November 7, 2025

Martin Makary, MD, MPH
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20993-002

Re: Comment to Supplement Citizen Petition FDA-2025-P-0377-0001 regarding the U.S. Food and Drug Administration's ("FDA") regulation of mifepristone (NDA 020687, ANDA 0901178, ANDA 216616)

Commissioner Makary,

Petitioners the American College of Obstetricians and Gynecologists, Society of Family Planning, and Society for Maternal-Fetal Medicine (hereinafter "Petitioners") hereby supplement their petition FDA-2025-P-0377-0001 with additional arguments outlined below in support of their requests that FDA remove the Mifepristone Shared System REMS Program, including but not limited to the three ETASU, or, in the alternative, at a minimum, refrain from taking any action imposing greater burdens on patient access to mifepristone or on the health care system related to the provision of mifepristone.[1] Petitioners further express support for other currently pending citizen petitions to the extent they raise the arguments below in support of access to mifepristone.

1. **FDA's ongoing review of mifepristone must be conducted transparently and consider the full body of sound scientific evidence regarding mifepristone's safety and effectiveness.**

As Department of Health and Human Services ("HHS") Secretary Robert F. Kennedy, Jr., recently confirmed, FDA is currently undertaking a review of mifepristone.[2] Petitioners make the

[1] Citizen Petition from Am. College of Obstetricians & Gynecologists, et al., FDA-2025-P-0377-0001 (Jan. 31, 2025) [hereinafter "ACOG Citizen Petition"], https://www.regulations.gov/document/FDA-2025-P-0377-0001.

[2] CNBC Television, *HHS Sec. Robert F. Kennedy Jr. Testifies Before Senate on Trump's Health Care Agenda – 9/4/25*, at 1:10:58–1:11:04 and 1:26:10–50 (Sept. 4, 2025) (statement of Sec'y Kennedy confirming FDA review of mifepristone "is progressing apace" and that FDA-conducted studies are "progressing" and "ongoing"), https://www.youtube.com/watch?v=2KW1mVChh-c; Letter from Robert F. Kennedy, Jr., HHS Secretary, & Martin A. Makary, FDA Commissioner, to State Attorneys General, at 1 (Sept. 19, 2025) ("HHS—through FDA—is conducting its own review of the evidence, including real-world outcomes and evidence, relating to the safety and efficacy of the drug."), https://www.thegatewaypundit.com/2025/09/trump-admin-rfk-jr-moves-address-assess-safety/.

following requests with respect to any such review:

- That, for all data reviewed by FDA during the course of the review, the source of all data and methods used in analyzing such data be publicly disclosed, fully explained, and made accessible to all interested stakeholders, including Petitioners, consistent with principles of replicability and the scientific method, and further, that for any study or analysis that FDA itself conducts,[3] the underlying data be made public.

- That FDA consider as part of the review the content of, attachments to, comments to, and all evidence cited within all pending citizen petitions and comments relating to the FDA's regulation of mifepristone, consistent with FDA's legal obligation to consider the "'whole record,'" which "includes everything that was before the agency pertaining to the merits of its decision."[4]

- That FDA consider the entire body of evidence supporting mifepristone's safety and effectiveness, which FDA itself has repeatedly acknowledged,[5] and which is reflected in more than two decades of robust research and more than 7.5 million safe uses by patients,[6]

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[3] *See, e.g.*, Letter from Sec'y Kennedy, *supra* note 2, at 1–2.

[4] *Portland Audubon Soc'y v. Endangered Species Comm.*, 984 F.2d 1534, 1548 (9th Cir. 1993) (quoting 5 U.S.C. § 706); *see also* 21 C.F.R. § 10.30(i)(1)–(2) (in considering citizen petitions, the record includes "[t]he petition, including all information on which it relies," and "[a]ll comments received on the petition, including all information submitted as part of the comments").

[5] *E.g.*, U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Rsch., No. 020687Orig1s020, Mifeprex Medical Review(s) 12 (Mar. 29, 2016) (mifepristone's "efficacy and safety have become well established by both research and experience, and serious complications have proven to be extremely rare").

