Nos. 23-235, 23-236

IN THE

Supreme Court of the United States

U.S. FOOD AND DRUG ADMINISTRATION, ET AL.,
Petitioners,

v.

ALLIANCE FOR HIPPOCRATIC MEDICINE, ET AL.,
Respondents.

and

DANCO LABORATORIES, L.L.C.,
Petitioner,

v.

ALLIANCE FOR HIPPOCRATIC MEDICINE, ET AL.,
Respondents.

On Writs of Certiorari to the United States Court of Appeals for the Fifth Circuit

BRIEF OF AMICI CURIAE PUBLIC CITIZEN AND CENTER FOR SCIENCE IN THE PUBLIC INTEREST IN SUPPORT OF PETITIONERS

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TABLE OF CONTENTS

TABLE OF AUTHORITIES

Regulations

Other Authorities

INTEREST OF AMICI CURIAE[1]

Amici are two Food and Drug Administration (FDA) watchdogs with a strong interest in ensuring that citizen petitions are used properly to bring meaningful new evidence regarding a drug's safety and effectiveness to the FDA's attention.

Public Citizen is a nonprofit consumer advocacy organization with members in all 50 states. Among other things, Public Citizen works to advance access to healthcare and to ensure strong protections for public health, and it has a strong interest in the safety and effectiveness of drugs marketed to patients in the United States. Since 1971, the physicians in Public Citizen's Health Research Group have studied the FDA's work and have filed dozens of citizen petitions challenging FDA approvals or labeling decisions, including more than 40 petitions asking the FDA to ban an approved drug because of safety risks. *See, e.g.*, Public Citizen, Petition to the FDA to Ban the Drug Hydroxyprogesterone Caproate (Makena), Approved for Prevention of Preterm Birth (Oct. 8, 2019), https://tinyurl.com/3bk9xkkr; Public Citizen, Petition to the FDA to Require a Black-Box Warning for the Osteoporosis Drug Prolia (Apr. 16, 2019), https://tinyurl.com/bdhy4tj9. These citizen petitions typically ask the FDA to act based on new peer-reviewed studies or new adverse event reports that cast fresh doubt on prior safety and effectiveness findings.

Founded in 1971, the Center for Science in the Public Interest (CSPI) is a science-based consumer advocacy organization devoted to improving the food

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[1] This brief was not written in any part by counsel for a party. No one other than amici curiae or their counsel made a monetary contribution to the preparation or submission of the brief.

system to support healthy eating. With independence and scientific rigor, CSPI works to reduce the impact and burden of preventable diseases. During its 52 years, CSPI has submitted numerous citizen petitions to the FDA seeking changes to regulations or industry guidance to better promote public nutrition. *See, e.g.*, CSPI, Citizen Petition Requesting that the U.S. Food and Drug Administration Develop Voluntary, Measurable Added Sugars Reduction Targets for Processed, Packaged, and Prepared Foods and Beverages (Apr. 25, 2023), http://tinyurl.com/y8eddmxj; CSPI, Citizen Petition Seeking FDA Rulemaking to Update the Required Nutrition Information at Chain Restaurants to Include Added Sugars for Standard Menu Items (Jan. 31, 2022), http://tinyurl.com/2a5rn936. These petitions, too, typically present the FDA with peer-reviewed studies or other scientific evidence that supports the requested action.

SUMMARY OF ARGUMENT

In the Food, Drug, and Cosmetic Act (FDCA), Congress tasked the FDA with assessing the safety and effectiveness of new drugs before they can be marketed, determining the uses for which such drugs can lawfully be marketed, and monitoring drugs' safety after marketing approval. In carrying out these duties, the FDA brings together teams of medical doctors, chemists, microbiologists, statisticians, pharmacologists, and other experts to review a vast amount of information about a medication's safety and effectiveness, including peer-reviewed scientific literature and the results of clinical trials conducted with oversight from institutional review boards.

Congress anticipated that this rigorous, science-based process would produce reliable outcomes that

protect and advance Americans' health, and it does. Consequently, courts have appropriately recognized that the bar for second-guessing the FDA's determinations as to whether and how a drug can be safely and effectively used must be extremely high, requiring either evidence of a meaningful procedural breakdown or a departure from accepted scientific principles, or newly discovered information that reasonably should alter the FDA's prior considered analysis.

