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.

DANCO LABORATORIES, L.L.C., PETITIONER

v.

ALLIANCE FOR HIPPOCRATIC MEDICINE, ET AL.

ON WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FIFTH CIRCUIT

BRIEF FOR THE ASSOCIATION OF AMERICAN MEDICAL COLLEGES IN SUPPORT OF PETITIONERS

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INTEREST OF AMICUS*

The Association of American Medical Colleges (AAMC) is a nonprofit association dedicated to improving the health of people everywhere through medical education, health care, medical research and community collaborations. Its members are all 158 U.S. medical schools accredited by the Liaison Committee on Medi-

* No counsel for any party authored this brief in whole or in part, and no person or entity, other than amicus curiae or their counsel made a monetary contribution intended to fund the preparation or submission of this brief.

cal Education, 13 accredited Canadian medical schools, approximately 400 academic health systems and teaching hospitals and more than 70 academic societies. The AAMC leads and serves America's medical schools, teaching hospitals and academic health systems (AMCs), and through these institutions and organizations represents hundreds of thousands of individuals across academic medicine, including full-time faculty members, medical students, resident physicians and graduate students and postdoctoral researchers in the biomedical sciences.

AAMC's members pioneer discoveries and innovations that save lives and transform health care. More than half of all research sponsored by the National Institutes of Health is conducted at medical schools and teaching hospitals. Research at AAMC member institutions brings new treatments from the laboratory to the patient bedside in impacted communities. Organ transplant, immunotherapies for cancer and laparoscopic surgery are just three of the many innovations in medical care pioneered at teaching hospitals. The advances growing out of this research save lives and improve the quality of life for millions of people.

The cutting-edge research and high-quality patient care for which AMCs are recognized depends in large part on the Food and Drug Administration (FDA)'s scientifically rigorous process for evaluating and approving new drugs. Doctors rely on the FDA's determinations regarding the safety and efficacy of drugs, including conditions of use and clinical data described in the FDA-approved prescribing information and FDA announcements regarding drug safety, to inform their treatment decisions. Additionally, patients rely on con-

tinued access to and availability of FDA-approved drugs on which their health depends. Accordingly, AAMC has a significant interest in the stability of the FDA's evidence-based, science-driven review and decision-making process on which its members rely to provide expert patient care and pursue state-of-the-art medical research that saves lives and improves health.

SUMMARY OF THE ARGUMENT

Congress has vested the FDA with sole authority to review and approve new drugs, including their conditions for distribution and use, through a multidisciplinary, science-based process. Where a court is reviewing whether FDA actions taken pursuant to its drug approval and oversight authority were arbitrary and capricious under the Administrative Procedure Act, and especially in matters like this involving public health, the court's review is appropriately deferential to scientific determinations that Congress has committed to the agency's expertise. The court may not, as the Fifth Circuit did here, substitute its view of the scientific evidence for the agency's own.

AAMC supports petitioners' arguments that the FDA's actions with respect to mifepristone that are at issue in this case were lawful. Namely, the FDA's decision to change the conditions of use, adverse event reporting requirements and in-person dispensing requirements for mifepristone were not arbitrary and capricious. AAMC agrees with petitioners that the Fifth Circuit's unprecedented second-guessing of the FDA's expert judgment about the conditions required to assure the safe use of mifepristone contradict this Court's

precedents and applicable administrative law principles.

AAMC writes separately to address the implications of the Fifth Circuit's decision beyond the particulars of mifepristone. It is of critical importance that the scientific review and regulatory decision-making process remains the purview of the expert agency (the FDA) to which Congress has delegated specific authority for the scientific review of medical products—not the judicial branch.

AAMC's member institutions bring about life-changing, cutting-edge medical treatments and improve patient care through scientific discoveries. The use, study, purchase and prescribing of FDA-approved products are critical to the institutions' core missions of research, clinical care and educating the future health care workforce. AMCs rely on the FDA's rigorous, science-driven drug approval process, as well as the continued availability of FDA-approved drugs, to guide research and investment decisions and inform medical practice.

