No. 26-1104

IN THE UNITED STATES COURT OF APPEALS
FOR THE FOURTH CIRCUIT

PARENT AA, et al.,

Plaintiffs-Appellees,

v.

UNITED STATES DEPARTMENT OF JUSTICE,

Respondent-Appellant.

ON APPEAL FROM THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MARYLAND

BRIEF OF PUBLIC HEALTH AND HEALTH LAW SCHOLARS AS *AMICI CURIAE* URGING AFFIRMANCE IN SUPPORT OF PLAINTIFFS-APPELLEES

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INTRODUCTION

Physicians' use of their judgment and expertise to prescribe drugs and devices for purposes other than those approved by the Food and Drug Administration ("FDA")—colloquially known as off-label use—is an indispensable feature of modern medicine. The FDA approves drugs as "safe and effective for specific indications." Christopher M. Wittich, Christopher M. Burkle & William L. Lanier, *Ten Common Questions (and Their Answers) About Off-Label Drug Use,* 87 Mayo Clinic Procs. 982, 982 (2012). Federal law then generally leaves prescribing decisions, including off-label use of FDA-approved drugs and devices for a patient's particular indication, to physicians acting under state law and professional standards. *See id.* at 982, 986–87.[1]

Off-label prescribing bridges the divide between cutting edge, quickly evolving clinical research findings and the FDA's often slower-moving regulatory scheme. *See id.*; Katrina Furey & Kirsten Wilkins, *Prescribing "Off-Label": What Should a Physician Disclose?*, 18 Am. Med. Ass'n J. Ethics 587, 588–89 (2016). As such, off-label prescribing is an essential feature of medicine: studies estimate that 12% to 38% of U.S. doctor-office prescriptions are for off-label use. *See* Hassan Z. Sheikh, Cong. Rsch. Serv., R45792, Off-Label Use of Prescription

[1] Physicians' prescribing of drugs for off-label uses is distinct from entities' *promotion* of drugs for off-label uses, the latter of which the FDA is authorized to regulate. *See* Wittich et al., *supra*, at 988–89.

Drugs, at 1 (2021). In fields such as oncology, pediatrics, psychiatry, and in the treatment of rare diseases, off-label uses are common and may supply the best available therapies for many patients.[2]

The Federal Food, Drug, and Cosmetic Act ("FDCA" or the "Act") authorizes the FDA's regulation of drugs and devices. Originally passed in 1938, the FDCA is a consumer-protection statute aimed at ensuring that drugs entering interstate commerce are safe, effective, and properly labeled. The Act authorizes the FDA to regulate—through criminal and civil penalties—drug manufacturers, distributors, and other entities that move drugs into and through the stream of commerce to ensure their safety and efficacy.

In contrast, it is a "long-held understanding that the FDCA generally does not regulate off-label prescribing." Lewis A. Grossman, Nathan G. Cortez & Patricia J. Zettler, *Using FDA Law to Threaten Medical Practice*, 394 New England J. Med. 524, 524 (2026). Courts interpreting the FDCA have consistently made clear that the Act was not intended to allow the federal government to interfere with physicians' clinical decisions regarding their individual patients,

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[2] *See* Wittich et al., *supra*, at 982–85, 989; Kathleen A. Neville & Am. Acad. of Pediatrics Committee on Drugs, *Policy Statement—Off-Label Use of Drugs in Children*, 133 Pediatrics 563, 565 (2014) (reaffirmed with data updates Nov. 2020); Nat'l Cancer Inst., *Off-Label Drug Use in Cancer Treatment* (last updated Jan. 13, 2022), https://perma.cc/3JEH-VU46; Albert Fung et al., *Off-Label Medication Use in Rare Pediatric Diseases in the United States*, 10 Intractable Rare Disease Res. 238, 239–40 (2021).

including off-label prescribing of drugs or devices. *See, e.g.*, *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 350–51 & n.5 (2001); *Sigma-Tau Pharms., Inc. v. Schwetz*, 288 F.3d 141, 147–48 (4th Cir. 2002). The FDA has long affirmed this interpretation. FDA, *Understanding Unapproved Use of Approved Drugs "Off Label"* (Feb. 5, 2018), https://perma.cc/V29A-ZY3V.

Nonetheless, the U.S. Department of Justice (the "Department") now attempts a sharp expansion of federal authority under the FDCA, issuing unprecedented and unauthorized subpoenas to numerous hospitals, including Children's National Hospital, regarding the provision of gender-affirming care. While the Department alleges they are investigating potential violations of the Act, the District Court correctly understood that the Department undertakes this effort because it politically disfavors this care and aims to use its investigative powers as one means of many to regulate it out of existence. *See* JA22–23.[3]

In nonetheless insisting these subpoenas validly serve to investigate potential FDCA violations, the Department has tested unprecedented theories under which hospitals and health care practitioners could supposedly be subject to civil or criminal liability under the FDCA for their provision of gender-affirming care, including their prescribing of puberty blockers and hormone therapies. These

[3] All Joint Appendix citations are to the Corrected Joint Appendix, ECF No. 17 (May 4, 2026).

theories—premised on significant expansions of federal authority over physicians' clinical decisions—ignore the traditional manner in which health care is regulated and practiced. The Department asks the Court to license its interference in physicians' provision of health care, which is legal under state law, to patients who have requested it. In passing the FDCA, Congress did not intend for the Department of Justice to coerce health care providers into abandoning legal, clinically appropriate health care (including off-label prescribing) through the threat of FDCA liability.