Respondents here challenge (among other things) a 2016 decision by the FDA to alter certain restrictions on the approved use of mifepristone upon finding that the changes would not compromise safety or effectiveness. The 2019 citizen petition in which respondents raised their challenges, however, suggested no flaw in the FDA's decisional process and cited no significant new evidence. Instead, the petition did exactly what courts have cautioned against: It disagreed with the FDA's 2016 safety and effectiveness findings by offering a competing assessment of the body of scientific data that the FDA had already evaluated in depth. If anything, the petition's few references to post-2016 studies served to confirm that the evidentiary backdrop against which the FDA took its 2016 actions remained essentially unchanged. Should the Court reach this case's merits, then, it should hold that the FDA did not act arbitrarily and capriciously in refusing respondents' request to reverse the 2016 changes to the restrictions on mifepristone's use.[2]

[2] This brief does not address the issue of respondents' standing, other than to note the strength of petitioners' arguments on that issue.

ARGUMENT

I. The FDA engages in rigorous and ongoing expert study of detailed scientific evidence when considering whether and under what conditions a drug is safe and effective for use.

The FDA's congressionally mandated role is to "protect the public health by ensuring," among other things, that "human and veterinary drugs are safe and effective." 21 U.S.C. § 393(b)(2)(B). When created in 1906, the FDA was limited to enforcing prohibitions on marketing adulterated or misbranded drugs, and it had "no power to demand, prior to marketing, any evidence that a drug was safe or would perform as the seller claimed." Richard A. Merrill, *The Architecture of Government Regulation of Medical Products*, 82 Va. L. Rev. 1753, 1758 (1996). But in 1938, after an adulterated drug poisoned more than 100 people, Congress empowered the FDA to assess the safety of new drugs before they could be sold. *Id.* at 1761–62. Since then, Congress has strengthened the FDA's premarket role, including by requiring the agency to consider a drug's effectiveness as well as its safety. *Id.* at 1764–68.

The FDA's role in ensuring safety and effectiveness begins early in the process of developing a new drug. *See* 21 U.S.C. § 321(p)(1) (defining "new drug" in relevant part as a drug that has not yet been "generally recognized[] among experts qualified by scientific training and experience … as safe and effective for use" under particular conditions). After "[a new] drug's sponsor (usually the manufacturer or potential marketer)" has "screened the new [drug] for pharmacological activity and acute toxicity potential in animals," and after the preclinical animal and toxicology trials have established that the drug is

"reasonably safe for initial testing in humans," the sponsor submits an Investigational New Drug application to the FDA. FDA, *Investigational New Drug (IND) Application* (July 20, 2022), https://tinyurl.com/hwwryzzr. The application must include data from the preclinical studies, information about the drug's composition and manufacture, and details about the sponsor's proposed clinical trials and the qualifications of the investigators who will be conducting them. *Id.* The FDA then has thirty days to review the application and to "provide[] comments intended to improve the quality" of the proposed trials and ensure that the trials meet federal standards. FDA, *Step 3: Clinical Research* (Jan. 4, 2018), https://tinyurl.com/yttstres.

After the FDA gives approval, the proposed clinical trials generally proceed in three phases. *See* 21 C.F.R. § 312.21. First, investigators conduct "closely monitored" studies of the drug's effects in approximately 20 to 80 subjects, with the aim of "determin[ing] the metabolism and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and, if possible, … gain[ing] early evidence on effectiveness." *Id.* § 312.21(a)(1). Second, investigators conduct "well controlled, closely monitored" studies on "usually … no more than several hundred subjects" to "evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks associated with the drug." *Id.* § 312.21(b). Finally, if the initial phases produce "preliminary evidence suggesting effectiveness of the drug," investigators conduct "expanded" studies with "several hundred to several thousand subjects" to "gather the additional

information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling." *Id.* § 312.21(c). Throughout the trials, the sponsor has an ongoing obligation to review "all information relevant to the safety of the drug," including information from clinical investigations, animal studies, scientific literature, and unpublished reports, *id.* § 312.32(b), and to notify the FDA of the clinical trials' progress and of evidence of any potential safety risks, *id.* §§ 312.32(c), 312.33.

