No. 21-348

In The
# Supreme Court of the United States

JOHNSON & JOHNSON, ET AL.,
PETITIONERS,

*v.*

MISSISSIPPI, EX REL. LYNN FITCH,
ATTORNEY GENERAL OF MISSISSIPPI.

*ON PETITION FOR WRIT OF CERTIORARI TO THE SUPREME COURT OF MISSISSIPPI*

## BRIEF FOR FORMER FDA OFFICIALS AS AMICI CURIAE SUPPORTING PETITIONERS

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## INTERESTS OF AMICI CURIAE[1]

Amici are former Food & Drug Administration (FDA) officials with a strong interest in promoting public health and safeguarding FDA's authority to ensure accurate, informative, and science-based product labeling. Amici appear in their personal capacities and not on behalf of their employers or any other entities or individuals.

Dr. Andrew C. von Eschenbach was FDA Commissioner from 2006 to 2009. He previously served as the Director of the National Cancer Institute at the National Institutes of Health, and spent three decades as a physician, surgeon, oncologist, and medical executive.

Dr. Stephen Ostroff served as FDA Deputy Commissioner for Foods and Veterinary Medicine, and twice led the agency as Acting Commissioner. He also previously served as FDA's Chief Scientist and as Deputy Director of the National Center for Infectious Diseases at the Centers for Disease Control and Prevention.

Dr. David Acheson served as the Associate Commissioner for Foods at FDA. He was also previously Chief Medical Officer at FDA's Center for Food Safety and Applied Nutrition, Chief Medical Officer at the Department of Agriculture Food Safety and Inspection Service, and Associate Professor at Tufts University,

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[1] No counsel for a party authored this brief in whole or in part, and no person other than Amici or their counsel made a monetary contribution to its preparation or submission. Petitioners and respondent granted blanket consent for the filing of amicus curiae briefs. The parties were timely notified of amici's intent to file this brief.

where he studied the molecular pathogenesis of foodborne pathogens.

Daniel Troy served as Chief Counsel for the FDA, where he led the legal office responsible for providing litigation, enforcement, and regulatory counseling across the entire agency. He is currently Chief Legal Officer and General Counsel of Valo Health.

Kalah Auchincloss served as Deputy Chief of Staff for two FDA Commissioners. She also previously served as Director of the Office of Unapproved Drugs and Labeling Compliance in FDA's Center for Drug Evaluation and Research (CDER), as a regulatory counsel at CDER, and as FDA's detailee to the Senate Committee on Health, Education, Labor, and Pensions.

Randall Lutter was FDA's Deputy Commissioner for Policy. He also previously served as senior science and regulatory advisor in FDA's Office of the Commissioner and as the agency's chief economist, as well as a senior economist at the federal Office of Management and Budget and the President's Council of Economic Advisers. He is currently a senior fellow at the Manhattan Institute.

Patrick Ronan was FDA's Chief of Staff from 2005 to 2007. He previously served as Assistant Commissioner of Legislation and Associate Commissioner of Legislation at FDA. He is now CEO of Validant.

Cynthia Schnedar served as Director of the Office of Compliance for FDA's CDER, where she led efforts to protect the American public from unsafe and ineffective drug products. Before joining FDA, she worked at the Department of Justice, where she specialized in compliance and enforcement issues.

## INTRODUCTION AND SUMMARY OF ARGUMENT

The FDA leverages extensive multidisciplinary expertise in regulating labels for foods, drugs, cosmetics, and medical devices. Congress granted the FDA this exclusive authority in recognition of the agency's unparalleled ability to evaluate the scientific basis for proposed warnings and clearly communicate relevant health risks to consumers across the country. Through decades of regulatory experience, data collection, and scientific research, FDA has established a suite of tools to make labeling decisions that are both thoroughly supported by scientific evidence and responsive to rapidly changing markets.

The Mississippi Supreme Court's decision threatens to upend this system. By stripping the FDA's labeling decisions of preemptive effect unless they first undergo notice-and-comment rulemaking, the decision leaves the agency with an impossible choice: sacrifice the flexibility it needs to oversee thousands of products in an ever-shifting market, or allow its scientifically sound warnings to be crowded out by conflicting state-imposed labels. As Petitioners ably demonstrate, Congress never intended such a result.