Permitting an individual court or judge to substitute his or her opinions for the FDA's expert judgment threatens to upset this established, and highly successful, science-driven process and undermines the very authority Congress granted to the FDA. The fragmented approach that would be permitted under the Fifth Circuit's decision—where the availability of drugs and their applicable conditions of use could vary by judicial district—would undercut more than eight decades of progress since the passage of the Federal Food, Drug, and Cosmetic Act, imperiling innovative, life-

saving research and product development and threatening patient care.

The Court should reaffirm faithfulness to the FDA's evidence-based process, rather than embark on a new path in which individual judges, without access to the scientific resources and expertise of the FDA, are permitted to substitute their own views for those of the experts that Congress has entrusted to protect the public health.

ARGUMENT

I. THIS CASE IS ABOUT JUDICIAL DEFERENCE TO AN AGENCY'S EXPERT EXECUTION OF CONGRESSIONALLY DIRECTED SCIENTIFIC DECISION-MAKING IN HIGHLY COMPLEX, TECHNICAL FIELDS

Unlike other cases that this Court is presently considering, such as *Loper Bright Enterprises* v. *Raimondo*, No. 22-451 (S. Ct. argued Jan. 17, 2024), this case does not concern judicial deference to an agency's legal opinion regarding the meaning of a statutory or regulatory text. Rather, this case concerns the proper role of judicial deference when reviewing, under an arbitrary and capricious standard, an agency's scientific judgment, made in the exercise of their core, Congressionally assigned technical expertise—especially when those decisions implicate the public health. Justice Kavanaugh has described as "[a] basic principle of administrative law," that "[i]n Administrative Procedure Act cases alleging arbitrary and capricious agency action, courts must be careful not to unduly second-guess an agency's scientific judgments." *Cytori Therapeutics, Inc.* v. *FDA*, 715 F.3d 922, 923 (D.C. Cir. 2013) (Ka-

vanaugh, J.). This Court should be wary of undermining that deference or otherwise elevating the opinions of judges without scientific training over the science-driven process employed by expert agencies like the FDA.

In general, "courts owe significant deference to the politically accountable entities with the 'background, competence, and expertise to assess public health.' " *FDA* v. *Am. Coll. of Obstetricians & Gynecologists*, 141 S. Ct. 578, 579 (2021) (Roberts, C.J., concurring) (quoting *South Bay United Pentecostal Church* v. *Newsom*, 140 S. Ct. 1613, 1614 (2020) (Roberts, C.J., concurring)). See also *Marshall* v. *United States*, 414 U.S. 417, 427 (1974) ("When Congress undertakes to act in areas fraught with medical and scientific uncertainties, legislative options must be especially broad and courts should be cautious not to rewrite legislation, even assuming, arguendo, that judges with more direct exposure to the problem might make wiser choices."). Put differently, while judges should "do" law, scientists should "do" science.

There is even greater cause for judicial deference to agency expertise where, as here, Congress has established and delegated to the FDA robust authority and the resources to evaluate and make decisions on the basis of complex scientific evidence. See Part II.A., *infra*. On the record before the Court, and for the reasons stated in the federal petitioners' brief, AAMC supports petitioners' arguments that the agency's decision to change the conditions of use, adverse event reporting requirements and in-person dispensing requirements for mifepristone were neither arbitrary nor capricious. Pet. 33-44. AAMC agrees with petitioners

that the Fifth Circuit's unprecedented second-guessing of the FDA's expert judgment about the conditions required to assure the safe use of mifepristone contradict this Court's precedents and applicable administrative law principles. Moreover, AAMC supports the arguments set forth in the briefs of numerous amici supporting certiorari regarding the demonstrated safety and efficacy of mifepristone, the critical role mifepristone plays in women's reproductive health and the detrimental impact the Fifth Circuit's decision would have on patient care and medical practice. See, *e.g.*, American College of Obstetricians & Gynecologists et al. Cert. Amicus Br. 7-23; Patient & Provider Advocacy Orgs. Cert. Amicus Br. 9-20.

