Nos. 24-1576(L), 24-1600, 24-1617

UNITED STATES COURT OF APPEALS
FOR THE FOURTH CIRCUIT

AMY BRYANT, M.D.,
Plaintiff-Appellee,
v.
TIMOTHY K. MOORE, *et al.*,
Intervenors/Defendants-Appellants,
and
JOSHUA H. STEIN, in his official capacity
as Attorney General for the State of North Carolina, *et al.*,
Defendants-Appellees.

On Appeal from the United States District Court for the
Middle District of North Carolina, No. 1:23-cv-00077-CCE-LPA

OPENING / RESPONSE BRIEF FOR AMY BRYANT, M.D.

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INTRODUCTION

For a small subset of approved drugs (known as "REMS drugs"), Congress charged the U.S. Food and Drug Administration with "[a]ssuring access" by identifying, and refining on an ongoing basis, the precise mix of regulatory controls that is "commensurate" with the drug's risks without being "unduly burdensome on patient access to the drug"—especially for "patients in rural or medically underserved areas"—or imposing unnecessary "burden[s] on the health care delivery system." 21 U.S.C. § 355-1(f)(2).

Exercising that statutory responsibility, FDA has spent more than two decades studying and evaluating mifepristone, a REMS drug used for medication abortion. FDA recognizes that mifepristone has a "well-characterized safety profile … with known risks occurring rarely." JA249; *see* JA236 (noting that "[s]erious adverse events" occur in no more than a fraction of a percent of patients). Mifepristone's safety profile is comparable to that of many "commonly used prescription and over-the-counter medications," such as aspirin, ibuprofen, and routine antibiotics. Nat'l Acads. of Scis., Eng'g, & Med., The Safety and Quality of Abortion Care in the United States 55, 58 (2018).

Based on its expert analysis, FDA has imposed a number of carefully calibrated restrictions on mifepristone, while expressly rejecting other restrictions as unnecessary and inappropriate. In particular, after years of intensive review of voluminous data, FDA has eliminated in-person requirements and authorized the provision of mifepristone through telemedicine—allowing a patient to consult with her healthcare provider remotely, pick up her prescription from a pharmacy that is federally certified to dispense mifepristone, take the medication in the comfort of her home, and remotely follow up with her provider, as warranted.

Although medication abortion is legal in North Carolina, the state has erected a series of barriers to patients' ability to access mifepristone that FDA expressly considered and rejected. For example, it has dictated that only physicians may prescribe mifepristone, even though FDA concluded that mifepristone "is safe and effective when prescribed by … physician assistants and nurse practitioners." JA238, JA253. North Carolina has also frustrated FDA's judgment that telemedicine is appropriate by requiring patients to have at least three in-person visits with a doctor in order to receive the drug: an in-person examination and

consultation, a second in-person visit where the patient must take the drug in the doctor's presence, and a third in-person follow-up visit. FDA, by contrast, has determined that federally certified mifepristone prescribers do not have to "physically meet with and examine the patient," but can "consult[] with the patient over the Internet," JA240–241; that patients can obtain mifepristone "by mail" or from "certified … pharmacies," JA264; and that "in-person follow-up with a healthcare provider" is unnecessary because "follow-up can be performed by telephone," JA243–244 (quotation marks omitted).

North Carolina's restrictions on mifepristone are preempted because they "upset the careful regulatory scheme established by federal law." *Geier v. Am. Honda Motor Co.*, 529 U.S. 861, 870 (2000) (quoting *United States v. Locke*, 529 U.S. 89, 106 (2000)). As the district court recognized, Congress "create[d] a comprehensive regulatory framework under which the FDA is responsible for deciding what terms are required for safe access to and use of [REMS] drugs while considering patient access and burdens on the health care system." JA632. It would undermine that system and defeat Congress's goals if every state could "second-guess the FDA's explicit judgment on how to manage risks from

and safely prescribe, dispense, and administer" REMS drugs, JA645, by imposing "restriction[s] … FDA explicitly considered and rejected … as unnecessary for safe use under the statutory regime imposed and required by Congress," JA640–641.

This conclusion is mandated by the Supreme Court's pathmarking decision in *Geier*. There, the Court held that a state airbag requirement was preempted because it conflicted with a federal agency's deliberate choice, exercising authority granted by Congress, to reject an "all airbag" standard and instead "allow[] manufacturers to choose among different passive restraint mechanisms." 529 U.S. at 878–79. *Geier* establishes that "when a state adopts a law that imposes a requirement a federal agency deliberately rejected because it conflicts with Congress's goals, [the state law] is preempted." JA615. Just as the agency in *Geier* "deliberately provided the manufacturer with a range of choices among different passive restraint devices," 529 U.S. at 875, FDA deliberately gave prescribers and patients a range of choices about how to provide and obtain mifepristone, including via telemedicine. Allowing states to impose a patchwork of inconsistent restrictions on mifepristone that FDA has considered and rejected would stand "as an obstacle to" the careful

balance between safety and patient access "that the federal regulation deliberately imposed." *Id.* at 881.

This conclusion is also supported by the Supreme Court's decisions addressing preemption under the general labeling provisions of the Federal Food, Drug, and Cosmetic Act, including *Wyeth v. Levine*, 555 U.S. 555 (2009). *Wyeth* held that a state could require a stronger warning for a non-REMS drug when FDA had "paid no more than passing attention to the question." *Id.* at 563. Although *Wyeth* did not involve a REMS drug and thus did not consider the unique statutory scheme that applies here, the Court still acknowledged that a state could be preempted from requiring a drug's labeling to include a warning that FDA had "consider[ed] and reject[ed]." *Id.* at 581 n.14; *see* JA651 ("[I]n *Wyeth*, the FDA had not considered and rejected the exact requirements the state [sought] to impose, a factor the Supreme Court deemed important enough to mention explicitly."). And the Supreme Court has since made clear that even for non-REMS drugs, states cannot require labeling changes that FDA considered and rejected. *Merck, Sharp & Dohme Corp. v. Albrecht*, 587 U.S. 299, 302–03 (2019).

Unable to overcome this controlling precedent, intervenors try to shift the focus to a different question: Whether Congress has ousted states from regulating REMS drugs *at all*. They claim (at 1) the district court effectively imposed field preemption by holding that "*any* state law that imposes a 'safety-related' protection" on a REMS drug is automatically preempted. But Dr. Bryant has not argued that all state regulations of REMS drugs are preempted, and the district court was clear that this case is about obstacle (not field) preemption. JA614 n.4. The court held that a state is preempted from imposing restrictions on a REMS drug that "FDA explicitly considered and rejected." JA640–641.

While the district court's preemption analysis was largely correct, the court erred by holding that some of the challenged restrictions are not preempted because they are not "directed to the risks of mifepristone" but instead relate to "broader health issues." JA635, JA639. As intervenors concede (at 4), *all* the challenged laws were enacted to address the supposed risks of "abortion-inducing drugs" like mifepristone (albeit without any evidence they are necessary to address any actual risks of the drug, which are minimal, *see* p. 1, *supra*). And North Carolina's statutory scheme makes clear that these restrictions, like

those the court found preempted, reflect the state's "disagreement with the FDA over what safety restrictions on the use of mifepristone are necessary." JA652.

Accordingly, Dr. Bryant asks this Court to affirm the judgment with respect to the restrictions the district court held are preempted and to reverse with respect to those the court held are not preempted.

JURISDICTION

The district court had jurisdiction under 28 U.S.C. §1331. It entered final judgment on June 3, 2024. JA657–659. Intervenors' notice of appeal was filed on June 20, 2024; Dr. Bryant's notice of cross-appeal was filed on June 28, 2024; and Attorney General Stein's notice of cross-appeal was filed on July 2, 2024. JA660–669. This Court has jurisdiction over the appeal and cross-appeals pursuant to 28 U.S.C. § 1291.

ISSUE

Can North Carolina obstruct patient access to a federally approved REMS drug by imposing restrictions that FDA has considered and rejected pursuant to the federal REMS statute and that frustrate FDA's efforts to facilitate patient access to the drug?

STATEMENT OF THE CASE

A. FDA's Statutory Responsibility for Assuring Access to REMS Drugs

Under the Federal Food, Drug, and Cosmetic Act ("FDCA"), FDA will approve a drug that is shown to be safe and effective when used as directed in the drug's labeling. 21 U.S.C. § 355(d). "[V]irtually all drugs come with complications, risks, and side effects," *FDA v. All. for Hippocratic Med.* (*AHM*), 602 U.S. 367, 392 (2024), so demonstrating safety does not require showing that a drug has no potential adverse effects. Rather, FDA will approve a drug as safe if the agency determines that its benefits to patients outweigh its risks. *Mut. Pharm. Co. v. Bartlett*, 570 U.S. 472, 476 (2013).

For most drugs, after its initial approval decision, FDA is not charged with the type of rigorous and continuous monitoring and updating of the drug's conditions of approval that Congress required for REMS drugs. "FDA has limited resources to monitor the [many thousands of] drugs on the market," so "manufacturers, not the FDA, bear primary responsibility for their drug labeling" and are "charged … with ensuring that [a drug's] warnings remain adequate as long as the drug is on the market." *Wyeth*, 555 U.S. at 571, 578–79. A state is thus

ordinarily free to require a drug's manufacturer to provide additional, stronger warnings that "FDA did not consider and reject," *id.* at 581 n.14, but is barred from requiring warnings that FDA *did* consider and reject, *see Merck*, 587 U.S. at 302–03.

For a small number of drugs, Congress mandated a much more intensive form of FDA oversight. For these drugs, a specific mix of regulatory controls—known as a Risk Evaluation and Mitigation Strategy ("REMS")—is needed to sufficiently manage the drug's risks. Congress has determined that, in order to provide patients with access to the broadest array of medicines, FDA should be able to approve these drugs subject to specific conditions, and that the agency also should regulate them with particular scrutiny.

In the Food and Drug Administration Amendments Act of 2007 ("FDAAA"), Congress codified FDA's authority to establish a REMS when the agency determines that one is necessary to ensure that a drug's benefits outweigh its risks. Pub. L. No. 110-85, § 901, 121 Stat. 823, 926 (enacting 21 U.S.C. § 355-1).[1] Under the REMS statute, FDA considers a

[1] Intervenors claim (at 8–9) that Congress enacted FDAAA in reaction to "the Vioxx controversy." While some parts of FDAAA—in particular. the provisions related to label changes based on new information after

range of statutory options and imposes the precise mix of regulatory controls that the agency concludes strikes the appropriate balance between ensuring safe use of the drug and avoiding undue burdens on patient access to the drug—especially for patients in rural or medically underserved areas—and on the healthcare delivery system.