Amici wish to impress upon the Court the exceptional importance of this issue. FDA rarely acts through notice-and-comment rulemaking, instead relying on its expert components to evaluate a multitude of issues, including labeling changes, through less formal channels. Citizen petition responses, like

the one here, are among the non-rulemaking mechanisms FDA uses to make scientifically sound judgments in a dynamic environment. The agency lacks time and resources to run every such decision through notice-and-comment rulemaking. But, according to the Mississippi Supreme Court, that reality means FDA must share labeling authority with all 50 states, any one of which can require a label specifically rejected by FDA as scientifically unsound.

This Court should grant review to clarify the law of preemption and prevent the Mississippi Supreme Court's decision from disrupting FDA's vital functions.

## ARGUMENT

### REQUIRING FDA TO ENGAGE IN NOTICE-AND-COMMENT RULEMAKING TO PREEMPT STATE LABELING REQUIREMENTS WOULD UNDERMINE THE AGENCY'S MISSION AND PUBLIC HEALTH

FDA's regulation of product labels is a vital part of its mission to protect public health. To carry out that mission, the agency relies on a variety of flexible tools, including citizen petition responses. Those procedures are thorough and science-based. Allowing (non-expert) states to require their own conflicting labels unless FDA engages in notice-and-comment rulemaking would hobble the FDA's regulatory efforts and harm consumers.

## A. FDA Plays A Critical And Exclusive Role In Regulating Product Labels

### *1. Congress created FDA to use scientific expertise to protect public health*

Since its earliest days as the Bureau of Chemistry,[2] the FDA has been charged with leveraging scientific expertise to protect American consumers from harmful or mislabeled products. *See* Pure Food and Drug Act, § 4, Pub. L. No. 59-384, 34 Stat. 768, 769 (1906) ("[T]he examinations of specimens of foods and drugs shall be made in the Bureau of Chemistry of the Department of Agriculture, or under the direction and supervision of such Bureau, for the purpose of determining from such examinations whether such articles are adulterated or misbranded within the meaning of this Act."). Congress expanded that authority throughout the twentieth century, entrusting FDA to regulate, among other things, cosmetics and their ingredients in the Federal Food, Drug, and Cosmetic Act of 1938 (FDCA), 21 U.S.C. §§ 361 et seq., thus further "bolster[ing] consumer protection against harmful products." *Wyeth v. Levine*, 555 U.S. 555, 574 (2009).

Now housed within the Department of Health and Human Services, FDA is multiple expert agencies

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[2] In 1927, Congress shifted the Bureau of Chemistry's regulatory functions to the newly created Food, Drug, and Insecticide Administration, which adopted its current name three years later. *See* FDA, *Milestones in U.S. Food and Drug Law History* (May 3, 1999), https://web.archive.org/web/20090521181634/http://www.fda.gov/opacom/backgrounders/miles.html.

rolled into one. It employs thousands of leading scientists, medical professionals, and supporting staff across its Centers for Biologics Evaluation and Research, Devices and Radiological Health, Drug Evaluation and Research, Food Safety and Applied Nutrition, Tobacco Products, Veterinary Medicine, and other subdivisions. FDA, *FDA Organization*.[3] Those Centers and offices conduct and review cutting-edge research that supports FDA's regulatory decisions and anticipates its future needs.

Among the Centers' most critical roles is evaluating or recommending proposed changes in safety standards and labeling requirements for products across FDA's broad jurisdiction. In this way, FDA's subject matter experts carry out the agency's congressional mandate to "promote" and "protect the public health" by regulating the contents and marketing of all the products it regulates, including foods, drugs, devices, and cosmetics. 21 U.S.C. § 393(b).

### *2. Congress exclusively entrusted labeling regulation to FDA's scientific experts*

Labeling regulations are central to FDA's public health mission. In the FDCA, Congress broadly prohibited "[t]he adulteration or misbranding of any food, drug, device, tobacco product, or cosmetic," 21 U.S.C. § 331(b), and authorized FDA to regulate labels for each of those product categories, *see* 21 U.S.C. § 343 (misbranded food); § 352 (misbranded drugs and devices), § 362 (misbranded cosmetics); § 387c

[3] https://www.fda.gov/about-fda/fda-organization.