As Appellees explain (Resp. Br. at 27–38, 42–47) and the District Court determined (JA19–23), these subpoenas lack a legitimate purpose under federal law and instead improperly seek to curb gender-affirming care. This Court should therefore affirm the District Court's Order. In so doing, this Court should reject the Department's interpretation of the FDCA, which would improperly enable the federal government to interfere with medical practice at large.

STATEMENT OF INTERESTS

Amici Curiae are leading scholars of health, public health, and health law who have published numerous treatises, books, and articles regarding the FDCA and the delivery, regulation, and accessibility of health care more broadly.[4] The

[4] No party's counsel authored this brief in whole or in part. No party or its counsel contributed money intended to fund the preparation or submission of this brief, and

signatories and their backgrounds are listed individually in the Motion for Leave to File that accompanies this brief. Collectively, *amici* have devoted significant portions of their careers to studying how federal health law, policy, and regulation affect patients, clinicians, and health systems, including the allocation of regulatory authority between the federal government, states, and health care professionals.

Amici have a strong interest in ensuring that the FDCA is interpreted correctly by the Government. They submit this brief in support of Appellees to provide the Court with insight into the Act's text, history, and purpose, from which the Department's interpretation significantly deviates.

Amici file this brief pursuant to Fed. R. App. P. 29(a) and Local R. 29(a). All parties to the appeal have consented to the filing of this brief.

ARGUMENT

I. Off-Label Prescribing is an Essential and Foundational Part of American Health Care

Off-label prescribing is essential for a wide range of medical specialties and treatment contexts. As FDA law scholars have observed, "off-label prescribing is so prevalent and necessary that much care would grind to a halt without it." Grossman et al., *supra*, at 525. In many cases, off-label uses of medications

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represent the accepted standard of care or the best available treatment option for a patient. *See* W.A. Meadows & B.D. Hollowell, *'Off-Label' Drug Use: An FDA Regulatory Term, Not a Negative Implication of Its Medical Use*, 20 Int'l J. Impotence Res. 135, 139 (2008). In some cases, "a physician may actually commit malpractice by not prescribing a drug off-label." *Id.*

Oncology provides a salient example. One study estimates that up to 75% of oncology drug use is off-label. Grossman et al., *supra*, at 525. The National Cancer Institute notes that oncologists may prescribe off-label to use approved medications or combinations of approved medications across various cancers, at different doses, or in children when medications have been approved for adults. *See* Nat'l Cancer Inst., *supra*. As the FDA recognizes, off-label prescribing may be useful when no approved drug exists for a condition, or if a patient has exhausted all other therapeutic options. FDA, *Understanding Unapproved Use of Approved Drugs, supra*. The need for off-label prescribing is thus even more pronounced for rare cancers, for which drug development is a particularly challenging, in large part due to the "difficulty [of] enrolling sufficient number[s] of patients to clinical trials," "decreased financial incentives for drug development," and limitations to conducting randomized control trials "due to small patient numbers or lack of appropriate therapy to use as a comparator." FDA, *OCE Rare Cancers Program* (last updated Jan. 27, 2025), https://perma.cc/A4DE-VJR3.

The widespread use of off-label prescribing in pediatric oncology reflects a broader reality across pediatric medicine. *See* Nat'l Cancer Inst., *supra*; Wittich et al., *supra*, at 982–85. One study estimated that up to 38% of all prescriptions written for children are off-label, and an expert with the Institute for Advanced Clinical Trials for Children noted that off-label medication accounts for 90% of prescriptions for newborns. *See* Patrick Boyle, *The Wish of Pediatricians: More Medications Deemed Safe for Kids*, Ass'n Am. Med. Colls. (June 21, 2022), https://perma.cc/T6UL-HDLU. In large part, the prevalence of pediatric off-label prescribing is the result of lags in FDA approvals for medication use by children, as clinical trials are often not available for pediatric populations. *Id.*; Fung et al., *supra*, at 238. Thus, allowing physicians to use their medical judgment in prescribing is a foundational component of pediatric care.