A REMS may include requirements such as a medication guide or patient package insert, a communication plan, or packaging and disposal requirements. 21 U.S.C. § 355-1(e). FDA can also require that a REMS include Elements to Assure Safe Use, or "ETASU." *Id.* § 355-1(f). ETASU may require that (i) prescribing healthcare providers have particular training or experience or be specially certified; (ii) pharmacies, practitioners, or healthcare settings that dispense the drug be specially certified; (iii) the drug be dispensed only in certain settings; (iv) the drug be dispensed only after documentation of safe-use conditions, such as laboratory test results; or (v) patients using the drug be subject to specified monitoring or enrolled in a registry. *Id.* § 355-1(f)(3); *see AHM,* 602 U.S. at 375. REMS with ETASU are imposed on a very limited

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approval—may have been motivated by that controversy, the REMS provisions address the distinct issue of restrictions that are necessary to enable drug approval. *Compare* 21 U.S.C. § 355(o) *with id.* § 355-1.

number of drugs. Of the more than 20,000 prescription drugs FDA has approved, FDA's website lists only 72 current REMS with ETASU.[2]

In enacting the REMS statute, Congress was focused on ensuring both that REMS drugs would be safe and that patients would not face unnecessary obstacles to accessing those drugs. The subsection authorizing REMS with ETASU is titled "Providing safe access for patients to drugs with known serious risks that would otherwise be unavailable." 21 U.S.C. § 355-1(f). Under the subheading "Assuring access and minimizing burden," Congress charged FDA with ensuring that any restrictions on a REMS drug are "commensurate with" specific identified risks of the drug, "not … unduly burdensome on patient access to the drug," and designed to "minimize the burden on the health care delivery system." *Id.* § 355-1(f)(2). In determining what restrictions are appropriate, FDA must "seek input from patients, physicians, pharmacists, and other health care providers" about how to avoid unduly burdening patients and providers. *Id.* § 355-1(f)(5)(A).

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[2] *See* FDA, Fact Sheet: FDA at a Glance (Jan. 2024), *available at* https://www.fda.gov/about-fda/economics-staff/fda-glance; *Approved Risk Evaluation and Mitigation Strategies (REMS)*, FDA.gov (2024), https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm.

The process of minimizing burdens on patient access "begin[s] during the REMS design phase," when drug sponsors must demonstrate that they have considered and sought to minimize potential burdens. FDA, Draft Guidance: REMS Assessment: Planning and Reporting 13–15 (Jan. 2019), *available at* https://www.fda.gov/media/119790/download. And FDA's role in protecting access does not end with its initial approval of a REMS. Instead, Congress charged FDA with continued monitoring and periodic reassessment of REMS and ETASU to ensure that they continue to reflect the least restrictive set of requirements necessary to protect both safety and patient access.

Every REMS thus includes a timetable for regular, comprehensive assessments, which must include consideration of "REMS burdens" and "barriers to patient access." *Id.* at 14–15; *see* 21 U.S.C. § 355-1(c)(1), (d). FDA reviews these assessments and requires modification of a REMS whenever necessary to "minimize the burden on the health care delivery system." *Id.* § 355-1(g)(4)(B). In addition, FDA must "periodically evaluate" ETASU to assess whether they are necessary to assure safe use, "are not unduly burdensome on patient access to the drug," and "minimize the burden on the health care delivery system," and FDA must

"modify" ETASU "as appropriate" in light of these evaluations. *Id.* § 355-1(f)(5)(B)–(C).

In short, for the narrow universe of REMS drugs, FDA rigorously analyzes both the risks associated with a drug and the burdens that various requirements would impose on patients in order to determine the least restrictive set of requirements that will ensure safety without unduly impeding patient access to the drug. FDA then robustly monitors each REMS drug to ensure that the right mix of controls is in place as more is learned about the drug.

B. FDA's Evolving Regulation of Mifepristone Under the REMS Statute

Mifepristone is the only drug that is FDA-approved for termination of pregnancy (in combination with a second drug, misoprostol), and it is subject to a REMS with ETASU. Since its initial approval in 2000, FDA has repeatedly examined, studied, and scrutinized mifepristone to ensure that it is subject to the least restrictive set of requirements necessary to protect both safety and patient access. As FDA has gathered more data, it has repeatedly updated the Mifepristone REMS, including to pare back restrictions that it determined were unnecessary for safe use and unduly burdensome on patients and providers. FDA has spent countless hours

over decades weighing the specific restrictions necessary to ensure that mifepristone is available to patients and used safely.

Twenty-four years ago, FDA approved mifepristone for use in medication abortion. JA620. FDA found that access to mifepristone was "important to the health of women," JA115, but that certain restrictions were necessary to assure safe use. FDA thus approved mifepristone subject to distribution restrictions under regulations that predated the REMS statute. JA620; *see* JA112–119. Congress codified FDA's REMS authority in 2007, and in 2011 FDA adopted the first Mifepristone REMS, incorporating the original regulatory restrictions as ETASU. JA620–621; *see* JA160–169 (2011 REMS).

The 2011 REMS required that mifepristone be provided only by or under the supervision of a specially certified physician with enumerated qualifications, such as the ability to accurately assess the duration of pregnancy and diagnose ectopic pregnancies, and who signed a Prescriber Agreement. JA621, JA642. "Doctors and patients also had to follow a strict regimen requiring the patient to appear for three in-person visits with the doctor." *AHM*, 602 U.S. at 375. The drug could be dispensed only in clinics, medical offices, and hospitals, and patients had

to take it in their provider's office and return for an in-person follow-up visit. JA621. The REMS-certified physician had to fully explain the procedure, give the patient a Medication Guide and Patient Agreement, and obtain the patient's signature on the Patient Agreement. JA621. The physician also had to report all "hospitalizations, blood transfusions, or other serious adverse events to the drug sponsor (who, in turn, was required to report the events to FDA)." *AHM*, 602 U.S. at 375; *see* JA621. The REMS did not require that every patient have an ultrasound, as FDA had "carefully considered" the question and determined that whether to perform an ultrasound should be left "to the medical judgment of the physician." JA116.

In 2016, as required by statute, FDA "assessed … whether each [Mifepristone] REMS element remain[ed] necessary," JA177, and, in light of the extensive data collected since the original approval 16 years earlier, modified the REMS to reduce barriers to patient access while maintaining safety. JA621–622; *see* JA219–225 (2016 REMS). FDA eliminated the physician-only requirement and began allowing other qualified healthcare providers to become certified to prescribe mifepristone. JA621–622. It retained the in-person dispensing

requirement, but it no longer required patients to take the drug in their provider's office and return for in-person follow-up. JA622. And it modified the reporting requirements so that providers had to report fatalities but not non-fatal adverse events, JA622—"a reporting requirement that was still more stringent than the requirements for most other drugs," *AHM*, 602 U.S. at 376. Providers could still report non-fatal adverse events voluntarily, and sponsors still had to comply with ordinary post-approval reporting requirements. JA220–222; 21 C.F.R. §§ 314.80–.81. Conversely, FDA did not approve the sponsor's request to remove the Patient Agreement from the REMS, because it determined that requiring a signed Patient Agreement Form "would not interfere with access and would provide additional assurance that the patient is aware of the nature of the procedure, its risks, and the need for appropriate follow-up care." JA227.

In 2021, FDA announced that it would not enforce the in-person dispensing requirement during the COVID-19 public health emergency. JA623. FDA also undertook "a full review of the Mifepristone REMS program." JA235. Following that review, FDA determined that further changes to the REMS were necessary to remove barriers to patient access

that were no longer appropriate. JA623; *see* JA235–236. Accordingly, in 2023, FDA approved a REMS modification that eliminated the in-person dispensing requirement. JA629–630; *see* JA77–89 (2023 REMS). FDA explained that in-person dispensing was "no longer necessary to assure the safe use of mifepristone." JA235.

At the same time, FDA added a pharmacy certification program to the REMS. Pharmacies that meet enumerated requirements and sign a Pharmacy Agreement can become federally certified to dispense mifepristone. JA623; *see* JA236; JA79–80, JA87–89. Consequently, the REMS now permits mifepristone to be dispensed "by or under the supervision of certified prescribers, *or* by certified pharmacies on prescriptions issued by certified prescribers." JA77 (emphasis added). FDA was clear that prescribers would no longer be required to see patients in person to provide mifepristone. JA351. FDA concluded that these changes would "continue to ensure the benefits of mifepristone for medical abortion outweigh the risks" without imposing unnecessary burdens "on healthcare providers and patients." JA351.

C. North Carolina's Restrictions on Mifepristone

Rejecting the regulatory framework imposed by Congress and FDA, North Carolina has imposed unnecessary and burdensome restrictions on the provision of mifepristone that are inconsistent with the federal REMS—including the same in-person and physician-only requirements that FDA expressly rejected. Under North Carolina law:

- Only a physician can prescribe mifepristone; a qualified non-physician who is certified to prescribe the drug under the federal REMS is prohibited from doing so in North Carolina. JA641 (citing N.C. Gen. Stat. §§ 90-21.83A(b)(2)(a), 90-21.83B(a)).
- The physician or another qualified professional must complete an in-person consultation with the patient at least 72 hours before providing the drug and obtain the patient's agreement to a consent form provided by the state. JA634 (citing N.C. Gen. Stat. § 90-21.83A(b)).
- The physician must examine the patient in person before providing the drug, and the patient must receive an ultrasound and a blood-type determination (which may require blood testing

in some cases). JA634–635 (citing N.C. Gen. Stat. §§ 90-21.83B(a), 90-21.83A(b)(2)(b), 90-21.93(b)(6)).

- The physician must dispense and administer the drug in person. JA641 (citing N.C. Gen. Stat. § 90-21.83A(b)(2)(a)).
- The physician or an agent of the physician must schedule an in-person follow-up visit for the patient and "make all reasonable efforts to ensure" that the patient attends. JA646 (quoting N.C. Gen. Stat. § 90-21.83B(b)).
- Physicians must report all adverse events related to the use of mifepristone, regardless of severity, to both the state and FDA. JA637, JA647 (citing N.C. Gen. Stat. § 90-21.93).

North Carolina threatens severe consequences for a physician who fails to comply with these restrictions, including criminal prosecution, civil penalties, and suspension or revocation of the physician's medical license. JA625 & n.10 (citing N.C. Gen. Stat. §§ 14-44.1, 90-21.88, 90-21.88A).

D. The District Court's Decision

Dr. Bryant is a physician with a medical practice in Orange County, North Carolina, who is certified to prescribe mifepristone under the

federal REMS. JA30–31. North Carolina's restrictions on mifepristone prevent her from providing the drug to her patients in a manner consistent with the REMS and her professional judgment. Dr. Bryant brought this suit seeking declaratory and injunctive relief against North Carolina Attorney General Joshua Stein and other officials charged with enforcing the state's restrictions. After the Attorney General agreed with Dr. Bryant that the restrictions are preempted, state legislators Timothy Moore and Philip Berger intervened to defend them. JA612.

