup.com/2019/12/06/abortion-reversal-is-not-only-b-s-but-is-dangerous-too/>.

⁷⁹ Creinin et al., *supra* note 75 (finding that patients suffered “serious blood loss” when deviating from the medication abortion regimen).

⁸⁰ *Medication abortion up to 70 days of gestation* *supra* note 22; LaMotte, *supra* note 15.

⁸¹ Grossman et al., *Continuing Pregnancy After Mifepristone*, *supra* note 18, at 210.

possibility of “abortion reversal” “may negatively affect the[ir] emotional and physical health.”⁸² Use of language like “abortion reversal” inherently pressures patients to “correct” a mistake, thereby enhancing abortion-related stigma, even though most patients “have high degrees of certainty about their decisions.”⁸³ Another study found that “experiences and fears of abortion-related stigma can result in lower self-efficacy, reduced perceptions of social support to help with abortion decision-making, increased use of denial and avoidance coping techniques, and avoidance of needed services.”⁸⁴ Abortion-related stigma also leads to heightened levels of stress, shame, and guilt, which can result in “reduced self-efficacy around decision making, decreased perceptions of social support, and increased psychological distress.”⁸⁵ Exposure to abortion-related stigma also decreases a woman’s likelihood of seeking reproductive health care, which can lead to negative, life-altering consequences.⁸⁶

⁸² Redd et al., *Medication Abortion “Reversal” Laws*, *supra* note 14, at 202 (“‘Reversal’ laws . . . require that patients receive medically inaccurate information about the possibility of reversing a [medication abortion].”).

⁸³ *Id.* at 210.

⁸⁴ Janet M. Turan & Henna Budhwani, *Restrictive Abortion Laws Exacerbate Stigma, Resulting in Harm to Patients and Providers*, 111 *Am. J. Pub. Health* 37, 38 (2020) (“Abortion-related stigma has been defined as ‘a negative attribute ascribed to women who seek to terminate a pregnancy that marks them, internally or externally, as inferior to ideals of womanhood.’”). *See also* Alison Norris et al., *Abortion Stigma: A Reconceptualization of Constituents, Causes, and Consequences*, 21 *Women’s Health Issues* S49 (2011), <https://doi.org/10.1016/j.whi.2011.02.010>, (providing an explanation as to why certain groups may feel abortion-related stigmatization).

⁸⁵ Redd et al., *supra* note 14, at 210.

⁸⁶ Turan, *supra* note 83, at 38. *See also* Adler, et al., *Changes in the Frequency of Barriers to Reproductive Health Care Between 2017 and 2021*, 6 *Jama Network*, Apr, 2023, at 2, <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2803644> (“Delaying or forgoing reproductive health care not only can result in morbidity but also, in situations such as untreated sexually transmitted infections, can result in an increased risk of serious complications, such as infertility and pelvic inflammatory disease.”).

IV. The Promotion of “Abortion Reversal” Misleads Patients.

ACOG’s ethical guidelines require that an “obstetrician–gynecologist must deal honestly with patients,” which includes “not misrepresenting himself or herself through any form of communication in an untruthful, misleading, or deceptive manner.”⁸⁷ The practice of “abortion reversal” fails to meet this standard, as its use is steeped in misleading information.

The term itself—“abortion reversal”—misleads patients. The use of the word “reverse” to describe this process is inherently misleading because there is no evidence that “progesterone therapy” negates a medication abortion.⁸⁸ As stated by ACOG and affirmed by courts across the country, it is misleading to state that it is possible “to reverse the effects of an abortion-inducing drug.”⁸⁹

Patients are also often misled by “abortion reversal” proponents into “wrongly assuming that there are reliable data to support this practice.”⁹⁰ This is not the case, and to indicate otherwise is a violation of ACOG’s ethical guidelines.⁹¹ Each clinician “has an obligation to obtain the informed consent of each patient” and to provide pertinent medical facts and recommendations consistent with good medical practice.”⁹² This information should include “alternative modes of treatment and

⁸⁷ *Code of Professional Ethics*, *supra* note 26, at 1.

⁸⁸ *Slatery*, 523 F. Supp.3d at 1005.

⁸⁹ *Stenehjem*, 412 F.Supp.3d at 1149-50.

⁹⁰ *Stenehjem*, 412 F.Supp.3d at 1134, 1142.

⁹¹ *Code of Professional Ethics*, *supra* note 26.

⁹² *Id.* at 2.

the objectives, risks, benefits, possible complications, and anticipated results of such treatment.”⁹³

Instead, those most likely to recommend “abortion reversal” to patients argue that progesterone has been used (including “off-label” use) during pregnancy for more than 50 years, suggesting that its use for other purposes proves that its use for “abortion reversal” is safe.⁹⁴ These clinicians do not inform patients of the significant potential risks associated with “abortion reversal” regimens, including hemorrhaging, or the lack of evidence that progesterone can actually reverse the effect of mifepristone.

Patients place a high level of trust in health care professionals and are likely to follow their recommendations.⁹⁵ When clinicians promote “abortion reversal”—an unsupported intervention—they risk eroding trust between physicians and their patients, particularly low-income patients and patients of color.⁹⁶ Thus, such

⁹³ *Id.*

⁹⁴ Delgado, et al., *A Case Series Detailing the Successful Reversal of the Effects of Mifepristone Using Progesterone*, *supra* note 38, at 8.

⁹⁵ *See Survey of Trust in the U.S. Health Care System*, NORC Univ. Chi. (2021), https://www.norc.org/content/dam/norc-org/pdfs/20210520_NORC_ABIM_Foundation_Trust%20in%20Healthcare_Part%201.pdf (finding that 90% of patients believe their physician is honest with them and respects them, which suggests that patients overwhelmingly believe their physician).

⁹⁶ *Id.* at 14 (finding that trust in one’s physicians increases as age and income increase, and that Black and Hispanic patients report a lower level of trust than similarly situated White patients). *See* Zella Hanson, *Trust in Gynecology: The Impact of Race & Socioeconomic Status in Women’s Health*, Duke Rsch. Blog (Nov. 3, 2020) <https://researchblog.duke.edu/2020/11/03/trust-in-gynecology-the-impact-of-race-ses-in-womens-health/> (providing an overview of systemic issues women of color and women with low socioeconomic status face regarding access to quality health care and bias by providers); *See also Joint Statement: Collective Action Addressing Racism*, *supra* note 53 (“As our nation confronts systemic racism and consequences of persistent inequities and disparate outcomes in health care, our organizations—which include the leading professional organizations in the fields of obstetrics and gynecology—are committed to changing the

recommendations fail to adhere to ethical guidelines that require that a patient-physician relationship be “built on confidentiality, trust, and honesty.”⁹⁷ As stated by the American Medical Association, “[b]ecause there is no credible, scientific evidence that a medication abortion can be reversed, physicians do not and cannot, without misleading them, tell their patients that it may be possible to reverse a medication abortion.”⁹⁸

* * *

“Abortion reversal” is not supported by credible scientific evidence, is misleading, and can be dangerous to the physical and mental health of patients. There is no safe and credible way for a clinician to recommend “abortion reversal” to a patient, and “abortion reversal” is not a generally accepted standard of practice.

culture of medicine, eliminating racism and racial inequities that lead to disparate health outcomes, and promoting equity in women’s health and health care.”).

⁹⁷ *Code of Professional Ethics*, *supra* note 22.

⁹⁸ Complaint ¶ 64, *Stenehjem*, 412 F.Supp.3d 1134.