Psychiatry and neurology are also dependent on off-label prescribing, largely because of the limited availability of FDA-approved treatment options for many serious mental illnesses and neurological diseases. *See* Shariful A. Syed et al., *The Law and Practice of Off-Label Prescribing and Physician Promotion*, 49 J. Am. Academy Psychiatry & L. 53, 54 (2021); *see, e.g.*, Hua Chen et al., *An Epidemiological Investigation of Off-Label Anticonvulsant Drug Use in the Georgia Medicaid Population*, 14 Pharmacoepidemiology. & Drug Safety 629, 629–30 (2005). In office-based clinical settings, studies report 31% of all

antidepressant, anticonvulsant, and antipsychotic prescriptions are written for off-label indications, and community-based studies suggest that 40% to 80% of patients receiving common psychotropics are treated off-label. Syed et al., *supra*, at 54. Additionally, tricyclic antidepressants, though not FDA-approved for neuropathic pain, are considered first-line treatment for that indication and are used off-label. Wittich et al., *supra*, at 983–85.

As these examples reveal, off-label prescribing is a necessary corollary of the FDA's regulatory process itself. Because FDA approval and labeling processes are time- and resource-intensive and necessarily limited in scope,[5] they cannot realistically encompass every clinically appropriate use of a drug for every patient population, condition, or evolving standard of care. *See* Wittich et al., *supra*, at 985; Furey & Wilkins, *supra*, at 588–89. Physicians therefore routinely rely on emerging evidence, clinical guidelines, and professional judgment to determine when an already approved product is appropriate for a new indication or patient population.

Off-label prescribing also plays a critical role in medical innovation. "Valid new uses for drugs already on the market are often first discovered through serendipitous observations and therapeutic innovations," and "effective and safe

[5] *See* FDA, *Development & Approval Process (Drugs)* (last updated Aug. 8, 2022), https://perma.cc/5WDD-ZW5C.

treatment options would often be overlooked or never discovered" without off-label prescribing. James Beck, *Off-Label Use in the Twenty-First Century: Most Myths and Misconceptions Mitigated*, 54 UIC J. Marshall L. Rev. 1, 18, 30–31 (2021) (internal citations omitted).

Off-label prescribing, like most medical interventions, carries risk. *See* Grossman et al., *supra*, at 525. Physicians are therefore obligated under state law to adequately explain the risks, benefits, and reasonable alternatives to a particular course of treatment, and to work with patients to select a treatment plan in the patient's best interest. *See* Furey & Wilkins, *supra*, at 590–92. Where off-label uses are the only treatment option available, those risks must be weighed against the risk of foregoing treatment altogether. *See id.* at 588–90. And, like many areas of medicine, a patient may elect a course of treatment with varied levels of "risk" because it best serves their needs or values. *See id.* at 590–92.

And off-label prescribing is not done without guardrails. Professional practice standards require that such prescribing be grounded in sound scientific evidence and clinical judgment. Am. Med. Ass'n, *Patient Access to Treatments Prescribed by Their Physicians, H-120.988* (2024), https://perma.cc/6XL7-LPRV.

All told, physicians prescribing drugs for off-label uses work in tandem with the FDA's function of safeguarding the drug supply. The FDA evaluates products for safety and efficacy at the product level, while physicians—who are properly

regulated by professional standards and clinical evidence and operating within state requirements, *see infra* at pp.14–15—translate those determinations into individualized treatment decisions for patients.

II. The FDCA Was Not Designed to Allow the Federal Government to Interfere with Physicians' Clinical Prescribing Decisions

Another significant reason for the prevalence of off-label prescribing is the FDCA itself. The FDCA was not designed and has not been interpreted to allow the federal government to interfere with physicians' clinical decisions to prescribe drugs or devices for off-label uses.

The FDCA is a consumer-protection statute aimed at ensuring that drugs, devices, and other articles entering interstate commerce are safe, effective, and properly labeled. By its text, the FDCA prohibits, with criminal and civil penalties, "the introduction or delivery for introduction into interstate commerce of any food, drug, device, tobacco product, or cosmetic that is adulterated or misbranded." 21 U.S.C. § 331(a); *see also, e.g.*, 21 U.S.C. § 331(b) (prohibiting the adulteration or misbranding of products in interstate commerce); 21 U.S.C. § 333 (setting out penalties for violations of § 331). A drug is "misbranded" if, among other things, its "labeling"—written, printed, or graphic materials that accompany drugs or devices and provide directions for their use—is false or misleading. 21 U.S.C. § 321(k), (m) (defining "label" and "labeling"); 21 U.S.C. § 352 (defining "misbranded").