Dr. Bryant's operative complaint was filed in August 2023, after the North Carolina legislature amended the relevant statutes. Intervenors moved to dismiss, and the district court held a hearing in January 2024. During that hearing, the parties agreed that there were no disputed questions of fact and that the motion to dismiss should be converted into cross-motions for summary judgment. The court allowed the parties to file supplemental briefs. JA612–613.

On April 30, 2024, the court ruled that many, but not all, of North Carolina's restrictions on mifepristone are preempted. The court recognized that in enacting the REMS statute, "Congress had the clear and manifest purpose of making the FDA responsible for deciding what

restrictions need to be imposed on the distribution of [REMS] drugs … and on the providers who prescribe and distribute those drugs." JA630. And it held that state laws that "undermine the national regulatory system established by Congress for evaluating and managing safe use and distribution of [REMS] drugs … are obstacles to the purpose of Congress" and are preempted. JA652. In particular, the court held that a state cannot "enact[] laws … [that] conflict with decisions made by the FDA explicitly finding such requirements to be unnecessary for safe use." JA652.

The court held that provisions of North Carolina law that require physician-only prescribing; in-person prescribing, dispensing, and administering; an in-person follow-up appointment; and reporting of non-fatal adverse events to FDA are preempted because they "second-guess the FDA's explicit judgment on how to manage risks from … mifepristone." JA645. The court held, however, that provisions requiring an in-person 72-hour advance consultation, an in-person examination, an ultrasound and blood-type determination, and reporting of non-fatal adverse events to the state were not preempted because, in the court's

view, those requirements are "not solely, or even primarily, directed to the risks of mifepristone." JA635.

After additional briefing, the court entered a final judgment and permanent injunction barring enforcement of the requirements the court held were preempted. JA657–659. Intervenors appealed, and Dr. Bryant and the Attorney General cross-appealed. JA660–669.

SUMMARY OF ARGUMENT

I. The district court properly held that most of North Carolina's restrictions on mifepristone are preempted. Under settled principles, state law is preempted if it stands as an obstacle to the accomplishment of the full purposes and objectives of federal law. Applying those principles here, the district court correctly held that because Congress charged FDA with assuring patient access to REMS drugs—especially for patients in rural or medically underserved areas—a state may not impose restrictions on a REMS drug that conflict with FDA's efforts to assure access to the drug. This follows from the Supreme Court's decision in *Geier* that a state cannot impose a mandate that a federal agency has rejected in favor of providing a broader range of choices. *Wyeth*, a case involving a less intensively regulated non-REMS drug, supports the same

conclusion: There, the Court held that a state was not precluded from requiring a stronger warning for the drug where FDA had not even considered, much less rejected, that warning.

North Carolina's restrictions are preempted because they second-guess FDA's explicit judgment and impose barriers to patient access that pose an obstacle to the federal REMS. The state bars qualified nonphysicians from prescribing the drug; requires that it be prescribed, dispensed, and administered in person; requires an in-person follow-up appointment; and requires that physicians report all adverse events to FDA, regardless of severity. FDA has considered and rejected each of these requirements, concluding they are unnecessary for safe use and impose unwarranted burdens on patients and providers. FDA has accordingly modified the federal REMS to enable nonphysician prescribing, pharmacy dispensing, and the use of telemedicine. North Carolina's restrictions frustrate FDA's efforts to facilitate patient access.

Intervenors' arguments are unpersuasive. They claim the district court applied field preemption, when in fact it held that under well-established principles of *obstacle* preemption, a state cannot restrict distribution of a REMS drug in ways FDA considered and rejected. They

claim *Wyeth* supports them, even though the Supreme Court emphasized that FDA had not even considered the warning at issue there. They ignore the overwhelming textual evidence that Congress intended FDA to assure patient access to REMS drugs. They gloss over the clear conflict between the state's restrictions and FDA's judgments. And they vastly overstate the consequences of the district court's ruling, when in reality, a ruling *upholding* the challenged restrictions would upend settled law.

II. The restrictions the district court upheld—those requiring (1) an in-person examination, ultrasound, and (in some cases) blood testing; (2) an in-person, 72-hour-advance consultation; and (3) reporting of all adverse events to the state—are also preempted. Like those the court struck down, these restrictions burden patient access to mifepristone in ways that conflict with the carefully balanced regulatory structure FDA imposed in the Mifepristone REMS, and they interfere with FDA's efforts to facilitate patient access to mifepristone via telemedicine. The court held that these restrictions avoid preemption because they are "unrelated to mifepristone," JA633, but that is wrong: The North Carolina statute and intervenors' own arguments leave no doubt that these restrictions are aimed squarely at mifepristone and

reflect the state's disagreement with FDA about how to balance safety and patient access for this particular REMS drug.

III. Intervenors' new argument that Dr. Bryant lacks a cause of action is forfeited and meritless. They did not raise this argument below, and this Court has held that an argument that a plaintiff lacks a cause of action is forfeited when not raised in the district court. In any event, Dr. Bryant has a well-established equitable cause of action to enjoin state officials from enforcing preempted state laws, and the FDCA does not displace that cause of action because Dr. Bryant is not seeking to enforce or restrain a violation of the FDCA.

IV. The district court did not abuse its discretion by enjoining the enforcement of any provisions of state law that impose the preempted requirements. The injunction is appropriately tailored to reach only the specific restrictions that the court concluded are unconstitutional. There is no risk of confusion, and courts routinely impose similar injunctions.

STANDARD OF REVIEW

This Court reviews de novo whether a state law is preempted by federal law. *Guthrie v. PHH Mortg. Corp.*, 79 F.4th 328, 336 (4th Cir. 2023). A district court's disposition of cross-motions for summary

judgment is also reviewed de novo. *Libertarian Party of Va. v. Judd*, 718 F.3d 308, 312 (4th Cir. 2013). The scope of a district court's injunction is reviewed for abuse of discretion. *Roe v. Dep't of Def.*, 947 F.3d 207, 231 (4th Cir. 2020).

ARGUMENT

I. The district court properly held that most of North Carolina's restrictions are preempted by federal law.

A. A state may not impose restrictions on a REMS drug that FDA considered and rejected as unnecessary for safety and unduly burdensome on patient access.

In our federal system, state law must yield to federal law, which is "the supreme Law of the Land." U.S. Const. art. VI, cl. 2. State laws are thus preempted when they "stand[] as an obstacle to the accomplishment of the full purposes and objectives of federal law." *Anderson v. Sara Lee Corp.*, 508 F.3d 181, 191–92 (4th Cir. 2007) (quoting *Worm v. Am. Cyanamid Co.*, 970 F.2d 1301, 1305 (4th Cir. 1992)). For preemption purposes, relevant federal law includes both statutes enacted by Congress and actions taken by "a federal agency acting within the scope of its congressionally delegated authority." *La. Pub. Serv. Comm'n v. FCC*, 476 U.S. 355, 369 (1986); *accord Geier*, 529 U.S. at 881. It is thus undisputed that "agency actions taken pursuant to the FDA's

congressionally delegated authority"—such as modifying a REMS—can preempt state law. *Merck*, 587 U.S. at 315.

Implied obstacle preemption is among the "ordinary principles of preemption" and is "well-settled." *Arizona v. United States*, 567 U.S. 387, 406 (2012); *see, e.g.*, *Perez v. Campbell*, 402 U.S. 637, 649 (1971) (tracing obstacle preemption to Chief Justice Marshall's recognition that state laws that "interfere with … the laws of Congress" violate the Supremacy Clause (quoting *Gibbons v. Ogden*, 22 U.S. 1, 211 (1824)); *McCulloch v. Maryland*, 17 U.S. 316, 436 (1819) (Marshall, C.J.) ("[T]he unavoidable consequence of that supremacy which the constitution has declared" is that "states have no power … to retard, impede, burden, or in any manner control, the operations of the constitutional laws enacted by [C]ongress."). While intervenors (at 19) dispute that obstacle preemption is "a valid basis for federal preemption," they admit that "existing precedent" offers no support for their position.

The Supreme Court's decision in *Geier*—which intervenors barely address—is a classic illustration of obstacle preemption. *Geier* held that a state law requiring auto manufacturers to equip every car with a driver-side airbag was preempted because it conflicted with a federal

agency's decision not to require airbags for all vehicles. 529 U.S. at 874–75, 881–82. Acting under the National Traffic and Motor Vehicle Safety Act, the Department of Transportation had promulgated a Federal Motor Vehicle Safety Standard that "deliberately sought variety" by "allowing manufacturers to choose among different passive restraint mechanisms," including seatbelts. *Id.* at 878. The agency had specifically rejected an "all airbag" standard as inconsistent with its safety goals. *Id.* at 879. Against this regulatory backdrop, the Supreme Court held that a state-law airbag requirement "would have presented an obstacle to the variety and mix of devices that the federal regulation sought" and "upset the careful regulatory scheme established by federal law." *Id.* at 870, 881 (quotation marks omitted). As the district court held, *Geier* establishes that state law is "preempted where [a federal] agency deliberately established [a] federal regulatory scheme and specifically considered and rejected [the] requirements that state law would impose." JA632.

Intervenors pay short shrift to *Geier* while emphasizing *Wyeth*, but *Wyeth* fully supports *Geier*'s approach to obstacle preemption. *Wyeth* involved a challenge to the FDA-approved labeling for Phenergan, a non-REMS drug; the Court thus did not have to consider the unique statutory

scheme that applies to REMS drugs. The defendant argued that obstacle preemption barred a state-law tort suit that would have required it to add a warning to Phenergan's label. The additional warning had never been proposed by Wyeth, and FDA "had paid no more than passing attention" to whether such a warning would be appropriate. 555 U.S. at 563. Wyeth, however, insisted that state law was preempted "regardless of whether there [was] any evidence that the FDA ha[d] considered the stronger warning at issue." *Id.* at 573–74.

In a 5–4 decision, the Supreme Court rejected that argument. Distinguishing *Geier*, the Court explained that there the agency's "contemporaneous record … revealed the factors the agency had weighed and the balance it had struck," including its deliberate decision to "[r]eject an 'all airbag' standard"; whereas in *Wyeth*, the record showed that "FDA did not consider and reject a stronger warning." *Id.* at 580–81 & n.14. The Court also explained that it was not surprising that FDA had not focused on the warning at issue, because FDA "has limited resources to monitor the [at that time] 11,000 drugs on the market," so state tort suits could help the agency identify "unknown drug hazards" that

otherwise would not come to its attention, as well as serve a "compensatory function" distinct from federal regulation. *Id.* at 578–79.

The Court recognized, however, that if FDA *had* clearly rejected the warning, then the state would be preempted from requiring it. *Id.* at 571; *see* JA651 ("[I]n *Wyeth*, the FDA had not considered and rejected the exact requirements the state [sought] to impose, a factor the Supreme Court deemed important enough to mention explicitly."). And the Court has since confirmed that "state law failure-to-warn claims are pre-empted … when there is 'clear evidence' that the FDA would not have approved the warning that state law requires." *Merck*, 587 U.S. at 310.