The issues before the Court in this case, however, go far beyond the specifics of an individual medication or its conditions of use. The scientific review and regulatory decision-making process must remain the purview of the federal agency to which Congress has entrusted specific authority for the scientific review and approval of medical products—not the judicial branch. That science-driven process has been the bedrock of medical innovations that have been and continue to be vital to patients' health and wellbeing. The Court should not lightly undermine that essential foundation of the American health care system.

II. The Fifth Circuit's Decision Would Jeopardize the Science-Driven FDA Approval Process and the Continued Availability of Approved Drugs

The use, study, purchase and prescribing of FDA-approved products are critical to AMCs' core missions

of research, clinical care and educating the future health care workforce. AMCs rely on the FDA's rigorous, science-driven drug approval process, as well as the continued availability of FDA-approved drugs, to guide research and investment decisions and inform medical practice. Permitting individual courts or judges to substitute their opinions for the FDA's expert judgments of the scientific record threatens to upset this established, and highly successful, evidence-based process and undermines the very authority Congress granted to the FDA.

A. Congress Has Vested the FDA with Broad Authority to Review and Approve New Drugs, Including Their Conditions for Distribution and Use, Through a Multidisciplinary, Science-Based Process

Through the Food, Drug, and Cosmetic Act of 1938, Pub. L. 75-717, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. 301 *et seq.*) (FDCA), Congress has vested the FDA with exclusive governmental authority to "protect the public health by ensuring that * * * drugs are safe and effective" and to "promote the public health by promptly and efficiently reviewing clinical research and taking appropriate action on the marketing of regulated products in a timely manner." 21 U.S.C. 393(b). In furtherance of this mission, the FDCA establishes a comprehensive regulatory framework for the review and approval of new drugs through the new drug application (NDA) process. 21 U.S.C. 355. The FDCA strictly prohibits the introduction or delivery for introduction into interstate commerce of any new drug unless and until the NDA for such drug has received FDA approval. 21 U.S.C. 355(a). Estab-

lishment of a national standard for drug approvals through the NDA approval process was based on Congress' recognition that the previous patchwork approach to regulating drugs was inadequate, as evidenced by an incident in 1937 where an untested drug led to the deaths of more than 100 people in 15 states. See, *e.g.*, Carol Ballentine, Off. of Pub. Affairs, U.S. Food & Drug Admin., *Sulfanilamide Disaster* (June 1981), https://www.fda.gov/about-fda/histories-product-regulation/sulfanilamide-disaster.

The NDA process requires that the FDA undertake a rigorous, science-driven evaluation of any NDA, as well as any new conditions for use of a previously approved drug submitted under a supplemental NDA (sNDA), to determine, *inter alia*, whether the drug is "safe for use" and will have the "effect[s] it purports or is represented to have" under the conditions of use prescribed in the labeling. 21 U.S.C. 355(d). Recognizing that no drug is devoid of safety risks, teams of scientific experts undertake a careful and balanced risk-benefit assessment to determine whether the benefits of the drug outweigh the potential risks. *Ibid.* See also U.S. Food & Drug Admin., *Guidance for Industry on Benefit-Risk Assessment for New Drug and Biological Products* (Oct. 2023), https://www.fda.gov/media/152544/download. The technical review process requires experts from relevant scientific disciplines (*e.g.*, medical, chemistry, pharmacology, statistics, clinical pharmacology) to analyze, interpret and synthesize the information and evidence in the application, including proprietary or unpublished information, as well as any additional information the applicant provides in response to FDA requests for information. See U.S.

Food & Drug Admin., *FDA's Drug Review Process: Continued* (Aug. 24, 2015), https://www.fda.gov/drugs/information-consumers-and-patients-drugs/fdas-drug-review-process-continued. The technical review process includes a thorough evaluation of the complete scientific record, including the clinical and non-clinical studies of the drug, associated study protocols, statistical analysis plans, clinical study reports and detailed data sets and the relationship between such studies in establishing the risk-benefit profile of the drug. See, *e.g.*, U.S. Food & Drug Admin., *Review Team Responsibilities* (Sept. 1, 2015), https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/review-team-responsibilities.