None of these provisions authorize the federal government to regulate health care practitioners' clinical judgment to prescribe FDA-approved drugs and devices for off-label uses. This has long gone unquestioned: in addition to the Act's text and Congress's intent, both the FDA and the Department have historically confirmed this interpretation.

a. Congress Did Not Intend for the FDCA to Interfere with Off-Label Use

The FDCA's legislative sponsors emphasized that, in regulating drugs in interstate commerce, they had no intent to "interfere at all with the ordinary legal practice of the [medical] profession." 79 Cong. Rec. 5019 (1935) (statement of Sen. Royal Copeland during Senate debate on S. 5), *reprinted in A Legislative History of the Federal Food, Drug and Cosmetic Act and Its Amendments*, vol. 4, at 57 (FDA 1979) [hereinafter *Legislative History of the FDCA*].[6] Congress reaffirmed this understanding in subsequent amendments to the FDCA. In 1971, Congressman Lawrence H. Fountain stated that "[t]he law, of course, was not intended to regulate the practice of medicine and should not be so used." *New Drugs Used for Nonapproved Purposes (Methotrexate for Psoriasis): Hearing Before the Intergovernmental Relations Subcomm. of the H. Comm. on Gov't*

[6] Senator Royal S. Copeland was the FDCA's original sponsor and as such, his contemporaneous statements can be probative legislative history. *See, e.g., United States v. Shirey*, 359 U.S. 255, 258–60 & n.4 (1959).

Operations, 92d Cong. 643 (1971), *reprinted in Legislative History of the FDCA*, app. H, at 643.

The Act's text speaks directly to the point of off-label prescribing. Congress revised the FDCA in 1997 to indicate "[n]othing in [the Act] shall be construed to limit or interfere with the authority of a health care practitioner to prescribe or administer any legally marketed device to a patient for any condition or disease within a legitimate health care practitioner-patient relationship." 21 U.S.C. § 396. The import is clear. A Joint Explanatory Statement of the Committee of Conference responsible for the amendments adding section 396 to the FDCA noted this provision was:

> intended by the conferees to emphasize that ***the FDA should not interfere in the practice of medicine***. Specifically, the conferees note that the off-label use of a medical device by a physician using his or her best medical judgment in determining how and when to use the medical product for the care of a particular patient ***is not the province of the FDA***.

H.R. Rep. No. 105-399, at 97 (1997) (emphasis added), https://perma.cc/8W7K-APZ6; *see also Judge Rotenberg Educ. Ctr., Inc. v. FDA*, 3 F.4th 390, 395 (D.C. Cir. 2021) ("Section 396 ensures that once the FDA permits a device to be marketed for one use, health care practitioners have the flexibility to draw on their expertise to prescribe or administer the device for any condition or disease, not just the use the FDA approved—in short, to practice medicine.").

In addition to section 396's explicit language regarding the off-label use of devices, courts have repeatedly held that the FDCA should not be read to prohibit physicians from prescribing either drugs and devices for off-label uses. Citing section 396 of the FDCA, the Supreme Court confirmed "the FDCA expressly disclaims any intent to directly regulate the practice of medicine," and cited scholarship confirming that "[p]hysicians may prescribe drugs and devices for off-label uses." *Buckman*, 531 U.S. at 350–51 & n.5. And, as this Court has reasoned: "[T]he longstanding practice of Congress, the FDA, and the courts [is] not to interfere with physicians' judgments and their prescription of drugs for off-label uses." *Sigma-Tau Pharms.*, 288 F.3d at 147.[7]

b. The FDCA's Protection of Off-Label Use Reflects Congress's Understanding of the Proper Locus of Physician Governance

The legislative history reveals Congress' understanding that protecting physicians' ability to prescribe off-label is essential for at least three reasons: (1) respect for states' regulation of medical practice, (2) the appreciation that physicians are best positioned to evaluate the individual circumstances of their

[7] Other circuits are in accord that the FDCA regulates manufacturers and does not prohibit off-label prescribing. *See, e.g.*, *Ass'n of Am. Physicians & Surgeons v. FDA*, 13 F.4th 531, 534 (6th Cir. 2021); *In re Celexa & Lexapro Mktg. & Sales Pracs. Litig.*, 915 F.3d 1, 5 (1st Cir. 2019); *In re Schering Plough Corp. Intron/Temodar Consumer Class Action*, 678 F.3d 235, 240 (3d Cir. 2012); *United States v. Caronia*, 703 F.3d 149, 153 (2d Cir. 2012); *Wash. Legal Found. v. Henney*, 202 F.3d 331, 333 (D.C. Cir. 2000).

patients, and (3) as discussed above, the importance of off-label prescribing to medical practice.

First, in line with other federal health care statutes,[8] the FDCA respects the longstanding principle that the regulation of medical practice is quintessentially a matter reserved to states. *See Hillsborough Cnty., Fla. v. Automated Med. Lab'ys, Inc.*, 471 U.S. 707, 720 (1985) (explaining that "regulation of health and safety matters is primarily, and historically, a matter of local concern"). Consistent with this principle, then-FDA Commissioner George Larrick acknowledged that the question about "the extent to which FDA can rely on the discretion of individual medical practitioners in balancing the advantages and hazards of a drug" "goes to the heart of the matter of States rights." *Drug Safety: Hearings Before a Subcomm. of the H. Comm. on Gov't Operations*, 88th Cong. 186 (1964) (exchange between Rep. Lawrence H. Fountain and Comm'r Larrick), *reprinted in Legislative History of the FDCA*, app. D, at 180. States primarily exercise this responsibility *ex ante* through state medical boards, which establish and enforce licensing requirements, investigate complaints, and oversee disciplinary actions, while medical malpractice

[8] Congress has likewise limited federal power vis-à-vis medical treatment decisions in other significant ways. *See, e.g.,* 42 U.S.C. § 1395 (opening the Medicare Act by proclaiming that "[n]othing in this subchapter shall be construed to authorize any Federal officer or employee to exercise any supervision or control over the practice of medicine").

lawsuits enforce medical standards *ex post. See Chiles v. Salazar*, 146 S. Ct. 1010, 1047, 1049 (2026) (Jackson, J., dissenting).