Under *Wyeth* and *Merck*, North Carolina could not require a manufacturer of mifepristone to incorporate the state's restrictions into the drug's FDA-approved labeling (nor, for that matter, could a manufacturer do so unilaterally). For example, if the state ordered the manufacturer to warn that mifepristone should be prescribed only by a physician, that it should be dispensed and administered in person, or that patients should return for an in-person follow-up visit, those requirements would be preempted because there is clear evidence that FDA has rejected them, so including them in the drug's labeling would

render it misbranded in violation of federal law. *See In re Zofran (Ondansetron) Prods. Liab. Litig.*, 57 F.4th 327, 342 (1st Cir. 2023) (state could not require warning that drug should not be used during pregnancy because FDA had rejected that position); *Cerveny v. Aventis, Inc.*, 855 F.3d 1091, 1105 (10th Cir. 2017) (similar).

To be sure, a state law requiring a manufacturer to make a labeling change that FDA has rejected would be barred under *impossibility* preemption (because the manufacturer would violate federal law if it made the change). But it would make no sense to say that a state that is preempted from requiring a manufacturer merely to *recommend* that a drug not be taken during pregnancy (as in *Zofran* and *Cerveny*) can undermine FDA's judgment even more by *banning* providers from prescribing the drug during pregnancy. While compliance might not technically be impossible, such a requirement would be obstacle-preempted under *Geier* because it would upset the federal regulatory scheme by imposing restrictions that FDA considered and rejected.

Here, the Court need not decide whether obstacle preemption would prevent such circumvention of FDA's judgment with respect to ordinary labeling (*e.g.*, whether it would prevent a state from imposing a

restriction on prescribers that FDA expressly considered and rejected including in the drug's label). At a minimum, obstacle preemption applies where, as here, the drug is subject to a REMS and not just ordinary labeling, because in the REMS statute Congress expressly tasked FDA with assuring patient access. *See* pp. 11–13, *supra*. Contrary to intervenors' suggestion, Congress clearly charged FDA with protecting and promoting patients' access to REMS drugs.

For starters, patient access to safe and effective drugs is a key objective of the FDCA as a whole. Congress defined FDA's mission as "promot[ing] the public health" by "promptly," "efficiently," and "timely" reviewing new-drug applications, which underscores that providing access to drugs is a key statutory objective. 21 U.S.C. § 393(b)(1); *see id.* § 379g note ("[P]rompt approval of safe and effective new drugs is critical to the improvement of the public health so that patients may enjoy the benefits provided by these therapies …."); *id.* § 356 note ("Patients benefit from expedited access to safe and effective innovative therapies."); *Zogenix, Inc. v. Patrick*, 2014 WL 3339610, at *4 (D. Mass. July 8, 2014) (state laws preempted when they "prevent the accomplishment of the FDCA's objective that safe and effective drugs be available to the public").

Beyond the FDCA as a whole, there is overwhelming textual evidence that ensuring patient access is a central objective of the REMS statute. *See North Carolina v. United States*, 7 F.4th 160, 165 (4th Cir. 2021) ("When discerning congressional intent, we begin with statutory text."). Under the heading "Assuring access and minimizing burden," Congress directed FDA to ensure that any restrictions imposed on a REMS drug are (i) "commensurate" with the drug's risks—meaning sufficient, but not greater than necessary, to assure safety; (ii) not "unduly burdensome on patient access to the drug," considering in particular "patients who may have difficulty accessing health care (such as patients in rural or medically underserved areas)"; and (iii) designed to "minimize the burden on the health care delivery system." 21 U.S.C. § 355-1(f)(2). Congress required FDA to consult with patients and providers about how to avoid unduly burdening "patient access to the drug" or "the health care delivery system." *Id.* § 355-1(f)(5)(A). And Congress commanded FDA to regularly reevaluate any restrictions and eliminate those that are unduly burdensome on "patient access to the drug" or "the health care delivery system." *Id.* § 355-1(f)(5)(B)–(C), (g)(2)(C), (g)(4)(B).

Contrary to intervenors' suggestion (at 19), the district court did not base its preemption analysis on speculation about "'abstract and unenacted legislative desires.'" It relied on the text Congress enacted, which makes plain that one of the statute's core purposes was ensuring that patients—and especially patients with difficulties accessing health care—can access REMS drugs without facing unduly burdensome restrictions. As the court recognized, Congress's "clear and manifest objective" was "to make the FDA responsible for deciding upon and implementing safety restrictions to balance safety, efficacy, patient access, and burdens on the health care system." JA631; *accord* JA646 (noting the "clearly stated congressional goals of (1) having the FDA in charge of managing risks associated with REMS drugs, (2) limiting restrictions on REMS drugs to those necessary for safety purposes, and (3) avoiding restrictions that impose unnecessary burdens on the health care system and patient access").

The district court thus correctly held that state law is preempted when it seeks to "second-guess the FDA's explicit judgment on how to manage risks from and safely prescribe, dispense, and administer REMS drugs" by imposing restrictions that "FDA explicitly considered and

rejected … as unnecessary for safe use under the statutory regime imposed and required by Congress." JA640–641, JA645.

B. North Carolina's restrictions have been rejected by FDA and impede FDA's efforts to make mifepristone more accessible to patients.

Applying these principles, the district court properly held that most of North Carolina's restrictions conflict with federal law because they "second-guess the FDA's explicit judgment on how to manage risks from and safely prescribe, dispense, and administer … mifepristone." JA645. Exercising its congressionally delegated responsibility, after careful review, FDA took steps to increase patient access to mifepristone—including access through telemedicine—by eliminating restrictions, such as in-person requirements, that the agency determined were unnecessary for safe use and unduly burdensome on patients and providers. It would frustrate the objectives of federal law if North Carolina could reimpose the same access barriers FDA sought to eliminate.

Intervenors do not dispute that North Carolina is imposing restrictions that "FDA explicitly considered and rejected" as part of its management of the Mifepristone REMS. Br. 30 (quoting JA640–641). But

they gloss over the specific conflicts the district court identified between those restrictions and FDA's decisions under the REMS statute.

1. *Physician-Only Restriction.* North Carolina requires that only physicians can "prescribe, dispense, or otherwise provide" mifepristone, excluding nonphysician practitioners who are licensed to prescribe drugs under state law. N.C. Gen. Stat. § 90-21.83A(b)(2)(a). Other provisions reinforce this requirement by referring to "the physician" who provides mifepristone. *E.g.*, *id.* § 90-21.93(b)(1).

This restriction squarely conflicts with FDA's judgment. Congress gave FDA "explicit statutory authorization" to decide what qualifications are needed to prescribe a REMS drug. JA642; *see* 21 U.S.C. § 355-1(f)(3)(A). At first, FDA determined that only physicians could become certified prescribers of mifepristone. JA642. But after extensively studying the issue, in 2016, FDA concluded that this limitation was unduly burdensome and modified the REMS to eliminate it. JA642–643. In 2021, FDA denied a citizen petition asking it to reimpose the physician-only requirement and reiterated its firm conclusion that mifepristone "is safe and effective when prescribed by midlevel providers,

such as physician assistants." JA238–239; *see* JA253 ("[W]e do not agree … that the healthcare provider needs to be a licensed physician.").

FDA did not just remove the physician-only restriction from the REMS; it also made a reasoned decision to grant prescribing authority under the REMS to a broader range of healthcare providers. JA77, JA82–85 (allowing providers other than physicians who meet the qualifications specified by FDA to become certified prescribers under the REMS). Yet a nonphysician who enters into a Prescriber Agreement and becomes federally certified to prescribe mifepristone is still prohibited from prescribing the drug in North Carolina. North Carolina's laws thus "run[] smack into [FDA's] regulations," *Nat'l Meat Ass'n v. Harris*, 565 U.S. 452, 467 (2012), by denying certified nonphysician prescribers the ability to do what they are certified to do under the federal REMS. *Cf. Sperry v. Florida ex rel. Fla. Bar*, 373 U.S. 379, 385 (1963) (a state may not "impose upon the performance of activity sanctioned by federal license additional conditions not contemplated by Congress"); *Barnett Bank of Marion Cnty., N.A. v. Nelson*, 517 U.S. 25, 33 (1996) (presuming that "Congress

would not want States to forbid, or to impair significantly, the exercise of a power" granted by federal law).[3]

2. *In-Person Dispensing and Administration.* North Carolina requires a physician providing mifepristone to "be physically present in the same room as the woman when the first drug or chemical is administered." N.C. Gen. Stat. § 90-21.83A(b)(2)(a). And it imposes strict-liability penalties on anyone who supplies mifepristone that is subsequently taken outside the presence of a physician, which effectively bars pharmacies (even those certified under the REMS) from dispensing mifepristone. *Id.* § 14-44.1(a)–(b).

FDA has considered and rejected the same in-person requirements. FDA originally required physicians to both dispense and administer mifepristone in person, but it later jettisoned those requirements after years of safe use and extensive review. It removed the in-person

[3] FDA's statement that for nonphysician practitioners to become certified prescribers under the Mifepristone REMS, they must be allowed to "prescribe medications" under their states' laws, JA470, does not help intervenors. FDA does not regulate general prescribing privileges under state law. But a state may not single out a REMS drug and prohibit practitioners who have prescribing privileges under state law from prescribing that particular drug, in conflict with FDA's judgment about the qualifications necessary to prescribe the drug.

administration requirement in 2016, allowing patients to take mifepristone at home or in the location of their choosing. JA622; *compare* JA168 *with* JA225. And in 2023, FDA eliminated the in-person dispensing requirement and replaced it with a pharmacy certification requirement. JA623–624; *compare* JA220 *with* JA78–80, JA87–89. As FDA explained, it "undertook a full review of the Mifepristone REMS Program" and concluded that "the in-person dispensing requirement is no longer necessary to assure the safe use of mifepristone" and that the REMS should "allow … dispensing of mifepristone by mail" or in person by certified pharmacies. JA235, JA264; *see also* JA351.

As with its elimination of the physician-only requirement, FDA did not simply remove the federal requirement of prescriber dispensing; it affirmatively granted dispensing authority to pharmacies that meet an enumerated list of qualifications and enter into a Pharmacy Agreement. JA79–80, JA84–85. The state's insistence that patients not be allowed to obtain mifepristone from pharmacies—even pharmacies that are certified to dispense the drug under the federal REMS—thus conflicts with FDA's expert judgment that mifepristone can be safely provided by pharmacies, undermines the agency's efforts to promote patient access

and reduce burdens on the healthcare system by enabling pharmacy dispensing and telemedicine, and nullifies FDA's affirmative grant of dispensing authority to REMS-certified pharmacies.

3. *In-Person Follow-Up.* North Carolina requires mifepristone prescribers to schedule in-person follow-up visits for patients 1–2 weeks after administration of the drug and to make and document "all reasonable efforts to ensure" that patients return for these appointments. N.C. Gen. Stat. § 90-21.83B(b); *see id.* §§ 90-21.83A(b)(4)(*l*), 90-21.93(b)(8)–(9).

