# 24-916(L)

## 24-1121(CON), 24-2360 (CON)

IN THE

# United States Court of Appeals

**FOR THE SECOND CIRCUIT**

TIFFANY RUTLEDGE, INDIVIDUALLY AND AS MOTHER, GENERAL GUARDIAN OF, ET AL., KRISTOPHER WHITE, BRIDGET MCCONNELL, ALEXANDER HOLLAND, CHRISTINE HOLLAND,

*Plaintiffs-Appellants,*

—against—

WALGREEN CO., COSTCO WHOLESALE CORPORATION, CVS HEALTH CORPORATION, CVS PHARMACY, INC., SAFEWAY, INC., WALMART INC., A DELAWARE CORPORATION, RITE AID CORPORATION,

*(Caption continued on inside cover)*

ON APPEAL FROM THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF NEW YORK

**BRIEF FOR *AMICUS CURIAE* CHAMBER OF COMMERCE OF THE UNITED STATES OF AMERICA IN SUPPORT OF DEFENDANTS-APPELLEES**

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*Defendants-Appellees*

## CORPORATE DISCLOSURE STATEMENT

The Chamber of Commerce of the United States of America states that it is a non-profit, tax-exempt organization incorporated in the District of Columbia. The Chamber has no parent corporation, and no publicly held company has 10% or greater ownership in the Chamber.

# TABLE OF CONTENTS

# TABLE OF AUTHORITIES

**Page(s)**

## Cases



## Statutes and Regulations

**Other Authorities**

## INTEREST OF *AMICUS CURIAE*[1]

The Chamber of Commerce of the United States of America (Chamber) is the world's largest business federation. It represents approximately 300,000 direct members and indirectly represents the interests of more than three million companies and professional organizations of every size, in every industry sector, and from every region of the country. An important function of the Chamber is to represent the interests of its members in matters before Congress, the Executive Branch, and the state and federal courts. To that end, the Chamber regularly files *amicus curiae* briefs in cases, like this one, that raise issues of concern to the nation's business community.

The Chamber's members have a strong interest in this case because it implicates the proper scope of federal preemption standards. The district court's preemption decision exposes businesses to potential liability for failing to add unknowable warnings to their products, rather than use the warnings crafted and adopted by the Food and Drug

[1] No counsel for any party authored this brief in whole or in part, and no entity or person, aside from *amicus curiae*, its members, or its counsel, made any monetary contribution intended to fund the preparation or submission of this brief. The parties have consented to the filing of this brief.

Administration (FDA). Such a regime would invite a fifty-state patchwork of labeling requirements for over-the-counter (OTC) drugs that would burden drug manufacturers and retailers and harm consumer health and safety. The Chamber therefore files this brief to urge the Court to reject that outcome.

## INTRODUCTION AND SUMMARY

Federal law grants the FDA the responsibility to decide which medicines may be sold to consumers and what must appear on those medicines' labels. More than 40 years ago, the FDA determined that the labels of certain OTC drugs should contain a "single national warning" relating to use during pregnancy and nursing "to ensure that OTC drugs are used safely and for their intended purpose[]" and that "consumers receive clear, unambiguous, and consistent information on the labeling." *Pregnant or Nursing Women; Delegations of Authority and Organization; Amendment of Labeling Requirements for Over-the-Counter Human Drugs*, 47 Fed. Reg. 54,750, 54,756 (Dec. 3, 1982). The FDA has never strayed from that commitment.

The district court's decision, holding that the FDA's determination does not preempt Plaintiffs' claims, is both wrong and dangerous. It is

wrong because the federal regulatory scheme for pregnancy-related warnings preempts state lawsuits that, like Plaintiffs', seek to impose liability on OTC drug manufacturers and retailers for failing to unilaterally add a warning different from the one that FDA has mandated. The district court's decision is dangerous because allowing cases like this to proceed will disrupt the federal regulatory scheme, unduly burden manufacturers, and lead to widespread confusion that threatens consumer health and safety.

## ARGUMENT

### I. PLAINTIFFS' STATE-LAW CLAIMS ARE PREEMPTED

Covered OTC drugs, including acetaminophen, are required to include the general pregnancy-related warning devised by the FDA unless and until the agency approves a more specific pregnancy-related warning through a New Drug Application (NDA) or monograph. And even when a specific warning is approved, it supplants—rather than supplements—the general warning. The district court failed to appreciate these fundamental facts. As a result, it failed to recognize that, under this regime, states have no ability to override the FDA's pregnancy-related warnings and supplement OTC labels with their own state-specific warnings. The district court was right to fear a "massive

shift," MDL.Dkt.589 at 23, but such a shift would come about only if this jurisdiction becomes the first to permit state-law liability where the FDA has already mandated both a warning and a process for agency approval to deviate from that warning.