These technical reviews do not merely rely on the information provided in the application, but require the FDA's scientific experts to undertake an independent analysis of the data and exercise their scientific judgment to make conclusions and recommendations regarding the product, including whether the application meets the statutory standards for approval. The technical review process ensures that any approval decisions are based on a comprehensive assessment of the evidence and the consensus of a multidisciplinary group of experts in the relevant scientific fields, rather than any single individual's opinion.

If, based on this scientific review process, the FDA determines that a drug meets these statutory standards for safety and effectiveness and the benefits of the drug outweigh the risks, the FDA will approve the NDA, allowing the drug to be marketed in the U.S.

Congress has vested the FDA with authority to make safety and effectiveness determinations and undertake the complex risk-benefit assessments required for approval. The FDCA neither defines nor provides precise standards for what it means for a drug to be "safe" or "effective" or when the benefits outweigh the risks. Rather, the FDCA explicitly assigns to the FDA the responsibility to apply the standards to individual products in an exercise of the FDA's scientific expertise and well-reasoned judgment. For example, regarding safety, the FDA may refuse to approve an NDA if "the Secretary finds * * * he has insufficient information to determine whether such drug is safe for use." 21 U.S.C. 355(d)(4). The statute does not elaborate on what level or type of information is "sufficient" to demonstrate a drug is safe; instead, Congress explicitly assigns to the FDA the task of determining whether the information is sufficient.

Similarly, regarding effectiveness, the FDCA permits the FDA to refuse to approve an NDA if "the Secretary finds * * * there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have." 21 U.S.C. 355(d)(5). Here, the FDCA defines the term "substantial evidence" as "evidence consisting of adequate and well-controlled investigations, including clinical investigations, by *experts qualified by scientific training and experience* to evaluate the effectiveness of the drug involved, on the basis of which it could *fairly and responsibly be concluded by such experts* that the drug will have the effect it purports * * * ." 21 U.S.C. 355(d) (emphasis added). That definition does not articulate specific requirements regarding the level of evidence necessary to meet this

standard but, again, relies instead on the FDA to exercise its judgment in making this efficacy determination, emphasizing that such decisions should be rooted in the judgment of experts who are scientifically trained to evaluate drugs. *Ibid.*

Congress has also authorized the FDA, as part of its risk-benefit assessment, to require an applicant to implement a risk evaluation and mitigation strategy (REMS) under certain circumstances to ensure the benefits of the drug outweigh the risks. 21 U.S.C. 355-1(a)(1)-(a)(2). Consistent with Congress' delegation of authority for product approval, the FDA is vested with authority to determine whether a REMS is necessary and what elements are required for a particular drug to assure safe use. Specifically, the FDA may impose a REMS for a specific drug if "the Secretary * * * makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks of the drug." 21 U.S.C. 355-1(a)(2). Similarly, the FDA may require that the REMS include one or more elements as part of the strategy (*e.g.*, medication guide, communication plan, disposal requirements) or require additional elements to assure safe use (*e.g.*, training for health care providers who prescribe the drug, limiting dispensing to certain health care settings), "if the Secretary determines" such elements are required. 21 U.S.C. 355-1(e)-(f).

In assessing whether a REMS is necessary for a particular drug and the elements required thereunder, the FDA is required to consider several factors, including the estimated size of the patient population, the expected benefit of the drug, the duration of treatment, the seriousness of any known or potential adverse

events and whether the drug is a new molecular entity. 21 U.S.C. 355-1(a)(1). Although the FDA is required to consider these factors, the statute vests the Secretary with the exclusive authority to apply these factors to the risk-benefit framework to make a determination that a REMS is required. *Ibid.* The FDA's decision to implement a REMS involves a complex, drug-specific inquiry that considers the risk-benefit profile of the drug, available clinical and post-marketing data related to the risk and the input of internal and external experts with specialized expertise relevant to the risk. See, *e.g.*, U.S. Food & Drug Admin., *Guidance for Industry on REMS: FDA's Application of Statutory Factors in Determining When a REMS Is Necessary* (Apr. 2019), https://www.fda.gov/media/100307/download.