(misbranded tobacco products). *See also* §§ 371-374 (providing FDA general authority to promulgate rules, conduct hearings, initiate investigations, and inspect facilities to enforce the FDCA).

Congress intended FDA's labeling decisions to set nationwide, uniform standards. For example, the Food and Drug Administration Modernization Act of 1997, §412, Pub. L. No. 105-115, 111 Stat. 2296 (1997), expressly preempted "any requirement for labeling or packaging of a cosmetic that is different from or in addition to, or that is otherwise not identical with, a requirement specifically applicable to a particular cosmetic or class of cosmetics under this chapter." 21 U.S.C. § 379s(a); *see also* § 379r (express preemption for nonprescription drug rules). This approach is consistent with Congress's goal for uniform labeling standards in other contexts. *See* § 360k (express preemption for medical device rules); § 343-1 (express preemption for food labeling); § 387p(a)(2) (express preemption for tobacco rules); *cf. PLIVA, Inc. v. Mensing*, 564 U.S. 604, 620-21 (2011) (finding implied preemption of state-law claims that conflict with FDA labeling rules for prescription drugs).

Those preemption rules reflect Congress's judgment that labeling standards should remain uniform throughout the United States. As the Senate Committee on Labor and Human Resources explained, because "[a]n essential element of a nationwide marketplace is a national uniform system of regulation," Congress "intended that the FDA provide national leadership in assuring the safety, effectiveness, and proper labeling

and packaging for nonprescription drugs and cosmetics marketed throughout the country." S. Rep. No. 105-43, at 63-64 (1997) (Senate Report). To fulfill that mission, it was vital that "State and local officials enforce the same regulatory requirements for products as do our Federal officials." *Id*. at 64.

### *3. Congress envisioned a strictly limited role for states in labeling regulation*

Congress saw a risk of serious harm if states imposed labeling requirements that FDA did not. The Senate Report was emphatic that "[d]ifferent or additional requirements a[t] the State or local level can work against our national marketplace, confuse consumers, raise prices, undermine public confidence in our regulatory system and in products important to the public health, and result in divergent public health protection throughout the country." *Ibid.*

That is not to say Congress envisioned no role for the states. Under the federal statutory scheme, "all States may vigorously enforce requirements for nonprescription drugs and cosmetics that are *identical* to the Federal requirements." S. Rep. No. 105-43, at 64 (emphasis added). And while states are not generally free to make their own rules, Congress set out particular avenues for them to follow when "a local problem could justify a different or additional regulatory requirement for nonprescription drugs or cosmetics in a particular State." *Id*. at 65.

First, § 379s permits states and localities to apply for an exemption from preemption. But such

exemptions require that FDA, after notice and comment, agree that the proposed labeling rule "protects an important public interest that would otherwise be unprotected," and would not violate federal law or "unduly burden interstate commerce." 21 U.S.C. § 379s(b). *See also* § 379r(b) (establishing state exemption procedure for non-prescription drug rules); § 360k(b) (same for medical devices); § 343-1(b) (same for nutrition labeling). Second, just like any other interested party, "[a] State, locality, or person may continue to take advantage of their right to petition the FDA" through its citizen petition process to ask FDA to evaluate a new labeling requirement. S. Rep. No. 105-43, at 65.

Those procedures—which channel regulatory action though the expert agency Congress tasked with protecting consumers nationwide—are the appropriate ways for states like Mississippi to seek labeling requirements beyond what FDA has required.