1. State-law claims are "impliedly pre-empted where it is impossible for a private party to comply with both state and federal requirements." *Mut. Pharm. Co. v. Bartlett*, 570 U.S. 472, 480 (2013). In the specific context of failure-to-warn claims against makers of FDA-regulated medicines, the "question for 'impossibility' is whether the private party could independently do under federal law what state law requires of it." *PLIVA, Inc. v. Mensing*, 564 U.S. 604, 620 (2011). Put another way, a state-law failure-to-warn claim may proceed only if the drugmaker has the ability under federal law to make the label change "unilaterally" without the FDA's approval. *Wyeth v. Levine*, 555 U.S. 555, 573 (2009).

The Supreme Court's preemption cases make clear that preemption is context-dependent and based on the applicable FDA regulatory scheme.

On one side, in *Mensing*, the Court decided that federal law preempts state-law claims against manufacturers of generic drugs. 564 U.S. at 608–09. A generic drug manufacturer "is responsible for ensuring that its warning label is the same as the brand name's" and has no ability to unilaterally alter the drug's label. *Id.* at 613. It was thus "not lawful under federal law" for the generic drug manufacturers "to do what state law required of them." *Id.* at 618.

On the other side, in *Wyeth*, the Court held that federal law did not preempt failure-to-warn claims against a manufacturer of a branded drug. Branded drug manufacturers hold an NDA under which the FDA approves the drug for marketing. Under that scheme, brand and generic manufacturers "have different federal drug labeling duties." *Mensing*, 564 U.S. at 613. According to the Supreme Court, there was no preemption for branded drug manufacturers because (1) changes-being-effected (CBE) regulations grant NDA holders unilateral authority to add warnings to their labels, and (2) the manufacturer had not presented "clear evidence" that "FDA would not have approved a change to [the manufacturer's] label." *Wyeth*, 555 U.S. at 571–73. Thus, the

manufacturers may have been able to do what the state-law claims would have forced them to do.

The lesson of *Mensing* and *Wyeth* is that preemption claims related to FDA labeling require careful attention to the applicable statutes and regulations. Indeed, in *Merck Sharp & Dohme Corp. v. Albrecht*, the Supreme Court explained that the holding in *Wyeth* "flow[ed] from [the Court's] precedents on impossibility preemption *and the statutory and regulatory scheme . . . reviewed*." 587 U.S. 299, 314 (2019) (emphasis added); *see also id.* ("[I]n *Wyeth*, we confronted that question [of impossibility preemption] *in the context of a particular set of circumstances*.") (emphasis added). Context matters, and there is no one-size-fits-all approach to impossibility preemption any time the FDA is involved.

2. By failing to properly contextualize the acetaminophen products and take account of their particular FDA regulatory scheme, the district court misread Supreme Court case law. The court asked the right question: "could the manufacturer have unilaterally changed the label" on its acetaminophen products without FDA approval? MDL.Dkt.145 at 17. But, in answering "yes," the district court failed to appreciate and

account for the regulatory features that prevent manufacturers from unilaterally changing pregnancy-related warnings on OTC drugs.

Most notably, the FDA has promulgated a regulation requiring a specific pregnancy warning and dictating a process for FDA approval of any different or more specific pregnancy-related warnings. That regulation requires covered OTC drugs to carry a "general warning" advising, with the first four words in bold: "**If pregnant or breast-feeding**, ask a health professional before use." 21 C.F.R. § 201.63(a). The label must use this "exact language," as a product that deviates from the prescribed warning is misbranded under federal law. 21 C.F.R. § 330.1(c)(2). The only circumstances in which a "specific warning" may be "used in place of" this general warning are when "a specific warning relating to use during pregnancy or while nursing has been established for a particular drug product in [an NDA] or for a product covered by an OTC drug final monograph."[2] 21 C.F.R. § 201.63(b). As the FDA explained in promulgating the rule, "adjustments regarding the

[2] As discussed further below, a monograph is a set of FDA regulations describing the conditions under which a category of drugs, such as acetaminophen products, may be marketed without a prescription. *See* 21 C.F.R. § 330.1; *see also* MDL.Dkt.145 at 8–10.

appropriate pregnancy-nursing warnings"—in other words, warnings different from the general warning—are "handled in the final OTC drug monographs and in the individual NDA[s]." 47 Fed. Reg. at 54,755. OTC drug monographs apply to an entire class of OTC drugs, as opposed to a single branded drug.