[6] *See, e.g.*, ACOG Citizen Petition, *supra* note 1, at 1–11, 18–20; Citizen Petition from Massachusetts, et al., FDA-2025-P-1576-0001, at 1–15 (June 5, 2025) [hereinafter "Massachusetts Citizen Petition"], https://www.regulations.gov/document/FDA-2025-P-1576-0001; Citizen Petition from Washington, et al., FDA-2025-P-3287-0001, at 5–10 (Aug. 20, 2025) [hereinafter "Washington Citizen Petition"], https://www.regulations.gov/document/FDA-2025-P-3287-0001; Comment from National Abortion Federation, FDA-2025-P-0377-0010, at 1–2 (Mar. 18, 2025) [hereinafter "NAF Comment"], https://www.regulations.gov/comment/FDA-2025-P-0377-0010; Comment from Planned Parenthood Federation of America, FDA-2025-P-0377-0018, at 2–3 (May 28, 2025) [hereinafter "PPFA Comment"], https://www.regulations.gov/comment/FDA-2025-P-0377-0018; Comment from Guttmacher Institute, FDA-2025-P-0377-0012, at 2 (Ap. 8, 2025) [hereinafter "Guttmacher Inst. Comment"], https://www.regulations.gov/comment/FDA-2025-P-0377-0012; Comment from UCSF Bixby Center for Global Reproductive Health, FDA-2025-P-0377-0015 (Apr. 22, 2025) [hereinafter "Bixby Ctr. Comment"], https://www.regulations.gov/comment/FDA-2025-P-0377-0015; Comment from UCLA Law Center on Reproductive Health, Law, and Policy et al. on behalf of 263 Reproductive Health Researchers, FDA-2025-P-0377-0230, at 1–7 (Aug. 27, 2025) [hereinafter "Reproductive Health

and to also consider evidence of the burdens the REMS and ETASU impose on patients and the health care system as required by 21 U.S.C. § 355-1(f)(2) and (g)(4).[7]

- That FDA ensure an opportunity for input into the review from stakeholders with medical and scientific expertise on mifepristone, including Petitioners and their members, in accordance with FDA's practice of considering stakeholder input in other drug regulatory decisions.[8]

2. Baseless claims by abortion opponents about mifepristone's safety, effectiveness, and impact on the environment provide no basis to maintain or increase restrictions on access to mifepristone.

As detailed in multiple citizen petitions and comments from expert medical associations and public health researchers currently pending before FDA, there is a substantial body of robust scientific evidence demonstrating that mifepristone is very safe, very effective, and essential to the public health—evidence that spans more than one hundred reliable medical studies and twenty-five years of safe use by more than 7.5 million individuals.[9] Against this overwhelming body of evidence, abortion opponents rely on a handful of deeply flawed publications to call for medically unnecessary and unduly burdensome restrictions on mifepristone access. The recent self-published, non-peer-reviewed document from the anti-abortion Ethics and Public Policy Center ("EPPC") is just the latest in a long line of attempts by anti-abortion organizations to manufacture attacks on mifepristone's safety and abortion access. Petitioners fully support and adopt the

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Researchers Comment"], https://www.regulations.gov/comment/FDA-2025-P-0377-0230; Comment from Reproductive Freedom for All, FDA-2025-P-0377-0016, at 1–3 (May 1, 2025) [hereinafter "RFA Comment"], https://www.regulations.gov/comment/FDA-2025-P-0377-0016.

[7] *See, e.g.*, ACOG Citizen Petition, *supra* note 1, at 6, 9–20; Massachusetts Citizen Petition, *supra* note 6, at 21–37; Washington Citizen Petition, *supra* note 6, at 3–4, 22–29; NAF Comment, *supra* note 6, at 2–3; PPFA Comment, *supra* note 6, at 3–4; Guttmacher Inst. Comment, *supra* note 6, at 1–3; Bixby Ctr. Comment, *supra* note 6; RFA Comment, *supra* note 6, at 2, 4–6; Comment from Legal Voice, FDA-2025-P-0377-0013 (Apr. 11, 2025), https://www.regulations.gov/comment/FDA-2025-P-0377-0013; Comment from Lee Hasselbacher & Debra Stulberg, FDA-2025-P-0377-0240 (Oct. 6, 2025), https://www.regulations.gov/comment/FDA-2025-P-0377-0240; Comment from Boston University School of Law's Program on Reproductive Justice et al., FDA-2025-P-0377-0242 (Oct. 11, 2025), https://www.regulations.gov/comment/FDA-2025-P-0377-0242.