Following clinical trials, a sponsor seeking FDA approval to sell and market the new drug must submit a New Drug Application (NDA), which must "tell the drug's whole story, including what happened during the clinical tests, what the ingredients of the drug are, the results of the animal studies, how the drug behaves in the body, and how it is manufactured, processed and packaged." FDA, *New Drug Application (NDA)* (Jan. 21, 2022), https://tinyurl.com/bdh9pmbx. The FDCA and FDA regulations require that the "data and information" in the NDA be reported "in sufficient detail to permit the [FDA] to make a knowledgeable judgment about whether to approve the NDA or whether grounds exist … to refuse to approve the NDA." 21 C.F.R. § 314.50(d); *see* 21 U.S.C. § 355(b). The NDA must also include a summary that is "written at approximately the level of detail required for publication in, and [that] meet[s] the editorial standards generally applied by, refereed scientific and medical journals." 21 C.F.R. § 314.50(c)(1).

Upon receiving an NDA, an FDA review team made up of "medical officers, chemists, statisticians, microbiologists, pharmacologists, and other experts" evaluates the materials. U.S. Gov't Accountability

Off., GAO-08-751, *Food and Drug Administration: Approval and Oversight of the Drug Mifeprex* 9 (2008), https://tinyurl.com/4ccdvv5y (hereafter, GAO, *Approval & Oversight*). Meanwhile, inspectors travel to clinical study sites to "look[] for evidence of fabrication, manipulation, or withholding of data." FDA, *Step 4: FDA Drug Review* (Jan. 4, 2018), https://tinyurl.com/bdcub9sj.

Ultimately, the review team compiles a recommendation that "analyze[s] the condition or illness for which the drug is intended and evaluate[s] the current treatment landscape," considers "clinical benefit and risk information submitted by the drug maker, taking into account any uncertainties that may result from imperfect or incomplete data," and assesses potential "[r]isk management strategies." FDA, *Development & Approval Process: Drugs* (Aug. 8, 2022), https://tinyurl.com/vajsn94c. These detailed recommendations typically span hundreds of pages of expert analysis. For example, an FDA integrated assessment of a recently approved NDA was 346 pages, the vast majority of which were devoted to in-depth analysis of the scientific studies informing the FDA's safety and effectiveness findings. *See* FDA, Ctr. for Drug Eval. & Res., *Integrated Review: FABHALTA (Iptacopan) Capsules* (Dec. 5, 2023), http://tinyurl.com/mt24aspz.

After the scientific reviews are complete, FDA managers independently assess the review team's recommendation on whether to approve the NDA. GAO, *Approval & Oversight* at 9. Congress has directed the FDA to disapprove an NDA that provides "insufficient information to determine whether [the] drug is safe for use" under the intended conditions, or that fails to present "substantial evidence"—defined to include "adequate and well-controlled investig-

ations, including clinical investigations, by experts qualified by scientific training and experience"—that the drug will "have the effect it purports or is represented to have." 21 U.S.C. § 355(d).

If the drug clears those and other hurdles, the FDCA directs that the FDA "shall" approve the NDA and allow the drug to enter the market. *Id.* § 355(c). In approving a new drug, the FDA specifies precise labeling and requires manufacturers to comply with detailed regulations. *See* 21 C.F.R. §§ 201.1–201.328, 210.1–210.3. In addition, the FDA is authorized to place restrictions on the drug's distribution to ensure that the drug is used in a manner that the FDA can be confident is safe. *See* GAO, *Approval & Oversight* at 10. Initially, the principal basis for restricted approval was a set of 1992 regulations collectively known as "Subpart H," under which the FDA can impose "such postmarketing restrictions as are needed to assure safe use," 21 C.F.R. § 314.520, of a drug that "ha[s] been studied for [its] safety and effectiveness in treating serious or life-threatening illnesses and that provide[s] meaningful therapeutic benefit to patients over existing treatments," *id.* § 314.500. In 2007 amendments to the FDCA, Congress made clear that the FDA may condition approval of any new drug on the adoption of "a risk evaluation and mitigation strategy" (REMS) if "necessary to ensure that the benefits of the drug outweigh the risks." 21 U.S.C. § 355-1(a)(1). Congress also specified that any drug that (like mifepristone) was subject to Subpart H restrictions at the time of the 2007 amendments was "deemed to have in effect an approved [REMS] under" the FDCA until the sponsor submitted, and the FDA approved, a REMS. *Id.* § 331 note.