Second, Congress understands that individual practitioners—guided by professional standards and clinical evidence and operating within state requirements—are best positioned to evaluate courses of treatment for their individual patients. As one Senator expressed during the Senate's consideration of the 2013 Drug Quality and Security Act, which amended sections of the FDCA: "I . . . want to clarify that nothing in this legislation will constrain a doctor's options to practice medicine . . . Doctors know their patients best and should have access to accurate information on the safety and quality of the drugs they use." 159 Cong. Rec. S8072 (daily ed. Nov. 18, 2013) (statement of Sen. Lamar Alexander); *see also id.* (statement of Sen. Thomas Coburn) ("I . . . want to express my concern that this legislation should not be used by the FDA to interfere with a doctor's ability to practice medicine and choose the best therapy for his or her patients.").

Third, and perhaps most importantly, Congress understands the distinct importance of off-label prescribing to medical practice. While amending the Act, members of Congress emphasized their understanding of the "tremendous importance [of off-label prescribing] to the patient," citing that "the American Medical Association has estimated that between 40 percent and 60 percent of all

prescriptions are for off-label uses of prescription drugs." 143 Cong. Rec. S12244 (daily ed. Nov. 9, 1997) (statement of Sen. William Frist).

Congress' consistent and longstanding decision to limit federal interference with physicians' clinical decisions reflects a core practical consideration: physicians must be able to exercise independent clinical judgment informed by the best-available scientific evidence and standards of care established by state medical boards and professional associations to provide high-quality, individualized patient care. The FDCA does not provide the federal government authority to interfere with this essential and foundational feature of health care, nor to dictate which of these clinical decisions it favors and which it disfavors.

c. The FDA and the Department of Justice Long Adopted This Read

The FDA itself has understood this reading of the FDCA for decades, confirming that the Act does not regulate medical judgment. *See* Legal Status of Approved Labeling for Prescription Drugs; Prescribing for Uses Unapproved by the Food and Drug Administration, 37 Fed. Reg. 16,503 (proposed Aug. 15, 1972) ("Throughout the debate leading to the enactment [of the FDCA], there were repeated statements that Congress did not intend the [FDA] to interfere with medical practice and references to the understanding that the bill did not purport to

regulate the practice of medicine as between the physician and the patient.").[9] In a 1974 congressional hearing regarding FDA practice, then-FDA Chief Counsel and *amici* Peter Barton Hutt put this plainly:

> The legislative history is clear that Congress intended FDA to regulate the shipment of a drug and the labeling for that drug and declined to permit the Food and Drug Administration to regulate the practice of medicine as between the physician and the patient, which is the use of that drug . . . ***Congress denied*** [the FDA] explicitly, both in 1938 and in [the 1962 amendments], ***any authority to regulate the practice of medicine in terms of the use of a drug by a physician once it is lawfully shipped with lawful labeling in interstate commerce***.

Use of Advisory Committees by the Food and Drug Administration: Hearing before a Subcomm. of the H. Comm. on Gov't Operations, 93d Cong. 347–48 (1974), *reprinted in Legislative History of the FDCA,* app. J, at 620–21 (emphasis added). Accordingly, "[f]rom the FDA's perspective, once the FDA approves a drug, healthcare providers generally may prescribe the drug for an unapproved use when they judge that it is medically appropriate for their patient." *Understanding Unapproved Use of Approved Drugs, supra*.

Perhaps most telling, the Department itself agrees. As Appellees note (Resp. Br. at 31), in a 2019 Memorandum Opinion for the Attorney General, the Department's Office of Legal Counsel wrote:

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[9] *See also* Labeling Requirements for Systemic Antibacterial Drug Products Intended for Human Use, 68 Fed. Reg. 6071 (Feb. 6, 2003) ("As FDA has long recognized, its role is neither to regulate physician conduct, nor to train physicians.").

> As a general matter, FDA does not regulate the practice of medicine, which includes "off-label" prescribing—that is, when physicians prescribe FDA-approved drugs or devices for non-FDA-approved uses … [t]hus, while the FDCA bars a manufacturer or distributor from selling any drug or device for an unapproved use, physicians may, with limited exceptions, prescribe and administer FDA-approved drugs and devices for unapproved uses.