## B. FDA's Labeling Decision-Making Process Balances Flexibility With Thorough Expert Review

### *1. FDA heavily relies on informal procedures to regulate product labels*

Complex and dynamic regulatory problems require agencies to remain flexible. While FDA sets some broadly applicable labeling standards by published rules, *see*, *e.g.*, 21 C.F.R. § 740.1(a) (2021) (requiring cosmetics to "bear a warning statement whenever necessary or appropriate to prevent a

health hazard"), the agency does not often engage in notice-and-comment rulemaking, and particularly not for specific labeling decisions about individual products. That choice is consistent with bedrock principles of administrative law, which call for agencies to adopt generally applicable rules that can then be adapted to novel circumstances through adjudication. "The APA does not require that all the specific applications of a rule evolve by further, more precise rules rather than by adjudication." *Shalala v. Guernsey Mem'l Hosp.*, 514 U.S. 87, 96 (1995). Indeed, "any rigid requirement to that effect would make the administrative process inflexible and incapable of dealing with many of the specialized problems which arise." *SEC v. Chenery Corp.*, 332 U.S. 194, 202 (1947).

To keep up with new research, rapid innovation, and an ever-shifting marketplace of products, FDA relies on a variety of flexible procedures to ensure accurate labeling and consumer safety over time. For prescription drugs, for example, the "[d]evelopment of final labeling" is "an iterative process between" drug makers and agency experts, with a series of communications regarding the "scientific, medical, and procedural issues that arise" in the course of FDA review. *See* Center for Drug Evaluation and Research, *CDER 21st Century Review Process: Desk Reference Guide*;[4] 21 C.F.R. § 314.102(a) (2021). Labeling decisions are not a single static event—industry participants have an ongoing responsibility to update

[4] https://www.fda.gov/media/78941/download.

labels in light of new information, and the FDA monitors products over time to ensure compliance with federal law.

Major safety concerns sometimes necessitate swift action. When the Center for Drug Evaluation and Research learns of a serious or life-threatening risk, it will quickly require manufacturers to include a "black box warning" on their labels. FDA, *A Guide to Drug Safety Terms at FDA* 2 (Nov. 2012).[5] These labeling changes are sometimes preceded by statements to the public about the agency's ongoing evaluation. *See*, *e.g.*, FDA Drug Safety Communication, *FDA requires warnings about increased risk of serious heart-related events, cancer, blood clots, and death for JAK inhibitors that treat certain chronic inflammatory conditions* (Sept. 1, 2021) (requiring updated warnings for certain arthritis medicines after issuing warning about increased risk of blood clots and death).[6] No less than other decisions, these emergency actions are the product of FDA's unique expertise. For example, recent guidance on breast implant labeling, which imposed a black box warning about implant-associated anaplastic large cell lymphoma, was developed with input from an expert advisory panel that heard testimony from dozens of cancer patients. *See* FDA, *FDA Issues Final Guidance for Certain Labeling Recommendations for*

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[5] https://www.fda.gov/media/74382/download.

[6] https://www.fda.gov/media/151936/download.

*Breast Implants* (Sept. 28, 2020);[7] Susan Kelly, *FDA finalizes black box warning for breast implants*, MedTech Dive (Sept. 29, 2020).[8]

In the cosmetics context, FDA might issue a targeted warning letter when a product's labeling causes it to be an unapproved new drug or misbranded. *See*, *e.g.*, FDA, *Warning Letter to Nature Essence Small Molecule Co., LTD* (Feb. 12, 2020).[9] Or it might recommend a labeling change through industry guidance addressing a specific category of ingredients. *See*, *e.g.*, FDA, *Guidance for Industry: Labeling for Cosmetics Containing Alpha Hydroxy Acids* (Jan. 10, 2005).[10] These kinds of decisions are typically made within FDA expert components. Flexibility to act quickly and respond to new information is vital to the agency's public health mission.

### *2. Citizen petition responses balance FDA's need for flexibility and expert review*

Although most labeling actions are appropriately taken through less formal procedures, the agency's

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[7] https://www.fda.gov/news-events/press-announcements/fda-issues-final-guidance-certain-labeling-recommendations-breast-implants.

[8] https://www.medtechdive.com/news/fda-finalizes-black-box-warning-for-breast-implants/586033/.

[9] https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/nature-essence-small-molecule-co-ltd-586327-02122020.

[10] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-labeling-cosmetics-containing-alpha-hydroxy-acids.

citizen petition process provides an important mechanism for the public to petition for labeling decisions that is short of notice-and-comment rulemaking. *See* 21 C.F.R. § 10.30 (2021). The citizen petition process allows states, businesses, and individuals to ask the FDA "to issue, amend, or revoke a regulation or order, or to take or refrain from taking any other form of administrative action." 21 C.F.R. § 10.25(a) (2021).