After careful consideration, FDA removed a similar requirement from the Mifepristone REMS in 2016. JA622; *compare* JA168 *with* JA225. FDA explained that it had studied the matter and concluded that medication abortion does not "always require[] in-person follow-up" and that "follow-up can be performed by telephone." JA242–244 (quotation marks omitted).

North Carolina's in-person follow-up requirement bars providers from following up with patients via telehealth, creating a barrier to follow-up appointments that burdens both patient and provider. Congress charged FDA with assuring that patients would be able to

access REMS drugs, and it directed the agency to give special consideration to patients in "rural or medically underserved areas." 21 U.S.C. § 355-1(f)(2)(C)(ii). Through its REMS modifications, FDA has looked to telemedicine to aid in that objective. Telemedicine improves a patient's ability to promptly and easily see their healthcare provider—especially for patients who may have to travel a long way or take time off from work to visit the provider in person—and it also reduces burdens on the healthcare system.[4] North Carolina's requirement impedes these federal goals.

4. ***Mandatory Adverse-Event Reporting to FDA.*** North Carolina requires physicians to report all "adverse event[s]" related to the use of mifepristone to FDA, regardless of their severity. N.C. Gen. Stat. § 90-21.93(c).

This requirement, too, imposes burdens that FDA has considered and rejected. When mifepristone was first approved, FDA imposed a heightened reporting requirement under which prescribers had to report all adverse events to the agency. But in 2016, FDA explained that it had

[4] *See* HHS, *Why Use Telehealth?*, https://telehealth.hhs.gov/patients/why-use-telehealth; HHS, *Telehealth for rural areas*, https://telehealth.hhs.gov/providers/best-practice-guides/telehealth-for-rural-areas.

"assessed approximately 15 years of adverse event reports … and determined that" continued mandatory reporting of nonfatal events was "not warranted" in light of "the well-characterized safety profile of [mifepristone], with known risks occurring rarely." JA249. FDA therefore modified the REMS to eliminate the requirement for prescribers to report nonfatal adverse events. *Compare* JA166 *with* JA223. North Carolina is reimposing a burden that FDA deliberately chose to remove.

This requirement is also preempted because a state cannot oversee the relationship between a federal agency and the entities the agency regulates. *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 347–48 (2001). In *Buckman*, the Supreme Court held that the FDCA preempted an attempt to use state tort law to regulate a device manufacturer's communications with FDA. The Court explained that "the relationship between a federal agency and the entity it regulates is inherently federal in character because the relationship originates from, is governed by, and terminates according to federal law." *Id.* at 347. Allowing state law to govern communications between regulated parties and FDA would "dramatically increase the burdens" on regulated parties—imposing "burdens not contemplated by Congress"—and would lead to FDA

receiving "a deluge of information that [it] neither wants nor needs." *Id.* at 350–51. Here too, North Carolina's reporting requirement would intrude on this inherently federal relationship, imposing burdens on mifepristone providers not contemplated by Congress and burying FDA in reports it has stated it does not need.[5]

C. Intervenors' arguments are unpersuasive.

Intervenors insist that North Carolina and other states must be able to express their "disagreement with the FDA over what safety restrictions on the use of [REMS drugs] are necessary," JA652, by enacting a patchwork of burdensome restrictions on those drugs that FDA considered and rejected. Their arguments are unpersuasive.

Intervenors' main tactic is to try to change the subject. Even though the district court clearly stated that field preemption is not at issue here, JA614 n.4, intervenors mischaracterize the court's decision as implicitly resting on field rather than obstacle preemption. They insist that the court held that "*any* state law that imposes a 'safety-related' protection

[5] Mifepristone sponsors still must report any "serious and unexpected" adverse events to FDA within 15 days and other adverse events annually. 21 C.F.R. § 314.80(c)(1)–(2). FDA has determined that this reporting paradigm is appropriate for identifying safety issues. *See* FDA, New Drug and Antibiotic Regulations, 50 Fed. Reg. 7452, 7471 (Feb. 22, 1985).

on [REMS] drugs" is preempted. Br. 1; *see also, e.g.*, *id.* at 15, 27–29. That is not true. The district court did not hold, and Dr. Bryant did not argue, that a state can never regulate a REMS drug in any way. Rather, the court held that North Carolina could not stand up "obstacles to Congress's purpose in creating a comprehensive federal regulatory scheme," JA655, by imposing restrictions on a REMS drug that FDA has "expressly considered and rejected," JA609, and that directly "conflict with decisions made by the FDA explicitly finding such requirements to be unnecessary for safe use," JA652. Intervenors' mischaracterization of the court's holding underlies many of their other arguments.

1. Intervenors' reliance on *Wyeth* is misplaced.

Intervenors first contend (at 20–22) that the Supreme Court's decision in *Wyeth* "rejected the claim Plaintiff makes here—that 'the FDCA establishes both a floor and a ceiling for drug regulation.'" Br. 21 (quoting 555 U.S. at 573–74). But Dr. Bryant did not argue, and the district court did not hold, that the REMS is an absolute "ceiling" that precludes even state regulations unrelated to the REMS. Instead, the court held that a state is preempted from imposing a restriction on a

REMS drug that FDA "considered and rejected … as unnecessary for safe use." JA640–641.

Wyeth does not suggest that a state is free to impose restrictions on a federally regulated drug that FDA considered and rejected. Just the opposite—as discussed above, the Supreme Court emphasized that "FDA did not consider and reject" the state-law warning at issue there. 555 U.S. at 580–81 & n.14; *see id.* at 563, 573–74; JA651 (noting that the Court "deemed [this] important enough to mention explicitly"). And the Court has since made clear that a state *cannot* require warnings that FDA *has* considered and rejected. *Merck*, 587 U.S. at 310.

Moreover, *Wyeth* did not involve a REMS drug; it concerned only standard FDA-approved labeling. 555 U.S. at 567 (noting that the FDCA amendments that included the REMS statute were enacted "after Levine's injury and lawsuit" and were not at issue). And the Court stressed that because FDA could not possibly monitor all (at that time) 11,000 approved drugs, the Court could not assume FDA had "performed a precise balancing of risks and benefits" with respect to the specific warning at issue. *Id.* at 575, 578. That reasoning points to the opposite conclusion here. Only a few dozen drugs have REMS with ETASU, and

Congress directed FDA to intensively monitor those drugs and update their REMS to ensure that any restrictions are necessary for safe use and not unduly burdensome. 21 U.S.C. § 355-1(f)(2), (f)(5), (g)(4). With respect to REMS drugs, Congress thus charged FDA with performing the "precise balancing of risks and benefits" that was absent from the routine labeling review at issue in *Wyeth*. 555 U.S. at 575.

Intervenors stress two aspects of the FDCA that the Supreme Court mentioned in *Wyeth*: the saving clause in the Drug Amendments of 1962, and the express preemption clause in the Medical Device Amendments of 1976 ("MDA"). Neither provision helps them. The Supreme Court has squarely held that "neither an express pre-emption provision nor a saving clause bars the ordinary working of conflict pre-emption principles," including obstacle preemption. *Buckman*, 531 U.S. at 352 (cleaned up) (rejecting argument that courts "should be reluctant to find a pre-emptive conflict … because Congress included an express pre-emption provision in the MDA"); *see Arizona*, 567 U.S. at 406 ("[A]n express preemption provision does *not* bar the ordinary working of conflict preemption principles or impose a special burden that would make [establishing preemption] more difficult …." (cleaned up)); *Geier*,

529 U.S. at 870–72 ("[T]his Court has repeatedly declined to give broad effect to saving clauses where doing so would upset the careful regulatory scheme established by federal law." (cleaned up)); *PCS Phosphate Co. v. Norfolk S. Corp.*, 559 F.3d 212, 220–21 (4th Cir. 2009).

In any event, the provisions intervenors cite do not apply to the REMS statute, which they predate by several decades. The saving clause is expressly limited to preemption *under the 1962 amendments* and says nothing about the scope of preemption under the REMS statute that Congress enacted 45 years later:

> Nothing in *the amendments made by this Act* to the Federal Food, Drug, and Cosmetic Act shall be construed as invalidating any provision of State law which would be valid in the absence of *such amendments* unless there is a direct and positive conflict between *such amendments* and such provision of State law.

Drug Amendments of 1962, Pub. L. No. 87-781, § 202, 76 Stat. 780, 793 (emphases added). This limitation was deliberate: Congress rejected an alternative proposal that would have applied to the whole FDCA. H.R. Rep. No. 87-2526, at 26 (1962) (Conf. Rep.) (Congress chose to "make[] the provision applicable only to the amendments"). The Court should reject intervenors' request to disregard this express limitation and

ascribe broader meaning to the 1962 clause. *See Int'l Paper Co. v. Ouellette*, 479 U.S. 481, 493 (1987) (saving clause that "merely sa[id] that 'nothing *in this section*' … shall affect an injured party's right to seek relief under state law" did not "preclude pre-emption of state law by other provisions of the Act"). As for the MDA, it is a wholly separate regulatory paradigm from that governing drugs, and the MDA's express preemption provision, 21 U.S.C. § 360k(a), is specific to medical devices. It sheds no light on what Congress intended when it enacted the REMS statute 31 years later.

2. Nothing in FDAAA or its legislative history precludes ordinary obstacle preemption.

Intervenors next argue (at 23–25) that "FDAAA's structure and context confirm that Congress did not intend to broadly preempt state law." But none of the evidence they cite suggests Congress did not want ordinary, background principles of obstacle preemption to apply to FDA's actions under the REMS statute.

Intervenors note (at 24–25) that in a different title of FDAAA, Congress expressly preempted certain state laws requiring registration of clinical trials. That provision has nothing to do with the REMS statute. And even if it did, "an 'express preemption provision does *not* bar the

ordinary working of conflict preemption principles.'" *Arizona*, 567 U.S. at 406 (brackets omitted) (quoting *Geier*, 529 U.S. at 869).

Next, intervenors claim (at 25) that Congress "declined to enact a generally applicable preemption provision" as part of FDAAA. For support, they cite an amicus brief in this case, which cites an amicus brief in another case, which cites a footnote in a law review article, which does not identify any preemption language Congress considered and declined to enact. *See* David A. Kessler & David C. Vladeck, *A Critical Examination of the FDA's Efforts to Preempt Failure-to-Warn Claims*, 96 Geo. L.J. 461, 468 n.27 (2008). Intervenors also cite a few "[f]loor statements by individual legislators," which are "among the least illuminating forms of legislative history," *Trump v. Hawaii*, 585 U.S. 667, 692 (2018) (cleaned up), and which suggest only that the speakers rejected *field* preemption.