Steven A. Engel, *Whether the Food & Drug Admin. Has Jurisdiction over Articles Intended for Use in Lawful Executions*, 43 Op. O.L.C. 81, 85 (May 3, 2019) (internal citation omitted).[10]

The Department has also conceded as such at times in this and related cases. *See* JA498 ("[O]ff-label prescribing itself is a generally permitted practice under federal law . . ."). But, as discussed below, the Department nonetheless seeks to regulate off-label prescribing in this one area of medicine: gender-affirming care.

III. Accepting the Department's Theories of FDCA Liability Would Undermine the Act and Significantly Harm Health Care

Despite Congress's and agencies' historical interpretations of the FDCA, in this and related cases, the Department has invoked an interpretation of the Act that would significantly expand federal authority over physicians' clinical decisions. Citing expansive theories of potential FDCA liability for health care providers as

[10] With regard to the "limited exceptions," Congress has created a few narrow statutory exceptions where off-label prescribing is itself unlawful. *See, e.g.*, 21 U.S.C. § 333(e) (prohibiting certain off-label uses of human growth hormone). However, none of these narrowly tailored exceptions are applicable here.

justification, the Department seeks to use its investigative powers to insert federal oversight into a clinical practice that is legal under state law.[11]

In reinforcing the general legality of off-label prescribing, JA498, the Department seemingly suggests that these cases (and the government's regulation of legal gender-affirming care) should be seen as unique. Yet, "the arguments the [Department] has made to support the subpoenas presage a troubling and drastic expansion of the FDCA into medical practice" beyond this one kind of care. Grossman et al., *supra*, at 524. If the Department is correct that providers could be liable, or even just investigated, for violations of the FDCA for prescribing medications for or counseling patients regarding gender-affirming care, there is no legal protection for any off-label prescribing or physicians' discussions with their patients about the same. Accepting the Department's arguments here would improperly enable it to use investigative powers to *de facto* oversee and chill legal medical practice. Armed with the license it seeks, it would require only the

[11] State law in each jurisdiction where Children's National Hospital operates protects access to gender-affirming care. *See* D.C. Code §§ 2-1401.02 (12A), 31-2703.01; Md. Exec. Order 01.01.2023.08; Va. Code Ann. § 38.2-3449.1. And, the subpoenas are just one piece in the federal government's project to oversee, regulate, and halt gender-affirming care in states where it is legal. Other such efforts to unilaterally decree medical practice with respect to gender-affirming care have been rejected by federal courts. *See Oregon v. Kennedy*, No. 6:25-cv-02409, 2026 WL 1048354 (D. Or. Apr. 18, 2026).

slightest shift in the political gaze of the federal government to expand its project to interfere with clinical care outside its current iteration.

a. Accepting the Department's Arguments Regarding the Scope of Federal Authority under the FDCA Would Threaten Off-Label Use

In defending its subpoenas, the Department has suggested that, while off-label prescribing is generally legal, off-label prescribing for gender-affirming care is legally suspect because "pediatric medical transition" has an "unfavorable risk/benefit profile" and "the widespread off-label use of these powerful drugs also undermines the regulatory system that Congress established to ensure that drugs are used consistent with sound scientific data." *See* JA498–99; *see also* JA510 (describing off-label prescribing for gender-affirming care as "uses that the FDA has never approved and that raise grave safety concerns" which "fall squarely within the Government's statutory mandate to protect the public from misbranded, adulterated, and unapproved drugs.")[12] Misreading the FDCA this way would eviscerate off-label use across medical specialties.

[12] As evidence for its assertions of safety concerns, the Department cites to a 2025 report published by this Administration. *See* U.S. Dep't of Health & Human Servs., *Treatment for Pediatric Gender Dysphoria: Review of Evidence and Best Practices* (Nov. 19, 2025). That report has been criticized by medical organizations and commentators for departing from positions adopted by major professional associations, as well as methodological concerns, including alleged lack of transparency regarding study-selection criteria, authorship, and evaluation of evidence quality. *See* Nadia Dowshen et al., *A Critical Scientific Appraisal of the Health and Human Services Report on Pediatric Gender Dysphoria*, 77 J.

As the Department has acknowledged, puberty blockers and gender-affirming hormone therapy have been approved by the FDA. *See* JA529 ("[T]hese prescription drugs are FDA-approved for other indications (e.g., precocious puberty, prostate cancer, hypogonadism, etc.) . . ."). That is the end of the analysis under the FDCA. If the Department can read into the FDCA some limitation on "widespread" off-label use, or off-label uses that present (purported) risks, nothing shields the myriad providers doing crucial and routine prescribing of off-label drugs across specialties, which, as discussed *supra* p. 9, often involves balancing the risks and benefits of using medications off-label with alternatives including patients not receiving care altogether. This would significantly harm patients with a host of conditions who are reliant on off-label uses of medications. "By suggesting that physicians may be committing a federal crime under the FDCA when they prescribe or administer a drug for an unapproved use, the [Department]—in its effort to deter gender-affirming care—calls into question patients' access to off-label uses of all drugs." Grossman et al., *supra*, at 525.