For all approved drugs, the sponsor has an ongoing duty to "review all adverse drug experience information" it obtains "from any source, foreign or domestic, including information derived from commercial marketing experience, postmarketing clinical investigations, postmarketing epidemiological/surveillance studies, reports in the scientific literature, and unpublished scientific papers." 21 C.F.R. § 314.80(b). The sponsor must report all "serious and unexpected" adverse experiences to the FDA within fifteen days of discovering them, *id.* § 314.80(c)(1)(i), and it must report all other adverse experience data at quarterly intervals for three years following approval and annually thereafter, *id.* § 314.80(c)(2)(i). Separately, the sponsor must file an annual report with the FDA with detailed information about new developments that cast light on the drug's safety or effectiveness or on the adequacy of its labeling. *Id.* § 314.81(b)(2).

Altogether, the FDA's evaluation of whether and how a drug can be safely and effectively used begins before any human subjects are involved and continues as long as the drug remains on the market. At every stage, the agency works pursuant to a statutory mandate to protect Americans' health and safety by applying expert scientific judgment to an accumulating body of clinical and observational evidence.

II. Because the FDA's safety and effectiveness findings involve specialized scientific expertise, they should generally be upheld absent compelling new evidence.

The rigor of the FDA's process in approving a new drug, determining the conditions under which it is safe to use, and continuing to monitor its safety thereafter underscores that these functions "require[] a

high level of technical expertise." *Kleppe v. Sierra Club*, 427 U.S. 390, 412 (1976); *see Schering Corp. v. FDA*, 51 F.3d 390, 399 (3d Cir. 1995) (explaining that "judgments as to what is required to ascertain the safety and efficacy of drugs fall squarely within the ambit of the FDA's expertise"). They are therefore "properly left to the informed discretion of the responsible federal agenc[y]." *Kleppe*, 427 U.S. at 412; *see Baltimore Gas & Elec. Co. v. Nat. Resources Def. Council, Inc.*, 462 U.S. 87, 103 (1983) (observing that "a reviewing court must generally be at its most deferential" when examining an agency's "predictions, within its area of special expertise, at the frontiers of science"); *Rempfer v. Sharfstein*, 583 F.3d 860, 868 (D.C. Cir. 2009) (noting that courts "owe considerable deference" to "a scientific judgment by the FDA"). The deference owed to the FDA's scientific determinations derives from both the FDA's subject-matter expertise and the rigor of the process through which Congress directed the FDA to bring that expertise to bear in assessing a drug's safety and effectiveness. *See, e.g.*, *Rutherford v. United States*, 806 F.2d 1455, 1461 (10th Cir. 1986) (recognizing Congress's intent "to give the [FDA] the primary jurisdiction to determine evidentiary matters concerning drugs about which it has a special expertise").

To be sure, the FDA is not infallible in making safety and effectiveness findings. For example, in unusual instances, impermissible considerations, rather than scientific judgment, could drive its decisionmaking. *See, e.g.*, *Tummino v. Torti*, 603 F. Supp. 2d 519, 545–46 (E.D.N.Y. 2009) (vacating denial of a citizen petition where the FDA Commissioner overrode the "strong[]" recommendations of an "Advisory Committee *and* FDA scientific review staff"

and instead succumbed to "pressure[] by the White House" to restrict a drug's sale in a way that the "overwhelming evidence" showed to be unnecessary). And later developments might reveal safety or effectiveness concerns that the FDA's rigorous initial process failed to identify. For this reason, Congress gave the FDA authority to withdraw approval of an NDA if, for example, "clinical or other experience, tests, or other scientific data show that [a] drug is unsafe for use," or if "new information" undermines the FDA's conclusion that there is "substantial evidence that the drug will have the effect it purports or is represented to have." 21 U.S.C. § 355(e).

Moreover, the FDA does not act alone in identifying new information that calls an approval or approved labeling into question. Any "interested person" may file a citizen petition urging the FDA to "issue, amend, or revoke" a decision. 21 C.F.R. § 10.25(a). Indeed, the FDA has eventually withdrawn approval of more than twenty drugs that Public Citizen, through citizen petitions written by its medical experts, urged the FDA to remove from the market, primarily based on post-marketing evidence raising significant safety concerns. *See*, *e.g.*, FDA, *FDA Drug Safety Communication: FDA Recommends Against the Continued Use of Propoxyphene* (Nov. 19, 2010), https://tinyurl.com/57wz46cx (FDA action in response to a Public Citizen petition).