The procedure for citizen petitions is similar to that deployed in many other informal agency adjudications. Petitioners supply a detailed factual and legal statement, "including all relevant information and views on which the petitioner relies." 21 C.F.R. § 10.30(b) (2021). Any "interested person may submit comments" on a public docket, which becomes part of the petition's formal record. 21 C.F.R. § 10.30(d) (2021). And, after careful consideration and independent review, FDA issues a response, either approving or denying the petition, dismissing it as moot, or providing a "tentative" explanation "indicating why the agency has been unable to reach a decision," such as the "need for additional information." 21 C.F.R. § 10.30(e) (2021).

FDA's petition responses are deeply researched and scientifically grounded regulatory documents that bring to bear the agency's full multidisciplinary expertise. *See*, *e.g.*, *Serono Lab'ys, Inc. v. Shalala*, 158 F.3d 1313, 1320 (D.C. Cir. 1998) (holding that FDA's denial of a citizen petition "rests on the 'agency's evaluations of scientific data within its area of expertise,' and hence is entitled to a 'high level of deference' ")

(citation omitted). One study of FDA citizen petitions found that an overwhelming majority were decided on scientific rather than legal grounds. Brian K. Chen et al., *Petitioning the FDA to Improve Pharmaceutical, Device and Public Health Safety by Ordinary Citizens: A Descriptive Analysis*, 11 PLOS ONE, no. 5, 2016, at 1, 8.[11] Petition responses account for the studies and data presented by petitioners, those raised in public comments, and the agency's own independent review of relevant medical and scientific literature. 21 C.F.R. § 10.30)b)-(e) (2021). Responses also frequently rely on the agency's unique repository of data, collected continuously through years of industry surveillance, product surveys, facility inspections, and other regulatory efforts. *See*, *e.g.*, App'x 90 (relying on FDA's independent survey of relevant products).[12] And citizen petition responses place a petitioner's particular request in the broader context of the agency's overall mission to promote public health across subject matter areas.

### *3. FDA's rejection of talc warning labels well illustrates the utility of citizen petition review*

FDA's 2014 response to the cosmetic talc petitions at issue here is a good example of the agency's review process working as intended. As FDA explained, its decision was based on a "careful review and

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[11] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4865109/pdf/pone.0155259.pdf.

[12] The appendix before the Mississippi Supreme Court is cited as "App'x."

consideration of the information submitted in [the] Petitions, the comments received in response to the Petitions, and review of additional scientific information." App'x 88. It addressed each of the citizen petitions' claims in turn, laying out the agency's thinking on talc's association with asbestos, its alleged carcinogenic qualities, and the asserted causal relationship between genital talc exposure and ovarian cancer.

First, the FDA addressed its "[c]hemistry [f]indings," which analyzed the possibility that "talc containing asbestos fibers such as tremolite asbestos or chrysotile" had contaminated cosmetic products. App'x 89. The agency rejected reliance on two studies from the late 1960s and early 1970s because they were out-of-date, and because the petitions "did not present any original data on the chemical composition of talc currently being used in cosmetics." App'x 89. Instead, FDA noted that it had performed its own "exploratory survey of currently marketed cosmetic-grade raw material talc and finished cosmetic products containing talc," and "found no asbestos fibers or structures in any of the samples." App'x 90. Even so, the agency stated that it would "continue to monitor for new information and take appropriate actions to protect the public health." App'x 90.

Next, FDA laid out its "[t]oxicology [f]indings" on talc without the presence of asbestos. Again, the agency explained that the studies cited by the petitions had serious flaws. App'x 90. FDA noted that a panel of experts at an FDA workshop with the International

Society of Regulatory Toxicology and Pharmacology had concluded that the primary study on which the petitions relied to establish talc's carcinogenicity "has no relevance to human risk." App'x 90-91. And FDA's own comprehensive review of toxicity research from 1990 to 2008 revealed that there was insufficient support for the proposed warning label. App'x 91.