In supporting documents, the Department has also suggested that providers prescribing and administering medications off-label could be interpreted to be

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Adolescent Health 342 (2025); *see also* G. Nic Rider et al., *Scientific Integrity and Pediatric Gender Healthcare: Disputing the HHS Review*, Sexuality Res. & Soc. Pol'y (2025), https://perma.cc/MN97-HMNF (criticizing the report's transparency and methodological rigor).

distributing or "caus[ing] the distribution of" a "new drug" into interstate commerce without an FDA-approved indication. *See* JA527–29. But Congress has been clear that it does not intend for hospitals and physicians prescribing and/or administering off-label medications to be the focus of the Act's distribution provisions. Section 331 of the Act, which prohibits introducing or delivering adulterated or misbranded food and drugs in interstate commerce, is directed at actors who place or move drugs in commerce (e.g., drug manufacturers, packers, and distributors), rather than physicians prescribing or administering approved drugs in individual patient care. *See, e.g.*, 21 U.S.C. § 331(a), (b); *Wash. Legal Found*, 202 F.3d at 332–33 (D.C. Cir. 2000) (describing the "asymmetrical . . . regulatory treatment" of off-label uses, as the FDCA prohibits a manufacturer from introducing a drug into interstate commerce with the intent that it be used for a non-FDA approved purpose, while "neither Congress nor the FDA has attempted to regulate the off-label use of drugs by doctors and consumers.").

Further, "the provision of the FDCA that prohibits 'the causing of' violations has never been read" to find providers prescribing off-label to "cause" drug manufacturers to misbrand or mislabel drugs for a new, unauthorized use. *See* Grossman et al., *supra*, at 525. Indeed, in 2021, the FDA amended its regulations regarding the "intended use" of drugs to clarify that a manufacturer "would not be regarded as intending an unapproved new use for an approved drug based solely on

that [manufacturer's] knowledge that such drug was being prescribed or used by health care providers for such use." 21 C.F.R. § 201.128.

The Department's interpretation of the FDCA would be devastating to care. It would require hospitals and physicians involved in all kinds of off-label prescribing—including National Cancer Institute designated centers and other providers that administer medications off-label through injectables, as the Department focuses on here, *see* JA529, to radically alter their clinical approaches. At base, this unprecedented interpretation of the FDCA would be to the severe detriment of patients and health.

b. Similarly, Accepting the Department's Arguments Would Threaten the Provider-Patient Relationship

The Department's suggestions that FDCA's labeling and branding requirements should apply to ordinary, oral informed consent discussions between physicians and their individual patients about off-label drug use is also dangerous for medical care. *See, e.g.*, Op. Br. at 18 ("[m]isleading or deceiving minors and their parents about the risks of gender-related treatments could similarly violate the FDCA"); *id.* at 46–47 (arguing the Department has evidence of cases "where providers failed to supply adequate labeling," "actively deceived patients and parents with false claims and statements regarding the drugs' effectiveness or alternatives, and misrepresented to minor patients and their parents the risks associated with . . . taking the drugs.").

To be sure, the Department's contention that providers are "actively deceiv[ing] patients and parents with false claims and statements," Op. Br. at 46–47, relies on the Administration's own Report that has been heavily criticized due to methodological and scientific-process concerns. *See supra* note 12. But even assuming deficiencies on the part of physicians to provide necessary medical information, these are issues of state tort law and physician licensure, not subject to federal enforcement under the FDCA. *See Chiles*, 146 S. Ct. at 1047 (Jackson, J. dissenting) (noting that state regulations go beyond medical procedures, *see supra* pp.14–15, and "defined the 'practice of medicine' to cover practitioner speech").[13]

Holding physicians liable under the FDCA for the information they orally communicate to their *patients* about off-label drugs in the clinical relationship would dramatically exceed the intended scope and focus of the FDCA. "[T]he FDA has long recognized that . . . clinicians' discussions with patients about these prescriptions" "are generally outside the scope of the statute." Grossman et al., *supra*, at 524; *see also* Beck, *supra*, at 84 (the FDCA doesn't create a requirement

[13] As the Eastern District of Pennsylvania reasoned regarding a related subpoena, "[t]he conduct the Department of Justice describes—miscoded diagnoses, allegedly incomplete disclosures, or purportedly misleading consent forms—concerns how drugs are used in practice, not how they are labeled, promoted, or distributed in commerce. Alleged deficiencies in those areas may implicate state informed consent or professional-discipline standards, but they do not establish an [FDCA] Section 331 violation . . . ." *In re Subpoena No. 25-1431-014*, 810 F. Supp. 3d 555, 579 (E.D. Pa. 2025), *appeal voluntarily withdrawn and dismissed*, No. 26-1134, ECF No. 26 (3d Cir. May 12, 2026).