When a citizen petition challenges the FDA's judgment on safety and effectiveness based only on disagreement with the FDA's expert evaluation of the existing scientific evidence, however, the FDA's denial of the petition will rarely, if ever, be arbitrary and capricious. "The scope of review under the 'arbitrary and capricious' standard is narrow[,] and a court is not

to substitute its judgment for that of the agency." *Motor Vehicle Mfrs. Ass'n of U.S., Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983). And the data-driven process that Congress directed the FDA to follow in assessing the safety and effectiveness of new drugs and determining the restrictions to be placed on their use is designed to produce rational results based on technical expertise.

The degree of scientific, medical, and mathematical expertise that goes into FDA decisions with respect to approval and regulation of a particular drug makes clear why, as then-Judge Kavanaugh wrote for a unanimous D.C. Circuit panel, "[a] court is ill-equipped to second-guess" the FDA's "scientific judgment." *Cytori Therapeutics, Inc. v. FDA*, 715 F.3d 922, 927 (D.C. Cir. 2013). And the stakes are high: Americans' health and lives depend, quite literally, on decisions whether to approve and how to regulate a particular drug. Accordingly, absent evidence in the administrative record casting grave doubt on the FDA's scientific judgment, courts properly respect the agency's decisions with respect to specific medical products. *See also* 21 U.S.C. § 355(h) (providing that the FDA's factual findings concerning disapproval of an NDA or withdrawal of approval, "if supported by substantial evidence, shall be conclusive").

III. Respondents' citizen petition failed to offer new evidence supporting reversal of the 2016 REMS modifications.

Respondents filed this case in November 2022, challenging (among other things) the FDA's March 2016 decision to make certain modifications to mifepristone's REMS and the FDA's December 2021 denial of respondents' 2019 citizen petition concerning

the modifications.[3] Because respondents filed the case more than six years after the March 2016 decision, their challenge to the decision is timely only by reference to the FDA's 2021 denial of their citizen petition. *See* 28 U.S.C. § 2401(a). The question here, then, is not whether the FDA's 2016 action was arbitrary and capricious, but whether the FDA was arbitrary and capricious in rejecting the citizen petition's challenges to that action. *Cf. United States v. L.A. Tucker Truck Lines, Inc.*, 344 U.S. 33, 37 (1952) ("[C]ourts should not topple over administrative decisions unless the administrative body … has erred against objection made at the time appropriate under its practice."). Review of the citizen petition and the FDA's response reveals no basis for holding that the FDA's rejection of respondents' challenges to the 2016 REMS modifications was arbitrary and capricious. The petition neither identified a process breakdown that caused the FDA to overlook critical data nor presented substantial new evidence that was unavailable in 2016.[4]

Importantly, the administrative record shows that, beginning with its evaluation of the NDA, the FDA

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[3] Also before the Court is the Fifth Circuit's affirmance of a preliminary injunction concerning the FDA's 2021 decision not to enforce certain restrictions on mifepristone's distribution. Amici agree with petitioners that the 2021 decision was lawful, but part III of this brief focuses on the 2016 REMS modifications.

[4] *See* Am. Ass'n of Pro-Life Obstetricians & Gynecologists, et al., Citizen Petition (Mar. 29, 2019), https://tinyurl.com/3xnpkyfw (hereafter, Citizen Petition); Letter from Patrizia A. Cavazzoni, FDA, Director, Ctr. for Drug Eval. & Res., to Donna J. Harrison, Am. Ass'n of Pro-Life Obstetricians & Gynecologists, et al. (Dec. 16, 2021), https://tinyurl.com/5evavs6k (hereafter, Response Letter).

subjected mifepristone to the same rigorous scrutiny that it applies to every new drug. *See* FDA, *Drug Approval Package: Mifeprex (Mifepristone) Tablet* (Sept. 28, 2000), https://tinyurl.com/5ejsucmw (linking to nearly 200 pages of detailed medical, chemistry, environmental, pharmacology, statistical, and clinical pharmacology biopharmaceutics reviews). The FDA's decision in 2016 to lift some of the restrictions that it had previously imposed on mifepristone came only after a comparable level of scientific inquiry: A 108-page medical review considered extensive clinical evidence of safety and effectiveness, including evidence of mifepristone's observed effects following its entry into the market. *See* FDA, Ctr. for Drug Eval. & Res., *Medical Review(s): Mifeprex* (July 2015), https://tinyurl.com/fsw4fst6 (hereafter, REMS Medical Review). The proposed changes underwent review by chemists, clinical pharmacologists, statisticians, and others. *See* FDA, *Mifeprex (Mifepristone) Tablets* (Mar. 29, 2016), https://tinyurl.com/4f3baukc (linking to 2016 approval documents). And a cross-disciplinary team leader synthesized these studies into an 87-page review document and concurred in the recommended REMS changes. *See* FDA, Ctr. for Drug Eval. & Res., *Cross Discipline Team Leader Review: Mifeprex* (Apr. 6, 2016), https://tinyurl.com/3yztydfm.