[8] *See, e.g.*, U.S. Food & Drug Admin., REMS Modification Notification (Isotretinoin) 1 https://www.fda.gov/media/174325/download [https://perma.cc/6RF4-XFA7] (citing "stakeholder feedback from prescribers, pharmacists, and patients"); U.S. Food & Drug Admin., Supplemental Approval (Zydelig) 1 (July 6, 2022), https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2022/205858Orig1s018ltr.pdf [https://perma.cc/7C5C-VD5Z] (citing "surveys of healthcare providers").

[9] *See, e.g.*, *supra* note 6.

arguments in other Citizen Petitions and comments currently pending before FDA that detail at length the profound methodological flaws, lack of transparency, and fatal biases infecting these claims.[10] FDA's regulatory decisions must be based on scientifically and medically sound evidence, not junk science.

Petitioners are also aware of unsubstantiated claims by abortion opponents that mifepristone causes harm to the environment or the water supply. FDA itself has previously and

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[10] Petitioners adopt and incorporate by reference the arguments in the following: Massachusetts Citizen Petition, *supra* note 6, at 16–21, 37–38; Washington Citizen Petition, *supra* note 6, at 10–22; Citizen Petition from GenBioPro, FDA-2025-P-2162-0001, at 15–20 (July 3, 2025) [hereinafter "GBP Citizen Petition"], https://www.regulations.gov/document/FDA-2025-P-2162-0001; Comment from Ushma Upadhyay, FDA-2025-P-0377-0017 (May 9, 2025), https://www.regulations.gov/comment/FDA-2025-P-0377-0017; Reproductive Health Researchers Comment, *supra* note 6, at 7–23; *see also* M. Creinin & D. Turok, *False Serious Adverse Events Claims with Medication Abortion*, Society of Family Planning: Science Unpacked (2025), https://societyfp.org/wp-content/uploads/2025/10/SFP_Science_Unpacked-FalseSeriousAdverseEvents-f.pdf. FDA has previously rejected arguments that suffer from the kinds of flaws infecting the EPPC paper and similar publications. *See, e.g.*, Letter from Patrizia A. Cavazzoni, M.D., Dir. Ctr. for Drug Evaluation & Rsch. to Donna J. Harrison, M.D., Executive Director American Association of Pro-Life Obstetricians and Gynecologists, at 36–37 (Dec. 16, 2021), https://downloads.regulations.gov/FDA-2019-P-1534-0016/attachment_1.pdf (FDA: "Heavy bleeding or hemorrhage after medical abortion is a small subset of bleeding and can require a surgical procedure due to ongoing pregnancy or incomplete expulsion; these are considered failed treatment rather than adverse events and are not characterized using the [Council for International Organizations of Medical Sciences'] definitions. Even if heavy, bleeding after medical abortion may not be considered a serious adverse event unless clinically diagnosed as hemorrhage or requiring a transfusion."); *see also, e.g.*, U.S. Food & Drug Admin., REMS Modification Rationale Review 29 (Dec. 16, 2021) (noting research in which the authors found "that half of the ED/urgent care visits did not entail any medical treatment and [opining] that the increased number of visits may have been due to the study participants living farther from the abortion providers"); L. Schummers et al., *Health Services Context And Methodological Approach Must Be Considered For Rigorous Examination Of Abortion Methods And Outcomes*, Comment to Liu et al., *Short-Term Adverse Outcomes After Mifepristone-Misoprostol Versus Procedural Induced Abortion: A Population-Based Propensity-Weighted Study*, 176 Annals of Int. Medicine 145 (2023), https://www.acpjournals.org/doi/abs/10.7326/M22-2568?journalCode=aim (noting, *inter alia*, that "emergency department ('ED') visits are not indicative of adverse events"); Liu et al., Author Response to Schummers et al., *supra*, https://www.acpjournals.org/doi/abs/10.7326/M22-2568?journalCode=aim (agreeing that "[ED] use after [induced abortion (IA)] is not the best barometer of IA safety, especially since ED use is more likely among young women residing in low-income or rural areas"); Ushma Upadhyay et al., *Abortion-Related Emergency Department Visits in the United States: An Analysis of a National Emergency Department Sample*, 16 BMC Med. 1, 7–9 (2018) (majority of abortion-related ED visits in large retrospective study involved "observation care only," likely because some patients do not realize that normal post-abortion symptoms include "ongoing uterine cramping and bleeding").