Finally, the petition response analyzed epidemiological and etiological findings on the link between genital application of talc and ovarian cancer. App'x 91-92. Once again taking a deep dive into the research, FDA explained that flawed study design, low confidence intervals, and the lack of "[a] cogent biological mechanism by which talc might lead to ovarian cancer" compelled the conclusion that "the evidence is insufficient for FDA to require as definitive a warning as [petitioners were] seeking." App'x 91-92. That conclusion was further confirmed by an "expanded literature search" evaluating studies published between 2008 and 2014. App'x 93.

The talc response demonstrates the strengths of the citizen petition review process. FDA used that mechanism to issue an authoritative nationwide labeling decision. It did so after conducting expert analysis, sharing relevant data, and conducting a thorough review of relevant scientific research.

#### *4. FDA's talc petition response preempts Mississippi's failure-to-warn claim*

The FDA's reasoned decision not to impose an ovarian cancer warning on cosmetic talc products

preempts contrary state claims, like Mississippi's, that would require such a warning.

Contrary to the Mississippi Supreme Court's view, the FDA's petition response is a legally authoritative regulatory decision with preemptive effect. This Court has made clear that preemptive force does not require "a specific expression of agency intent to pre-empt, made after notice-and-comment rulemaking." *Geier v. Am. Honda Motor Co., Inc*, 529 U.S. 861, 885 (2000). Rather, it is sufficient that the petition response was an "agency action carrying the force of law" and taken pursuant to "congressionally delegated authority." *Merck Sharp & Dohme Corp. v. Albrecht*, 139 S. Ct. 1668, 1679 (2019).

The Mississippi Attorney General's theory of liability is thus expressly preempted because it is "not identical" with—and indeed, is entirely antithetical to—the FDA's reasoned judgment in the talc petition response. 21 U.S.C. § 379s(a). And it is impliedly preempted because it necessarily conflicts with the FDA's "'authoritative' message" that no warning was required. *Sprietsma v. Mercury Marine*, 537 U.S. 51, 67 (2002). No matter what category of preemption applies, federal law does not permit Mississippi to require inclusion of a warning on talc products that FDA specifically rejected as unsound.

The answer would be the same if the FDA's decision against an ovarian cancer warning on talc cosmetics had come not through the citizen petition process but rather in a less formal action by an FDA

component. While that question is not presented in this case, those labeling decisions are also "agency action[s] carrying the force of law" and taken pursuant to "congressionally delegated authority." *Merck*, 139 S. Ct. at 1679. That means they also would preempt purported state-law requirements to impose FDA-rejected warnings.

### C. Allowing States To Regulate Labels Absent Federal Rulemaking Would Have Grave Consequences

As Petitioners persuasively argue, the Mississippi Supreme Court's decision to "effectively limit[] agencies to notice-and-comment rulemaking if they want their decisions enforced nationwide" will hamstring regulatory efforts in a variety of contexts. Pet. 28. The damage to FDA's public health mission is grave. Such a rule hobbles the agency's flexibility, forcing it to choose between rigid rulemaking that is often logistically impossible or having its expert judgments lost in a sea of contradictory state-required labels. This Court's intervention is urgently needed to avoid such a result.

#### *1. Notice-and-comment rulemaking is not dynamic enough for labeling decisions*

FDA's jurisdiction covers an increasingly complex range of ingredients, additives, cosmetics, medicines, and devices. Responsible for products that account for roughly a fifth of all U.S. consumer spending, FDA regulates more than $2.8 trillion in goods manufactured or handled in some 270,000 facilities. FDA,

*FDA at a Glance* (Nov. 2020).[13] Exponential growth in science and technology has demanded an increasingly complex regulatory response, and FDA now relies on a variety of tools, including artificial intelligence and predictive analytics to keep pace. FDA, *Fiscal Year 2022 Justification of Estimates for Appropriations Committees* 6 (2021).[14]

Requiring FDA to deploy notice-and-comment rulemaking for every action it intends to have preemptive effect would seriously undermine the agency's effectiveness. To start, FDA lacks sufficient resources to funnel every regulatory action through notice-and-comment rulemaking. The agency's budget is already spread thin across its ever-widening array of responsibilities, which currently include responses to the national opioid crisis and the COVID-19 pandemic. *Id.* at 1. It is simply not possible for the agency to convert every product-specific labeling decision it now makes into notice-and-comment rules. Even with unlimited money and staffing, there often would be insufficient time to respond to changes in the market or new information quickly enough to adequately protect public health.