The conditions of an initial approval, including a REMS, are subject to modification as new data becomes available. Such data may come from a variety of sources including clinical trials, real-world evidence studies, post-marketing adverse event reporting, patient and physician reports and the FDA's own monitoring processes. Indeed, the FDCA requires the FDA to conduct routine, comprehensive assessments of REMS to assess whether the elements of the REMS assure the safe use of the drug, are not unduly burdensome on patient access and minimize the burden on the health care delivery system. 21 U.S.C. 355-1(f)(5).

The FDA is permitted to require modifications to the REMS at any time to add, modify or remove elements from the approved strategy to, *inter alia*, ensure the benefits of the drug outweigh the risks, minimize the burden on the health care delivery system of complying with the strategy or accommodate different,

comparable aspects of the elements to assure safe use. 21 U.S.C. 355-1(g)(4). These are the only factors the FDA is required to consider when modifying a REMS—nothing in the statute requires the agency to rely on specific evidence or evaluate the cumulative effects of proposed modifications in a single study, as the Fifth Circuit suggests. Pet. App. 44a-45a. The FDA has repeatedly exercised its broad authority to modify and remove REMS programs without relying on any specific clinical data, as other amici have explained. See Food & Drug L. Scholars Cert. Amicus Br. 11-12.

The FDA's comprehensive, multidisciplinary, science-driven process guides the entire product lifecycle and the same rigorous standards that apply to the initial approval apply equally to subsequent approvals of sNDAs and other modifications to the application, including modifications to REMS.[1]

If, following approval, the FDA determines that the risks of a drug outweigh the benefits, even with appropriate labeling and other protections, the FDA may initiate an action to withdraw its approval of the drug. Specifically, the FDCA requires the FDA to withdraw an NDA approval "if the Secretary finds * * * that clinical or other experience, tests, or other scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved." 21 U.S.C. 355(e). Although the statute

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[1] Indeed, this comprehensive, multidisciplinary, science-driven process is evident in the agency's initial and supplemental approvals for mifepristone, as well as FDA's decision to modify the REMS. See Pet. 34-38, 41-44; see also Food & Drug L. Scholars Cert. Amicus Br. 7-8, 13-15.

assigns to the FDA the responsibility to make the finding that a drug is unsafe, it does not allow the FDA to make such a scientific determination on a whim, without due process. Rather, the FDA is required to provide "due notice and opportunity for hearing to the applicant" prior to withdrawal, or in exceptional cases where the Secretary determines there is an imminent hazard to the public health warranting the immediate suspension of an approval, provide the applicant with an opportunity for an expedited hearing following such suspension. *Ibid.*

B. AMCs Rely on the FDA's Evidence-Based, Science-Driven Process for the Review and Approval of New Drugs

As part of the drug approval process discussed above, the FDA undertakes a comprehensive review of the scientific data to make expert-based judgments regarding the safety and efficacy of the drug and the conditions for distribution and use. See Part II.A., *supra*. Entities like AMCs that conduct complex biomedical research not only rely on the FDA's rigorous review process to support clinical practice, but also depend on the FDA's decision-making process to determine where to make investments in new research. Thus, AMCs' continued ability to rely on these processes is vital to both advancing scientific discovery and patient care.

AMCs play a pivotal role in the research and development of drugs across all stages of the product lifecycle. Numerous innovative therapeutics were initially discovered by researchers at AMCs and subsequently licensed or otherwise transferred to pharmaceutical partners for clinical development. See, *e.g.*,