Respondents' citizen petition disagreed with the FDA's expert analysis of the medical literature available at the time of the 2016 REMS modifications, but it offered virtually no new information and no discussion of the FDA's detailed analysis in adopting the modifications. Nearly all the evidence the petition cited in opposing the modifications predated 2016 and, therefore, failed to show that the body of available

scientific evidence had meaningfully changed since the FDA concluded that the REMS modifications would not compromise patient safety.

The petition's challenges to the 2016 modifications identified only a handful of new facts:

- The petition cited data showing that, as of the end of 2018, ninety-seven women in the United States with ectopic pregnancies had received mifepristone (even though mifepristone's labeling is required to state that it is contraindicated for ectopic pregnancies), and two of these women had died after the ectopic pregnancy went undiagnosed. Citizen Petition at 5 (citing FDA, *Mifepristone U.S. Post-Marketing Adverse Events Summary Through 12/31/2018*, at 1, https://tinyurl.com/3utjk7ur). But 89 of these ectopic pregnancies, and both of the fatalities, were reported and addressed by FDA experts *before* the FDA made the 2016 modifications. *See* REMS Medical Review at 82, 84. The FDA had thus already weighed these risks in 2016.
- The petition cited a 2018 study for the proposition that complications from medication abortions are more frequent for people who undergo the procedure at home rather than in a healthcare facility. Citizen Petition at 8 (citing Isabelle Carlsson, et al., *Complications Related to Induced Abortion: A Combined Retrospective and Longitudinal Follow-Up Study*, BMC Women's Health (Sept. 25, 2018), https://tinyurl.com/26t36cjz). The FDA, though, explained that the study found "no statistically significant difference" in complication rates for medication abortions that take place at home,

as compared to those that take place in a hospital. Response Letter at 15. And the FDA had already "assessed serious adverse events … as reported in [respondents'] literature" when initially adopting the REMS modifications. *Id.*

- In arguing that the FDA should not have eliminated the requirement that a patient return to her healthcare provider for a follow-up examination after taking mifepristone, the petition cited a 2017 study explaining the need to ensure that postpartum patients who are Rh-negative receive a certain medication. Citizen Petition at 9 (citing Am. Coll. of Obstetricians & Gynecologists, *Practice Bulletin No. 181: Prevention of Rh D Alloimmunization* (Aug. 2017), https://tinyurl.com/43urspd8 (hereafter, ACOG, *Practice Bulletin*)). As the study noted, the importance of providing such care has been known since the 1970s, *see* ACOG, *Practice Bulletin* at 59—before the challenged decision. *See also* Citizen Petition at 9 (citing a 2003 study for the same point). And the FDA's response to the petition—explaining why an in-person "follow-up clinic visit" is not necessary for a patient to obtain the necessary treatment, Response Letter at 18—cannot reasonably be described as arbitrary and capricious.
- Finally, the petition *critiqued* two 2018 studies that suggested that follow-up visits after a medication abortion might not be necessary. *See* Citizen Petition at 9–10. The FDA obviously did not rely on these post-2016 studies in crafting its 2016 REMS modifications. Accord-

> ingly, any flaws in the studies would not call into question the FDA's earlier decisionmaking.

In short, the citizen petition's 14-page discussion of the 2016 REMS modifications presented no new information that called into question the FDA's decision to make those modifications based on the expert evaluation of its medical officers, chemists, pharmacologists, statisticians, and clinical pharmacology biopharmaceutics experts. Nonetheless, the FDA walked point by point through the petition's arguments in a 40-page, single-spaced response that addressed the cited material and reaffirmed the substantial evidentiary basis for the FDA's 2016 action. Comparison of the two documents strongly demonstrates that denial of the 2019 petition was not arbitrary and capricious.

* * *

Although Public Citizen and CSPI in their 50-year histories have disagreed with FDA decisions dozens of times, the case law and Congress both correctly recognize that attempts to overturn an FDA decision with respect to a drug's safety and effectiveness properly face a high bar. With respect to the 2016 REMS, respondents fall well short of that high bar.

CONCLUSION

The decision below should be reversed.

Respectfully submitted,

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