correctly denied multiple anti-abortion petitions raising these baseless claims.[11] As recently as January 2025, FDA reported the results of its own new environmental analysis applying current mifepristone use rate data, FDA's current environmental analysis guidance, and "conservative calculations," which found that any exposure level from mifepristone use is "so low that it is predicted to have *no* effect on the environment, including threatened and endangered species" (emphasis added).[12] As such, speculative claims about environmental harm provide no legitimate basis to retain or increase REMS or ETASU restrictions on mifepristone. Particularly where anti-abortion commenters are not raising similar concerns about alleged harm to the environment or the water supply of the thousands of medications used in far greater quantities than mifepristone, it is clear that these claims are a pretext for seeking to further restrict access to mifepristone.

3. Any attempt to withdraw or suspend approval of mifepristone would be unlawful and wholly without scientific support.

Petitioners are aware of citizen petitions opposing access to mifepristone currently pending before FDA that include requests to either suspend or permanently revoke mifepristone's approval.[13] For all the same reasons that mifepristone's well-established safety profile falls short of what is required for a REMS or ETASU at all,[14] any claim that mifepristone's approval should be withdrawn or suspended is without merit. Such actions are strictly limited by statute to instances in which evidence demonstrates that a drug is "unsafe for use under the conditions of use" for which it was approved, that a drug has "not [been] shown to be safe for use" under such conditions, that there is a "lack of substantial evidence" of effectiveness under such conditions, or that the drug poses an "imminent hazard to the public health." 21 U.S.C. § 355(e). Mifepristone's safety and effectiveness have been proven time and again, by more than one hundred robust scientific

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[11] Patrizia A. Cavazzoni, M.D., Dir., Ctr. for Drug Evaluation & Rsch., Food & Drug Admin., Response to Citizen Petition Docket No. FDA-2023-P-3328, FDA-2023-P-3328-0004 (Jan. 15, 2025), https://www.regulations.gov/document/FDA-2023-P-3328-0004; Patrizia A. Cavazzoni, M.D., Dir., Ctr. for Drug Evaluation & Rsch, Food & Drug Admin., Response to Citizen Petition Docket No. FDA-2023-P-1528, FDA-2023-P-1528-0005 (Jan. 15, 2025), https://www.regulations.gov/document/FDA-2023-P-1528-0005; Patrizia A. Cavazzoni, M.D., Dir., Ctr. for Drug Evaluation & Rsch, Food & Drug Admin., Response to Citizen Petition Docket No. FDA-2023-P-2872, FDA-2023-P-2872-0004 (Jan. 15, 2025), https://www.regulations.gov/document/FDA-2022-P-2872-0004; *see also* GBP Citizen Petition, *supra* note 10, at 21-25.

[12] Cavazzoni, Response to Citizen Petition Docket No. FDA-2023-P-3328, *supra* note 11, at 16–17.

[13] Citizen Petition from Am. Ass'n of Pro-Life Obstetricians & Gynecologists, et al., FDA-2025-P-3288 (Aug. 13, 2025), https://www.regulations.gov/docket/FDA-2025-P-3288; Citizen Petition from James Brinkruff, FDA-2025-P-1242 (May 12, 2025), https://www.regulations.gov/docket/FDA-2025-P-1242.

[14] *See, e.g.*, *supra* Section 2; ACOG Citizen Petition, *supra* note 1, at 3–18; GBP Petition, *supra* note 10, at 26–30.

studies and the experience of more than 7.5 million patients across a quarter of a century. Any attempt to withdraw, stay, or suspend mifepristone's approval would be plainly unlawful.

Sincerely,

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