The reality is that early drafts of the REMS statute contained express *anti*-preemption language (*i.e.*, a saving clause), but Congress *removed* that language after numerous parties, including FDA, objected to it. *See, e.g.*, *Discussion Drafts Concerning User Fee Act Reauthorization: Hearing Before Subcomm. on Health, H. Comm. on*

Energy & Com., 110th Cong. 50 (2007) (statement of Rep. Pitts) ("Would it not be counterproductive to public health for States to impose different REMS requirements than those imposed by the FDA?"); *id.* (statement of Randall Lutter, Deputy FDA Comm'r (expressing concern about "State actions that may be contradictory to or inconsistent with FDA actions on safety and effectiveness"); *id.* at 66 (statement of Caroline Loew, Sr. Vice Pres., Sci. & Regul. Affairs, PhRMA) (objecting to "[t]he anti-preemption language" because it "would undermine the intent of the REMS bill to reinforce FDA's control" and "enable each State to require warnings the FDA specifically rejected based on its scientific review"). Congress's deliberate removal of an anti-preemption provision in response to these objections weighs strongly against any inference that it did not want ordinary obstacle-preemption principles to apply.

Intervenors nonetheless claim (at 23) that FDAAA's only purpose was "to *increase* drug regulation," ignoring Congress's express commands to FDA to minimize burdens on patient access and the healthcare system. They say (at 23–24) that the access-related provisions of the REMS statute are irrelevant to preemption because they are framed as "limits … on the *federal* agency" and are not directed to the states. That

argument fails to appreciate that this case is about *implied* preemption. If Congress had explicitly prohibited (or tasked FDA with prohibiting) unduly burdensome state-law restrictions on REMS drugs, this would be an *express* preemption case.

The absence of an express directive to the States simply aligns this case with other implied-preemption cases. For example, the statute in *Geier* directed "[t]he Secretary" of Transportation to "establish … appropriate Federal motor vehicle safety standards" and said nothing about the states. 15 U.S.C. § 1392(a) (1988). That did not stop the Court from concluding, under "ordinary pre-emption principles," that a State could not impose the same all-airbag standard the Secretary had deliberately rejected. 529 U.S. at 871; *see id.* at 884 (conflict preemption does not require "an express statement of pre-emptive intent"); *PLIVA, Inc. v. Mensing*, 564 U.S. 604, 621 (2011) ("The Supremacy Clause … makes federal Law 'the supreme Law of the Land' even absent an express statement by Congress.").

Intervenors contend (at 26) that, in light of the presumption against preemption and the major questions doctrine, obstacle preemption cannot apply under FDAAA absent a "clear statement of preemptive

intent" in the statute. That, too, is wrong. The presumption against preemption does not require a "clear statement" for obstacle preemption, and the major questions doctrine does not apply here.

With respect to the presumption against preemption, courts do not assume that Congress would want states to be able to enforce laws that stand as an obstacle to federal law. The opposite is true: Courts presume that "Congress would *not* want" states to "impair significantly" the operation of federal law. *Barnett Bank*, 517 U.S. at 33 (emphasis added). So it is well settled that "express congressional authorization to displace state law" is not required for obstacle preemption. *Fid. Fed. Sav. & Loan Ass'n v. de la Cuesta*, 458 U.S. 141, 154 (1982); *see Crosby v. Nat'l Foreign Trade Council*, 530 U.S. 363, 374 n.8 (2000) (presumption against preemption is overcome where state law "presents a sufficient obstacle" to federal law); *Nat'l Home Equity Mortg. Ass'n v. Face*, 239 F.3d 633, 637 (4th Cir. 2001) ("Even when Congress' intent is unclear, state law must nevertheless yield when it conflicts with federal law."). The dissent in *Geier* invoked the same presumption, to no avail. 529 U.S. at 894 (Stevens, J., dissenting).

As for the major questions doctrine, it is irrelevant for at least two reasons. First, the doctrine is a tool for deciding whether an agency has authority to take a challenged action; it does not affect whether a concededly valid agency action gives rise to obstacle preemption. *See West Virginia v. EPA*, 597 U.S. 697, 724 (2022) (doctrine addresses the problem of "agencies asserting highly consequential power beyond what Congress could reasonably be understood to have granted"). In every case where the Supreme Court has applied the doctrine, a party was challenging some agency action that it claimed exceeded the agency's statutory authority. *Id.* at 721–22 (surveying cases). Here, however, it is undisputed that Congress authorized FDA to promulgate and revise the Mifepristone REMS. The major questions doctrine does not speak to the preemptive effect of FDA's actions.

Second, this case does not involve a matter of "vast economic and political significance" capable of triggering the major questions doctrine. *Id.* at 716 (quotation marks omitted). The Supreme Court has applied the doctrine cautiously and only in cases involving a "transformative expansion in [an agency's] regulatory authority," *id.* at 724 (quotation marks omitted)—for example, where an agency claimed power to force a

nationwide transition away from the use of coal, *id.* at 735; release 43 million borrowers from their obligations to repay $430 billion in student loans, *Biden v. Nebraska*, 600 U.S. 477, 501 (2023); require 84 million Americans to obtain a COVID vaccine, *Nat'l Fed'n of Indep. Bus. v. Dep't of Lab.*, 595 U.S. 109, 112–13 (2022) (per curiam); impose a nationwide moratorium on evictions, *Ala. Ass'n of Realtors v. HHS*, 594 U.S. 758, 759–60 (2021) (per curiam); demand permits for millions of offices, schools, and churches, *Util. Air Regul. Grp. v. EPA*, 573 U.S. 302, 328 (2014); or ban cigarettes nationwide, *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 130 (2000).

Intervenors make no attempt to show that this case involves the kind of sweeping, transformative regulatory expansion that has led the Supreme Court to invoke the major questions doctrine. On the contrary, this case involves only the modest question of whether, in connection with abortions that are legal in North Carolina, the state can impose specific restrictions on mifepristone (like requiring patients to take it in a doctor's office instead of at home) that FDA has rejected as unduly burdensome and that interfere with the operation of the federal REMS (*e.g.*, by preventing pharmacies that are federally certified to dispense

mifepristone from doing so). The answer to that question is important to patients and their doctors, but it is hardly a matter of such "vast economic and political significance" as to trigger the major questions doctrine.

3. North Carolina's restrictions do not "complement" federal law.

Intervenors argue (at 29–32) that North Carolina's restrictions "complement" federal law, even though FDA has rejected the very same restrictions as unnecessary and inappropriate. They do not.

Intervenors first claim (at 29–30) that "[i]t is undisputed" that the challenged restrictions "protect 'safety,'" and they say the district court held the restrictions preempted "because they decrease mifepristone's risks." That is false. Dr. Bryant obviously disputes that the restrictions enhance safety; FDA found that they do not; and the district court said only that "intervenors justify [the] restrictions on safety grounds," not that the restrictions actually increase safety. JA649.

Intervenors then pivot to claim (at 30–31) that the restrictions at least do not "make mifepristone *less* safe" and that in rejecting similar restrictions, FDA "did not find them *harmful*." That, too, is false. FDA *did* find the restrictions harmful: It found they would hurt patients by unduly burdening patient access to mifepristone, making it harder for

patients to obtain a drug that is "important to the[ir] health." JA115. For example, in-person requirements can delay or deter patients from receiving appropriate and necessary medical care, and over-reporting of minor adverse events can make it harder for FDA to identify genuine safety issues. Moreover, even if North Carolina's restrictions and the federal REMS could be said to share the same "ultimate goal" of promoting safety, the state restrictions would still be preempted because they "interfere[] with the methods" by which FDA has chosen to pursue that goal. *Gade v. Nat'l Solid Wastes Mgmt. Ass'n*, 505 U.S. 88, 103 (1992) (quotation marks omitted).

When intervenors finally (and fleetingly) turn to the actual issue in this case—whether states are preempted from imposing restrictions on REMS drugs that FDA has determined to be unwarranted—they have no persuasive response to *Geier*. *See* Br. 30–32. They argue that in *Geier*, "[t]he Department of Transportation had 'deliberately provided the manufacturer with a range of choices among different passive restraint devices,'" whereas here, "Congress did not intend to provide a 'range of choices' regarding high-risk REMS drugs." *Id.* at 31 (quoting *Geier*, 529 U.S. at 875 & *Wyeth*, 555 U.S. at 580).

That statement is inaccurate—Congress expressly gave FDA a range of choices for how to regulate REMS drugs, *see* 21 U.S.C. § 355-1(e), (f)(3)—but more fundamentally, it misunderstands the analogy between this case and *Geier*. In *Geier*, it was *the agency*, exercising authority delegated by Congress, that deliberately sought to give car manufacturers a range of choices about how to ensure driver safety. Likewise here, FDA, exercising authority delegated by Congress in the REMS statute, deliberately sought to give prescribers and patients a range of choices about how to provide and obtain mifepristone: by meeting with a federally certified prescriber, who may or may not be a physician, in person or via telemedicine, and by obtaining the drug from the prescriber or from a federally certified pharmacy.

Here, as in *Geier*, state law would limit the range of choices the responsible federal agency sought to provide. The two cases are on all fours, so *Geier* is controlling.

4. Intervenors get the impact of a preemption ruling here exactly backward.

Finally, intervenors resort (at 32–34) to making dire predictions about how affirming the district court's decision will affect other states' laws, but they fail to show that any serious disruption will result. They

continue to misrepresent the decision as imperiling "*any* state law that touches a REMS drug," Br. 32, when in fact it is far more limited. When it comes to the impact of the court's actual holding—that states may not impose restrictions on REMS drugs that FDA considered and rejected—intervenors have little to say. They concede that only a handful of states have sought to impose restrictions on mifepristone that are similar to North Carolina's. *See* Br. 32–33. And while they cite a few state laws regarding opioids that they claim would be preempted, *id.* at 33, they make no attempt to show that those laws impose restrictions on opioids that FDA considered and rejected.

In reality, a decision *rejecting* preemption here would be a highly disruptive sea-change in the law. This should be an easy case for preemption—it involves FDA's intensive, ongoing oversight of a REMS drug, and state laws that restrict distribution of that drug in ways FDA expressly considered and rejected, making the district court's decision quite narrow. On the other hand, the implications of a decision reversing the district court would be astonishingly broad. If there is no preemption here despite the detailed Mifepristone REMS, then *a fortiori*, states will be free to impose restrictions on all 20,000+ non-REMS drugs that reflect

disagreement with FDA's evaluation of the scientific evidence concerning those drugs. A state could, for example, prohibit the use of a drug for indications or populations for which FDA has determined the drug is safe and effective, ban methods of administering the drug that FDA has approved, or require prescribers to give warnings about the drug that FDA has concluded are not justified. The Court should not invite such a patchwork of inconsistent state laws, which would undermine the federal regulatory scheme and harm patients.

II. The other challenged restrictions are also preempted.

Despite getting the preemption analysis mostly right, the district court held that some of North Carolina's restrictions on mifepristone were not preempted—specifically, those requiring that (1) the patient undergo an in-person examination, an ultrasound, and (in some cases) blood testing before being prescribed the drug; (2) the provider consult with the patient in person at least 72 hours before providing the drug to explain its benefits and risks; and (3) any and all adverse events be reported to the state.