Ashley J. Stevens et al., *Role of global public sector research in discovering new drugs and vaccines*, J. Tech Transfer (Apr. 27, 2023), https://link.springer.com/article/10.1007/s10961-023-10007-z. Even after out-licensing or transferring a product candidate to a pharmaceutical partner, AMCs typically remain involved throughout the clinical research process. AMCs lead almost half of all clinical trials conducted in the U.S. See, *e.g.*, Urtė Fultinavičiūtė & Irena Maragkou, *Profit vs inquiry: Clash of objectives in academic and commercial trials*, Clinical Trials Arena (Nov. 16, 2023), https://www.clinicaltrialsarena.com/features/academic-commercial-clinical-trials/. Additionally, AMCs continue to invest in research activities post-approval, including by conducting FDA-required post-approval studies in partnership with commercial sponsors, as well as other studies evaluating new therapeutic uses, potential safety risks and comparative effectiveness of available therapies. *Ibid.* See also *e.g.*, Gregory K. Robbins et al., *Comparison of Sequential Three-Drug Regimens as Initial Therapy for HIV-1 Infection*, 349 New Eng. J. Med. 2293 (Dec. 11, 2003), https://www.nejm.org/doi/full/10.1056/nejmoa030264 (describing results from a post-approval study conducted at numerous AMCs comparing treatment regimens for first-line HIV-1 infection). AMCs' continued ability to conduct these studies depends in part on their ability to rely on the FDA's science-based determinations of safety and efficacy and the availability of approved products.

The FDA's approval process not only guides AMCs in selecting products for research but helps protect their research investments. Specifically, AMCs invest

in research and development activities based on the expectation that once a drug is approved, it will be lawful to sell the drug in the United States for years to come, unless new evidence is identified by or submitted to the FDA that would provide grounds for withdrawal of approval. Indeed, many license and acquisition agreements between AMCs and their pharmaceutical partners contain milestone and royalty payments triggered by FDA approval or other post-approval benchmarks. See, *e.g.*, Vladimir Drozdoff & Daryl Fairbairn, *Licensing Biotech Intellectual Property in University–Industry Partnerships*, Cold Spring Harbor Persps. Med. (Mar. 2015), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4355252/. These agreements provide opportunities for AMCs to reinvest in future research, but depend on the stability of the FDA regulatory scheme, approval process, and mechanisms for evaluating post-approval evidence of drugs' safety and efficacy in clinical practice. See also Pharma. Res. Mfrs. of Am. et al. Cert. Amicus Br. 19-20.

Further, AMCs and health care providers nationwide rely on the FDA's assessment of clinical data and determination of a drug's safety and effectiveness, as well as the continued availability of approved products, to inform clinical decision-making and medical practice. Additionally, AMCs and academic societies undertake similar science-driven assessments in developing recommendations for clinical care, such as clinical treatment pathways and guidelines. These recommendations depend on stability in the FDA's drug approval process in that they assume that approved products will remain available for use in clinical practice unless

the FDA determines there are grounds to withdraw approval.

C. Substituting the Opinions of the Courts, Including Individual District Judges, in Place of the FDA's Evidence-Based, Science-Driven Review and Regulatory Decision-Making Process Is Not Only Unprecedented, But Dangerous

Permitting an individual court or judge, who is not scientifically trained or bound by a science-based process, to substitute their opinions for the FDA's expert judgment undermines the scientific rigor and multidisciplinary nature of the FDA's approval process. Judges and courts lack the requisite expertise to make the complex risk-benefit determinations that are fundamental to the drug approval process. Moreover, the judicial process is not conducive to the type of review required to assess all available scientific evidence, especially when courts are asked to assess FDA approval decisions that occurred many years prior. The FDA has authority to consider all evidence and information in the scientific record, including proprietary or unpublished information, as well as to request that sponsors provide additional evidence or studies as part of the NDA review process. As noted above, Part II.A., *supra*, the FDA also has at its disposal experts from wide ranging disciplines both within the agency and through advisory bodies to help inform its judgments. Judges, by contrast, have none of this. Judicial review is constrained to the arguments and materials provided to the court, and the judge must make the decision alone, aided only by non-technical law clerks.

If permitted to stand, the Fifth Circuit's decision would subvert the comprehensive, uniform federal regulatory scheme established by Congress through the FDCA. Instead of a single, national agency decision regarding the safety and efficacy of a drug, the ruling would potentially permit either a single district court judge lacking the scientific training and expertise of the FDA to make that decision for the nation, or—perhaps even worse—lead to fragmented outcomes district-by-district with different judges drawing different conclusions, thereby creating uncertainty regarding which decision controls and leading to arbitrary discrepancies in the available treatment options from geography to geography.