"above and beyond the usual informed consent duties pertaining to the material medical risks and benefits" to inform patients that drugs are being prescribed for an off-label use). As the Fifth Circuit has held, the FDCA should not be read to apply liability for improper labeling or misbranding (under 21 U.S.C. § 331(k)) to physicians communicating solely with patients about off-label prescriptions. *See United States v. Evers*, 643 F.2d 1043, 1052–53 (5th Cir. 1981) (reasoning that the Act is concerned with whether an actor is providing adequate information about prescription drugs to prescribing physicians, not whether an actor is providing adequate information to patients).[14]

Moreover, to the extent the Department suggests that any communication from providers to patients that discusses benefits of using medications off-label for gender-affirming care would violate federal law, this would violate the First Amendment. As the Supreme Court recently described, government action that prescribes what views a medical provider may or may not express is viewpoint discrimination. *Chiles v. Salazar*, 146 S. Ct. at 1024. As the Court reasoned:

[14] Even in the instances in which written instructions for medications are required to be provided directly to patients, the FDA has confirmed that such labeling is distinct from doctor-patient communications. *See* Prescription Drug Product Labeling; Medication Guide Requirements, 63 Fed. Reg. 66378, 66386 (Dec. 1, 1998) ("FDA agrees that health care providers should be the primary source of information about medications for their patients. The purpose of written information is to reinforce and supplement, not to interfere with, the doctor-patient relationship.").

> History is littered with examples of official efforts to manipulate and control professional speech—including the content of doctor-patient discourse—in ways designed to increase state power, suppress minorities, and muzzle unpopular ideas. And the dangers associated with censorship . . . are no less acute in the fields of medicine and public health than they are anywhere else.

Id. at 1024–25 (internal citations and quotations omitted). "Manipulate and control professional speech—including the content of doctor-patient discourse" to "suppress minorities" is precisely what the Department is trying to do here.

Most importantly, interfering with physician-patient communication and decision-making is harmful to patients across medical practice. Physicians' ability to freely communicate with their patients is essential both legally and ethically, to ensure patients receive and understand all information necessary to make autonomous medical decisions in their best interest. *See Informed Consent*, AMA Code of Medical Ethics, https://perma.cc/8WBY-5GSG (last visited June 29, 2026). The FDCA should not be read to allow the federal government to interfere in these conversations.

c. Finding the Department's FDCA Theories to be a Legitimate Justification for these Subpoenas Would Broadly Chill Health Care

Given the scope of the Department's FDCA theories, providers across medical specialties reliant on off-label prescribing could be chilled by the threat of receiving a federal subpoena. The Department should not be enabled to transform the FDCA into a tool for scrutinizing and deterring the exercise of routine, legal

medical judgment.[15] Authorizing the Department to act in this way would reshape medicine beyond gender-affirming care: it would permit federal officials to use investigative tools to regulate and restrict "off-label prescribing practices that are disfavored by whatever administration is in power, even when these practices are supported by scientific evidence and deemed medically appropriate by doctors." Grossman et al., *supra*, at 525. This Court should not allow the federal government to interfere into routine, evidence-based clinical decisions, on a political whim, in the guise of a statute that was never intended to regulate medical judgment.

CONCLUSION

For the foregoing reasons and those provided in Appellees' briefing, this Court should affirm the District Court's Order. The Department is seeking to use its investigatory and subpoena powers to interfere in the legitimate provision of legal, evidence-based care in the routine course of a physician-patient clinical relationship. The FDCA draws a clear line between federal regulation of medical products and physicians' clinical decisions, and retaining this division is essential for the provision of health care. Because the Department can point to no other

[15] Were the Department to argue that it would not exercise this authority in other medical applications, this only underscores that, as Appellees have argued, Resp. Br. at 42–48, and the District Court found, the Department issued these subpoenas with the improper purpose of seeking to regulate an area of medical practice that it politically disfavors.

legitimate purpose for its investigation under the FDCA, and for all other reasons outlined in Appellees' briefing, the District Court's judgment should be affirmed.

Dated: July 14, 2026

Respectfully submitted,
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CERTIFICATE OF COMPLIANCE

I certify the following in accordance with Fed. R. App. 32(g)(1) and 29(a)(5):

1. This brief complies with the type-volume limits because, excluding the parts of the document exempted by Fed. R. App. P. 32(f) (i.e., cover page, disclosure statement, table of contents, table of authorities, certificate of counsel, signature blocks, proof of service, addendum), this brief contains 6,437 words.

2. This brief complies with the typeface requirements of Fed. R. App. P. 32(a)(5) and the type style requirements of Federal R. App. 32(a)(6), because it was prepared in a proportionally spaced serif typeface using Microsoft Word in 14-point font size and Times New Roman type style.

Dated: July 14, 2026

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CERTIFICATE OF SERVICE

I certify that on July 14, 2026, I electronically filed the foregoing document with the Clerk of Court of the United States Court of Appeals for the Fourth Circuit by using the EM/ECF system. I certify that all participants in the case are registered CM/ECF users and that service will be accomplished by the CM/ECF system.

Dated: July 14, 2026

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