While FDA does not publish official numbers cataloguing its regulatory decisions, amici know from their experience at the agency that FDA makes thousands of product-specific decisions every year, including decisions to update or retain product labels.

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[13] https://www.fda.gov/media/143704/download.

[14] https://www.fda.gov/media/149616/download.

Even with a rapid notice-and-comment process, putting even a fraction of those decisions through rulemaking would overwhelm the agency's available resources. And that would force FDA to divert resources from other critical functions like reviewing potentially lifesaving medical product innovations and monitoring the marketplace for products that pose a public health threat. Requiring notice-and-comment to give targeted labeling decisions preemptive effect is completely unworkable.

### *2. States lack the expertise necessary to make scientifically sound labeling decisions*

The alternative of abandoning preemption and allowing states to adopt their own labeling requirements would be equally harmful. States lack the critical expertise and experience necessary to render scientifically sound judgements on the safety and efficacy of FDA-regulated products. As explained above, FDA's labeling decisions, including the petition denial here, are the product of extensive medical and scientific expertise, institutional knowledge, and long-term data collection. State attorneys general are no substitute for FDA's wealth of experience on these matters.

Science and technology are advancing rapidly in all areas of FDA's broad jurisdiction. Keeping pace requires a dedicated and extremely skilled staff of scientists and experts. For example, in 2009 FDA approved the use of milk from a goat with intentional

genomic alterations designed to express a human biologic to treat patients with a rare disease called antithrombin deficiency. Andrew Pollack, *F.D.A. Approves Drug From Gene-Altered Goats*, N.Y. TIMES (FEB. 6, 2009).[15] Today, product manufacturers can not only quickly and efficiently alter animal genomes, but also use regenerative medicine to grow animal cells in a lab for human food or other purposes. FDA, *Food Made with Cultured Animal Cells* (Oct. 2020).[16] And in 2020 alone, FDA received more than 230 applications to begin clinical trials for cellular and gene therapies. Ned Pagliarulo, *FDA seeking more consistency from cell, gene therapy developers, top official says*, BioPharmaDive (May 19, 2021).[17] These therapies are at the cutting edge of science, using living cells and manipulated genes to cure the rarest and hardest-to-treat diseases. Andrew Pollack, *Setting the Body's 'Serial Killers' Loose on Cancer*, N.Y. TIMES (Aug. 1, 2016);[18] Jerome Groopman, *A Stunning Breakthrough in the Fight Against a Devastating Blood Disease*, THE NEW YORKER (April 18, 2018).[19] FDA is also increasingly overseeing the use of artificial intelligence to

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[15] https://www.nytimes.com/2009/02/07/business/07goatdrug.html.

[16] https://www.fda.gov/food/food-ingredients-packaging/food-made-cultured-animal-cells.

[17] https://www.biopharmadive.com/news/fda-marks-gene-therapy-consistency/600445/.

[18] https://www.nytimes.com/2016/08/02/health/cancer-cell-therapy-immune-system.html.

[19] https://www.newyorker.com/science/elements/a-stunning-cure-for-one-of-the-worlds-most-devastating-blood-diseases.

diagnose and monitor diseases. FDA, *Artificial Intelligence and Machine Learning (AI/ML)-Enabled Medical Devices* (Sept. 2021).[20] These are just a few of the areas in which FDA will face dramatic new regulatory challenges in the coming decades. Leaving those decisions to the political whims of 50-plus state and local regulators instead of the expert agency Congress created to monitor emerging technologies would badly undermine public health.

FDA is also the only regulatory body that can monitor the entire life cycle of a product and understand the context of a particular market. For example, when FDA considers whether to add a warning to a drug, it considers how that particular warning compares to others, what level of evidence was required in comparable circumstances, which warnings were previously rejected, whether certain warnings may deter use of a drug that is overall safer or more effective than other available treatments, and whether diverting demand to another drug could cause a shortage. Likewise, the Center for Food Safety and Applied Nutrition evaluates warning labels for chemicals, metals, additives, and ingredients in the context of every other risk in our food and cosmetic products, applying particular standards of evidence and reliability, and considering the frequency and duration of exposure.