Institutions and providers across the nation would be uncertain about the impact of a single court ruling nullifying the approval of a drug or restricting the distribution of that drug on their ability to prescribe the drug and would not know the outcome or timing of subsequent appeals processes. Moreover, providers might reasonably be concerned about the risk of medical malpractice liability stemming from the prescription of drug between an initial court ruling disputing the safety of a drug and a later FDA action compelled by the courts. The undermining of the national authority of the FDA to determine which drugs are safe and effective might invite legal challenges against providers that call into question established standards of care involving the use of FDA-approved drugs. Concerns regarding such a fragmented approach are what led to the passage of the FDCA and permitting such approach would undercut 85 years of progress. See p. 8, *supra*.

Additionally, the Fifth Circuit's ruling, if upheld, would allow judges and courts to set aside the FDA's scientific determinations of safety and efficacy and impact the continued availability of approved drugs, which health care providers rely on to provide critical patient care. Allowing courts to make such decisions would have a chilling effect on patient care as providers would be prevented from using drugs for the uses that the FDA has deemed safe and effective. Moreover, providers would be prevented from using the drug for any appropriately supported off-label uses, which in some cases are the medically recognized standard of care, as the FDA itself has previously acknowledged. U.S. Food & Drug Admin., *Guidance for Industry on Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices* (Jan. 12, 2009), https://www.regulations.gov/document/FDA-2008-D-0053-0127. For example, few cancer drugs are approved for pediatric use at the time of initial FDA approval. See Dylan Neel et al., *Timing of first-in-child trials of FDA-approved oncology drugs*, 112 Eur. J. Cancer 49 (Mar. 28, 2019), https://doi.org/10.1016/j.ejca.2019.02.011. Most life-saving treatments for children with cancer are based on chemotherapy agents approved for use in adults and often for other forms of cancer. See, *e.g.*, Carmen-Maria Rusz et al., *Off-Label Medication: From a Simple Concept to Complex Practical Aspects*, 18 Int'l J. Environ. Res. & Publ. Health 10447 (Oct. 4, 2021), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8508135/. Additionally, for many rare, life-threatening diseases, there are no FDA-

approved treatment options, meaning that providers must use medicines off-label, based on the available clinical evidence, to treat patients with these conditions. *Ibid.*

Permitting courts to interfere with the practice of medicine in this way—by restricting access to or availability of medicines for both approved uses and appropriately supported off-label uses—can have life-threatening consequences, particularly if patients lose access to their prescribed medications without any prior notice. The level of uncertainty this type of judicial overreach will create is untenable and could damage the ability of health care providers to prescribe medications with the confidence that they would continue to be available in the future. This would jeopardize the health and well-being of all patients and interfere with the practice of evidence-based medicine.

Permitting judges and courts to second-guess the FDA's scientific expertise and regulatory process—by imposing novel evidence requirements not mandated by statute and insisting upon seemingly perfect scientific data where such data rarely exists, see Danco Br. 43-44; Pet. 14-15—incorrectly suggests that the FDA's decisions are arbitrary and disregards the scientific and technical complexity inherent in the judgments the FDA makes regarding drug safety and efficacy. Upholding the Fifth Circuit's decision here would invite challenges to other drug approvals and REMS decisions and discredit the significance of and trust in the FDA approval process, which is generally viewed as the gold standard for drug review. Erosion of the public trust in the FDA approval process would potentially lead patients to question whether the drugs their phy-

sicians recommend are safe and effective, sowing mistrust between patients and their providers.

The FDA's evidence-based, science-driven process for evaluating new drug approvals, label revisions and the application or revision of REMS programs has served the American public well since the FDCA's enactment. The Court should reaffirm faithfulness to that process, rather than embark on a new path in which individual judges, without access to the scientific resources and expertise of the FDA, are permitted to substitute their own views for those of the scientific experts that Congress has entrusted to protect the public health.

CONCLUSION

For the foregoing reasons, the judgment of the Court of Appeals should be reversed.

Respectfully submitted.

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