These requirements are preempted for the same reasons as those the court struck down: because they impose burdensome restrictions on

a REMS drug that FDA considered and rejected; conflict with "FDA's explicit judgment on how to manage risks from and safely prescribe, dispense, and administer" mifepristone, JA645; and obstruct FDA's efforts to improve patient access and reduce burdens on the healthcare system by authorizing federally certified prescribers to prescribe mifepristone via telemedicine. The district court nonetheless held that these requirements escape preemption because they are "unrelated to mifepristone." JA633. That is wrong—as intervenors concede (at 4), these restrictions, like those the court held preempted, are targeted at managing the supposed safety risks of "abortion-inducing drugs." And they do so in ways that FDA has determined are unnecessary and inappropriate.

A. The in-person examination and in-person consultation requirements are preempted.

North Carolina requires that before providing mifepristone, a physician must "examine the woman in person." N.C. Gen. Stat. § 90-21.83B(a). Other restrictions reinforce the in-person examination requirement: The physician must document the results of an ultrasound of the patient "used to estimate gestational age," *id.* § 90-21.93(b)(6); *see also id.* § 90-21.83A(b)(2)(b), and "[d]etermine the woman's blood type"

(which could require in-person testing in some cases if a patient does not know her blood type), *id.* § 90-21.83B(a)(2). In addition, North Carolina requires that a provider consult with the patient "in person" at least 72 hours before the patient takes mifepristone to explain the use and risks of mifepristone and obtain "informed consent." *Id.* § 90-21.83A; *see also id.* § 90-21.90(a).

FDA has considered and rejected requiring an in-person examination for patients receiving mifepristone. In 2021, FDA denied a citizen petition asking it to modify the Mifepristone REMS to "require certified providers to physically meet with and examine the patient." JA241. FDA explained that "evaluation of patients for contraindications to medical abortion does not necessarily require direct physical contact with the certified prescriber and can be done in different types of healthcare settings," including by "consult[ing] with the patient over the Internet." JA240–241; *see* JA264. Therefore, "[c]ertified prescribers do not have to be physically present with the patient." JA241.

FDA also denied a request in the same citizen petition that it "mandat[e] that gestational age be assessed by ultrasound," emphasizing that "determination of gestational age does not always require an

ultrasound." JA240. FDA referred to its denial of a similar citizen petition in 2016, where the agency explained that it had "carefully considered the role of ultrasound" and determined that it was "inappropriate" to "mandate how providers clinically assess women for duration of pregnancy and for ectopic pregnancy," noting that "[t]hese decisions should be left to the professional judgment of each provider." JA138; *see* JA116. And while FDA has not explicitly addressed blood testing, its rejection of such a requirement is encompassed in its determination that mifepristone can be prescribed safely without an in-person examination, including through telemedicine. *See, e.g.*, JA240–241, JA264.[6]

FDA has also expressly rejected the notion that informed consent to the use of mifepristone requires an in-person consultation. From its

[6] In imposing ETASU, FDA is authorized to require "evidence or other documentation of safe-use conditions, such as laboratory test results," 21 U.S.C. § 355-1(f)(3)(D). FDA has required blood testing in other REMS, but it has never imposed any lab-testing requirements for mifepristone. Intervenors' contention (at 5) that blood testing is "necessary because Rh-negative blood type can cause serious complications" also contravenes the scientific evidence. *See, e.g.*, Sarah Horvath et al., *Induced Abortion and the Risk of Rh Sensitization*, 330 JAMA 1167, 1171 (2023), *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10524155/ (concluding that "Rh testing and provision of Rh immune globulin should not be undertaken prior to receiving induced abortion care at less than 12 weeks' gestation" and noting that the World Health Organization agrees).

inception, the Mifepristone REMS has addressed informed consent by requiring prescribers to "review[] the Patient Agreement Form with the patient, fully explain[] the risks of the treatment regimen," "answer[] any questions the patient may have before receiving the medication," and "place the signed Patient Agreement Form in the patient's medical record." JA253; *see* JA227 (Patient Agreement provides "assurance that the patient is aware of the nature of the procedure, its risks, and the need for appropriate follow-up care"); JA288 (Patient Agreement "standardiz[es] the medication information on the use of mifepristone that prescribers communicate to their patients" and ensures that providers "counsel a patient appropriately").

Originally, the patient had to sign the Patient Agreement and provide informed consent "in [the provider's] presence." JA225 (2016 REMS); *see* JA158, JA168. But in 2021, FDA concluded that "[a] certified prescriber can … review the Patient Agreement Form with the patient, fully explain the risks of the mifepristone treatment regimen, and answer any questions, as in any consent process, without physical proximity." JA241 (footnote omitted); *see* JA264 ("Healthcare providers … are responsible for the well-being of their patients regardless of mode of

evaluation or dispensing of medication."). FDA therefore modified the REMS to specify that the Patient Agreement may be provided "electronically." JA86; *see* JA307 n.*w* (Patient Agreement "can be signed in person or through other means.").

In short, FDA has expressly concluded that federally certified mifepristone prescribers can prescribe the drug via telemedicine and need not meet with the patient in person, either to perform a physical examination or to obtain informed consent. North Carolina, by requiring an in-person examination and consultation, is "impos[ing] requirements that [FDA] ha[s] affirmatively and clearly rejected as unnecessary [and] inappropriate." JA628. These requirements are squarely preempted under *Geier*. Exercising its congressionally delegated responsibility for assuring patient access and minimizing burdens on the healthcare system, FDA "deliberately provided … a range of choices" about how mifepristone can be prescribed (in person or via telemedicine). 529 U.S. at 875. Allowing states to restrict those choices would "upset the careful regulatory scheme established by federal law." *Id.* at 870 (quoting *Locke*, 529 U.S. at 106).

Not only that—North Carolina's requirement that the informed-consent consultation take place 72 hours before the patient takes mifepristone conflicts with FDA's 2016 decision to "extend the maximum gestational age" for mifepristone's indicated use "to 70 days," JA232, because it effectively shortens the approved period by three days. The 72-hour requirement flatly prohibits patients at 68 or 69 days of gestation from deciding to use mifepristone. And the requirement that the consultation take place in person, rather than via telemedicine as authorized by FDA, makes it harder for patients nearing that gestational age to get care in time. These requirements stand as obstacles to Congress's goals of improving patient access and reducing burdens on the healthcare system. As FDA has recognized, North Carolina's requirements do not make the drug safer; they just make it harder to obtain.

B. The district court's reasons for upholding these requirements are incorrect.

The district court's decision to uphold North Carolina's in-person examination and consultation requirements, while recognizing that the state's other in-person requirements are preempted, is puzzling. The court purported to distinguish the two sets of requirements on a basis

intervenors have never argued: It claimed that the non-preempted requirements are "unrelated to mifepristone" and concern only "general patient health and welfare and informed consent." JA633; *see* JA635 (reasoning that unlike the preempted requirements, the non-preempted requirements are "not solely, or even primarily, directed to the risks of mifepristone"); JA609 (the non-preempted requirements "focus more on the practice of medicine"). This distinction does not bear scrutiny.

For one thing, intervenors have never claimed that the in-person examination and consultation requirements are "unrelated" to "managing the safety risks of mifepristone." JA633, JA637. Just the opposite—they have been adamant that *all* the challenged restrictions are about protecting patients from mifepristone's supposed health risks. For example:

- In their motion to dismiss, intervenors claimed that "[s]afety reasons abound for the challenged laws," citing a study about "complications from chemical abortions." Dkt. 84 at 12; *see id.* at 16 (insisting on North Carolina's right to enact "additional safety measures to protect [its] citizens from drugs with identified

risks"); *id.* at 27 (claiming the challenged laws "promot[e] safety and protection from" mifepristone because it is "dangerous").

- In their supplemental district-court brief, intervenors claimed that the challenged laws are all "safety measures" enacted to "protect … consumers from dangerous drugs." Dkt. 100 at 1; *see id.* at 11 (asserting that North Carolina has "a legitimate and important interest in making sure [REMS drugs] are prescribed and distributed safely"); *id.* at 14 (insisting that "the challenged provisions … make abortion drugs safer").
- In their opening brief on appeal (at 4–5), intervenors continue to characterize the in-person examination and consultation requirements as regulations of "abortion-inducing drugs" that are necessary to avoid "serious complications."

Intervenors have never claimed that these requirements are not "directed to the risks of mifepristone," JA635—not even after the district court *sua sponte* suggested that might be a basis for upholding them. It is far too late for intervenors to do so now.

In any event, the notion that these requirements are not about managing mifepristone's risks is plainly wrong. These are not general,

broadly applicable provisions governing "the practice of medicine," JA609; they are specific restrictions narrowly targeted at "medical abortion" and the "[d]istribution of abortion-inducing drugs" like mifepristone. N.C. Gen. Stat. §§ 90-21.83A & 90-21.83B (section titles). The district court's contrary conclusion misunderstood the laws at issue.

For one thing, the court appears to have thought that "verify[ing] that [the] pregnancy exists" and "provid[ing] medically indicated diagnostic tests" are purposes "unconnected to safe use of the drug." JA635–636 (quotation marks omitted). That is incorrect. FDA recognizes that mifepristone is "not … appropriate" for "patients who are not pregnant," JA265, and the REMS requires certified prescribers to be able to "accurately assess the duration of the pregnancy," JA240. But FDA has concluded that prescribers can "confirm[] the patient's … pregnancy" without being "physically present with the patient." JA241. Similarly, the "diagnostic tests" required by North Carolina law are those that are necessary "to determine whether the woman has a heightened risk of complications" from mifepristone. N.C. Gen. Stat. § 90-21.83B(a)(3). Such testing is obviously linked to "safe use of" the drug, JA635, and is addressed by FDA's conclusion that "evaluation of patients for

contraindications to medical abortion" does not require an in-person examination, JA264; *see* JA240–241.

The court also appears to have thought that confirming the patient's "informed consent" to the use of mifepristone is a matter beyond the scope of the REMS. JA636; *see* JA639 (suggesting that "FDA's REMS choices" were not "focused on" ensuring "informed consent"). That, too, is wrong. As explained above, informed consent has always been a critical part of the REMS, as reflected in the requirements related to the Patient Agreement. *See* JA264 (FDA explaining that "many factors … contribute to patient safety, including … informed consent"). Contrary to what the district court thought, FDA *did* focus on informed consent—and in doing so, it expressly concluded that obtaining a patient's informed consent to the use of mifepristone does not require "physical proximity." JA241.

North Carolina's in-person examination and consultation requirements are thus directly at odds with FDA's judgment about how to ensure safe access to mifepristone and, therefore, with Congress's goals in delegating the REMS authorities to FDA. These requirements are aimed squarely at addressing health and safety risks of mifepristone

that FDA concluded could be appropriately managed without in-person contact between the patient and the federally certified prescriber.