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[20] https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-aiml-enabled-medical-devices.

### *3. Allowing all 50 states to require their own product warning labels would harm consumers*

Permitting states to require warnings that FDA has not adopted—or, as here, specifically rejected—inflicts a special kind of harm. It is well-documented that overwarning poses a significant barrier to effective regulation. As this Court has observed in a variety of contexts, "*[m]eaningful* disclosure does not mean *more* disclosure," and instead requires consideration of "the need to avoid informational overload," *Ford Motor Credit Co. v. Milhollin*, 444 U.S. 555, 568 (1980) (citation, quotation marks, and alterations omitted). Congress, too, has long recognized that overwarning "invit[es] indifference to cautionary statements on packages of substances presenting a real hazard." H.R. Rep. No. 86-1861 (1960) *as reprinted in* 1960 U.S.C.C.A.N. 2833, 2837. And countless tort scholars have concluded that "[o]verwarning effectively amounts to the manufacturer 'crying wolf,'" making consumers "less likely * * * to heed" legitimate warnings. Robert G. Knaier, *An Informed-Choice Duty to Instruct?*, 88 CORNELL L. REV. 814, 853 (2003).[21]

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[21] *See also* Jeff Todd, *A Rhetoric of Warning Defects*, 54 S. TEX. L. REV. 343, 374, 377 (2012) (overwarning "can reduce the efficacy of warnings"); James A. Henderson, Jr. & Aaron D. Twerski, *The Products Liability Restatement in the Courts: An Initial Assessment*, 27 WM. MITCHELL L. REV. 7, 16, 19 (2000) (overwarning "diminish[es] the significance of warnings and tend to clutter warning labels with useless information"); W. Kip Viscusi, *Individual Rationality, Hazard Warnings, & the Foundations of Tort Law*, 48 RUTGERS L. REV. 625, 665-66 (1996)

Consistent with that view, FDA has long recognized that decisions *not* to require labeling are a critical part of its regulatory mission. That is because overwarning causes consumers to overlook important, scientifically-founded safety information. *See*, *e.g.*, *Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices*, 73 Fed. Reg. 49,603, 49,605-06 (Aug. 22, 2008) (unfounded statements in FDA labeling may crowd out "more important warnings," causing them to be "overshadow[ed]"). And warnings that are not grounded in science discourage beneficial use of products. *See ibid.* ("[O]verwarning * * * may deter appropriate use of medical products.") Congress tried to avoid such problems by expressly preempting different or additional state labeling requirements.

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When FDA labeling decisions are stripped of preemptive effect, the agency becomes just one of more than 50 regulators nationwide, fighting to be heard over a cacophony of conflicting information. Such an

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("[e]xcessive warnings are not innocuous" because they "further dilute the warnings for the real hazards."); James A. Henderson, Jr. & Aaron D. Twerski, *Doctrinal Collapse in Products Liability: The Empty Shell of Failure to Warn*, 65 N.Y.U. L. REV. 265, 297 n.135 (1990) ("Overwarning causes users and consumers to discount or ignore warnings that should be heeded" and leads to "wastefully high avoidance costs."); Michael D. Green, *When Toxic Worlds Collide: Regulatory & Common Law Prescriptions for Risk Communication*," 13 HARV. ENVTL. L. REV. 209, 223-24 (1989) (overwarning "tend[s] to reduce the attention that is paid to all warnings, thereby reducing their overall effectiveness").

outcome seriously harms the American public. Without clear guidance, consumers cannot know which of many products labels or warnings to trust. And Congress's "essential" goal of establishing a "national uniform system of regulation" to ensure "the safety, effectiveness, and proper labeling and packaging for nonprescription drugs and cosmetics marketed throughout the country" will be dismantled. S. REP. No. 105-43, at 63.

## CONCLUSION

The petition for a writ of certiorari should be granted.

Respectfully submitted,

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