Moreover, even if North Carolina's requirements were not (as they plainly are) targeted at managing the risks of mifepristone, a state cannot avoid preemption by restricting access to mifepristone under laws regulating "general patient health and safety" or "broad regulation[s] of the medical profession." JA633. On the contrary, "it is a black-letter principle of preemption law that generally applicable state laws may conflict with and frustrate the purposes of a federal scheme just as much as a targeted state law." *Saleh v. Titan Corp.*, 580 F.3d 1, 12 n.8 (D.C. Cir. 2009); *accord Geier*, 529 U.S. at 885–86, 881 (applying obstacle preemption even though airbag requirement was an application of state's general tort law); *United States v. California*, 921 F.3d 865, 880 (9th Cir. 2019) ("Obstacle preemption … attaches to any state law, regardless of whether it specifically targets the federal government."). If that were not the rule, a state could preemption-proof its laws by crafting them in general terms.

Targeted or not, North Carolina's requirements stand as obstacles to FDA's chosen means of increasing access to mifepristone, particularly

for underserved patients. As part of its robust REMS reviews, FDA has carefully considered data regarding the safe use of mifepristone by telemedicine (*e.g.*, JA298–314), and has sought, consistent with its duty under the REMS statute, to reduce burdens on patient access to mifepristone—particularly for "patients who have difficulty accessing health care," 21 U.S.C. § 355-1(f)(2)(C)(ii)—by facilitating telemedicine. A state cannot frustrate the agency's efforts by second-guessing FDA's judgment and mandating the very same in-person visits that FDA has rejected as unnecessary and overly burdensome.

C. The requirement to report all adverse events to the state is preempted.

Just as North Carolina requires physicians to report all mifepristone-related adverse events to FDA, regardless of severity, it requires that the same information be reported to the state. N.C. Gen. Stat. § 90-21.93(c). As explained above, FDA has rejected such mandatory reporting as unnecessary for safety and unduly burdensome in light of "15 years of adverse event reports" and "the well-characterized safety profile of [mifepristone], with known risks occurring rarely." JA249.

In light of FDA's conclusion, the district court correctly held that North Carolina's reporting-to-FDA requirement was preempted. But it

held that the reporting-to-the-state requirement was not preempted because it is a general "regulation of the practice of medicine." JA638. That is incorrect. The state has not imposed this extraordinarily burdensome reporting requirement with respect to all drugs. Instead, it has targeted mifepristone for a safety-related burden that FDA expressly considered and rejected.

III. Intervenors' argument that Dr. Bryant lacks a cause of action is forfeited and meritless.

For the first time on appeal, intervenors assert (at 34–36) that Dr. Bryant lacks a cause of action for her preemption claim. Intervenors forfeited this argument by failing to raise it in the district court. And even if it were preserved, their argument would lack merit.

This Court's decision in *Hicks v. Ferreyra*, 965 F.3d 302 (4th Cir. 2020), is controlling and leaves no doubt that intervenors' new argument is forfeited. In *Hicks*, the defendants raised on appeal a "late-breaking argument" that the plaintiff's claim "should have been dismissed at the outset because he lacks a cause of action." *Id.* at 309. But, like intervenors here, "[a]t no point during the lengthy proceedings in the district court [had they] argue[d] or even suggest[ed] that [plaintiff] lacked a cause of action." *Id.* This Court held that because the availability of a cause of

action is "not an issue that implicates a court's subject-matter jurisdiction," "standard forfeiture and waiver principles" applied. *Id.* at 310–11; *accord Steel Co. v. Citizens for a Better Env't*, 523 U.S. 83, 89 (1998) ("It is firmly established … that the absence of a valid (as opposed to arguable) cause of action does not implicate subject-matter jurisdiction.").

Under those principles, this Court will consider a new issue on appeal only if the proponent of the issue establishes "fundamental error," meaning an error "so serious and flagrant that it goes to the very integrity of the proceedings." *Hicks*, 965 F.3d at 310 (quotation marks omitted). "This rigorous standard is an even higher bar than the 'plain error' standard applied in criminal cases." *Id.* Intervenors do not and cannot claim that standard is met here. *See also Air Courier Conf. v. Am. Postal Workers Union, AFL-CIO*, 498 U.S. 517, 522–23 & n.3 (1991) (refusing to consider unpreserved argument that Congress did not "intend[] to allow a certain cause of action" because "[w]hether a cause of action exists is not a question of jurisdiction").

In any event, intervenors' new argument is meritless. As they acknowledge (at 35), Dr. Bryant has an equitable cause of action under

Ex parte Young, 209 U.S. 123 (1908), that allows her to "petition a federal court to enjoin State officials … from engaging in future conduct that would violate the Constitution." *Antrican v. Odom*, 290 F.3d 178, 184 (4th Cir. 2002). Intervenors claim this cause of action is precluded because the FDCA provides that "all such proceedings for the enforcement, or to restrain violations, of [the FDCA] shall be by and in the name of the United States." 21 U.S.C. § 337(a). But Dr. Bryant did not sue to enforce or restrain a violation of the FDCA; she sued to prevent state officials from enforcing state laws that violate the Supremacy Clause.

Section 337(a) does not apply to a suit like Dr. Bryant's. Part of the FDCA subchapter "Prohibited Acts and Penalties," section 337 follows provisions that authorize civil and criminal penalties for conduct that violates the FDCA, such as distributing adulterated or misbranded foods and drugs. *See generally* 21 U.S.C. § 331 *et seq*. When section 337(a) refers to "*such* proceedings" to enforce or restrain FDCA violations, it is referring to the kinds of enforcement proceedings authorized in that subchapter. *See Wikimedia Found. v. Nat'l Sec. Agency/Cent. Sec. Serv.*, 14 F.4th 276, 297 (4th Cir. 2021) (the word "such" refers to matters "previously indicated" (quotation marks omitted)). Section 337(a) might

be relevant if Dr. Bryant were seeking to hold North Carolina officials liable for distributing misbranded drugs. But an action to restrain state officials from enforcing preempted state laws is not a proceeding to enforce or restrain violations of the FDCA.

Intervenors' reliance on *Armstrong v. Exceptional Child Center, Inc.*, 575 U.S. 320 (2015), is similarly misplaced. The plaintiffs there claimed that state officials were violating the Medicaid Act by reimbursing certain providers at improperly low rates. The Court held that "[t]wo aspects of [the Act] establish[ed] Congress's intent to foreclose equitable relief" for such claims. *Id.* at 328 (quotation marks omitted). First, Congress had provided an administrative remedy for the plaintiffs' claims by authorizing the Secretary of Health and Human Services to withhold Medicaid funds from states that underpaid providers. *Id.* And second, the "sheer complexity associated with enforcing" such a broad, vague, and "judgment-laden" statute rendered it "judicially unadministrable" and indicated that Congress meant the administrative remedy to be exclusive. *Id.* at 328–29. Neither reason applies here: Congress has not provided any alternative remedy to prevent the

enforcement of state laws preempted by the FDCA, and no one disputes that such preemption claims are judicially administrable.

IV. The district court did not abuse its discretion by enjoining the state from enforcing the preempted requirements.

The district court enjoined defendants from enforcing certain enumerated statutes as well as "any other provisions of North Carolina law" that impose the requirements the court held were preempted. JA658. Intervenors take issue only with the "any other provisions" language, which they claim (at 37–38) makes the injunction "unclear" and forces them to "guess at which North Carolina laws" are preempted. The district court did not abuse its discretion.

"Once a constitutional violation is found, a federal court is required to tailor the scope of the remedy to fit the nature and extent of the constitutional violation." *Ostergren v. Cuccinelli*, 615 F.3d 263, 288–89 (4th Cir. 2010) (quotation marks omitted). Here, Dr. Bryant challenged certain categories of "restrictions imposed by North Carolina on the provision of mifepristone." JA70. And the district court held that North Carolina law is preempted insofar as it imposes particular restrictions or requirements; the court's preemption analysis was not limited to specific code sections. JA640–649, JA655–656.

The court properly tailored the injunction to reach only the specific requirements it had concluded were unconstitutional, regardless of where in North Carolina's codebooks those restrictions might be found. Courts routinely issue similar injunctions. *See, e.g.*, *De Leon v. Abbott*, 791 F.3d 619, 625 (5th Cir. 2015) (affirming injunction prohibiting enforcement of "any other laws or regulations prohibiting a person from marrying another person of the same sex" (quotation marks omitted)); *Latta v. Otter*, 771 F.3d 456, 476–77 (9th Cir. 2014) (directing district court to enjoin state from enforcing "any constitutional provision, statute, regulation or policy preventing otherwise qualified same-sex couples from marrying"); *Gen. Synod of United Church of Christ v. Resinger*, 12 F. Supp. 3d 790, 792 (W.D.N.C. 2014) (permanently enjoining North Carolina officials from enforcing "any other source of state law that operates to deny same-sex couples the right to marry"). Intervenors cite no case holding that an injunction framed in this way is an abuse of discretion.

Nor can intervenors plausibly claim confusion. The injunction spells out in plain English exactly what requirements North Carolina is barred from enforcing. It provides that state officials cannot (1) "prohibit

any healthcare provider other than a licensed physician from providing mifepristone," (2) "require that mifepristone be provided in person," (3) "require scheduling an in-person follow-up visit after providing mifepristone or efforts to ensure such a follow-up appointment," or (4) "require the reporting of non-fatal adverse events related to mifepristone to the FDA." JA658. Intervenors do not point to any ambiguity in this language, nor did they ask the district court to clarify it. And intervenors' claim (at 38) that this language "extend[s] to … statutes that no court has found to 'violate federal law'" is wrong—the district court held that *any* state law imposing these preempted requirements violates the Supremacy Clause.

By contrast, limiting the injunction to specific statutory sections would be a recipe for confusion and mischief. A prosecutor might claim that some other provision embodies the same preempted requirement. For example, references to "the physician" providing mifepristone are scattered throughout various provisions of North Carolina law, any of which might be cited as imposing the preempted physician-only requirement. Or the legislature might seek to evade the injunction by recodifying the same preempted restrictions in different code sections.

Indeed, it is hard to imagine why a party would object to this aspect of the injunction, other than to facilitate circumvention of the district court's ruling.

STATEMENT IN SUPPORT OF ORAL ARGUMENT

Dr. Bryant requests oral argument. Given the importance of the issues presented, Dr. Bryant submits that oral argument would assist the Court in its decisional process.

CONCLUSION

This Court should affirm with respect to the restrictions the district court held were preempted, reverse with respect to the restrictions the court held were not preempted, and remand for the court to permanently enjoin enforcement of the latter.

Respectfully submitted,

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CERTIFICATE OF COMPLIANCE

This brief complies with the type-volume limitation of Fed. R. App. P. 28.1(e)(2)(B) because it contains 15,189 words, excluding the parts of the brief exempt by Federal Rule of Appellate Procedure 32(f).

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/s/Eva A. Temkin
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