This regulatory scheme fundamentally changes the preemption analysis in this case as compared to *Wyeth*. As Justice Breyer explained, *Wyeth* was not a case where FDA had promulgated a "specific regulation[] describing . . . labeling requirements" that "serve as a ceiling as well as a floor." 555 U.S. at 582 (Breyer, J., concurring). Here, by contrast, that is exactly what the FDA has done. Covered OTC drugs must convey the general pregnancy-related warning *unless* the agency has approved a more specific warning in an NDA or monograph. And if the FDA has approved a more specific warning, then that specific warning appears "in place of" the general one. This regime therefore leaves no room for state tort law to mandate warnings not approved by the FDA that supplement—rather than supplant—the general warning.

Moreover, for OTC monograph products like those at issue here, there is no analogue to the CBE regulation from *Wyeth*. That regulation

allows manufacturers of branded drugs approved under an NDA to *unilaterally* "make [a] labeling change" under certain circumstances. *Wyeth*, 555 U.S. at 568. Manufacturers likely could not use the CBE regulation to change pregnancy-related warnings in any event, because the pregnancy warning regulation applies to OTC products regulated by NDAs and monographs alike. But for products governed by monographs, nothing like the CBE process even exists. Instead, the monograph approval process applies to "*classes* of OTC drug products and their active ingredients," and establishes conditions under which *classes* of drugs—not individual drugs—may be marketed. MDL.Dkt.145 at 8 (emphasis added). So, if a drug company wants a label that "deviate[s] in any respect from a monograph that has become final," it must either file an NDA for FDA approval, 21 C.F.R. § 330.11, or request that the FDA revise the monograph for the relevant class of drugs, *see* 21 U.S.C. § 355h(b)(5). That is materially different from *Wyeth*: there is no explicit regulatory pathway for individual drug companies to change or supplement pregnancy-related warnings on a label on their own and without FDA approval.

That inability to unilaterally change a drug label is irreconcilable with a central feature of the district court's analysis. The district court believed that finding preemption here would "enact . . . a sweeping change to FDA policy" that manufacturers bear responsibility for their labels. MDL.Dkt.589 at 23. The opposite is true. Allowing state-law liability here—where the FDA has already mandated both a warning and a process for agency approval to deviate from that warning—would amount to a "sweeping change." From the promulgation of the pregnancy warning regulation in 1982 until now, OTC drugs have borne *only* FDA-approved pregnancy warnings. The district court did not cite any contrary example. *Cf.* MDL.Dkt.145 at 16 ("Neither the Supreme Court nor any circuit court has addressed preemption in the context of drugs regulated under the monograph system."). That is telling, and this case should not be the first to open the door to empowering all fifty states to add their own warnings and thereby undercut the FDA's careful regulation.

## II. PERMITTING LIABILITY FOR A FAILURE TO ADD DIFFERENT STATE PREGNANCY WARNINGS WOULD UNDERCUT THE FEDERAL SCHEME AND HARM CONSUMERS.

The district court's decision risks burdening manufacturers and harming consumers in significant ways. Permitting liability for failing to supplement the FDA's pregnancy-related warnings would simultaneously encourage labels with too much information and labels that are not uniform from state to state—all to the detriment of the federal regime.

The first problem is too much information. The FDA has to strike a difficult balance when it regulates OTC labels: a label needs to communicate a host of risks and benefits essential to the safe and effective use of the medicine, but it must do so in a way that consumers understand. To strike that balance, the FDA permits "only information for which there is a scientific basis to be included in the FDA-approved labeling" and "guards against the exaggeration of risk, or the inclusion of speculative or hypothetical risks." *In re Zofran (Ondansetron) Prods. Liab. Litig.*, 57 F.4th 327, 330 (1st Cir. 2023) (citations omitted).

Getting the balance right is critical to consumer safety and health. Consumers have difficulty processing—and may even disregard—labels

that are replete with warnings, especially speculative or theoretical ones. "The resulting information overload would make label warnings worthless to consumers." *Robinson v. McNeil Consumer Healthcare*, 615 F.3d 861, 869 (7th Cir. 2010); *see also Over-The-Counter Human Drugs; Labeling Requirements*, 64 Fed. Reg. 13,254, 13,255 (Mar. 17, 1999) (applying "research on reading behavior and document simplification" to redesign OTC labels). When the "meaningful risk information" "lose[s] its significance" on a cluttered label, or is missed by a consumer, there are obvious and "negative effect[s] on patient safety and public health." *Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products*, 71 Fed. Reg. 3,922, 3,935 (Jan. 24, 2006) (citation omitted). At the same time, "[e]xaggeration of risk could discourage appropriate use of a beneficial drug." *Id.* The FDA therefore knows that it must "prevent overwarning, which may deter appropriate use of medical products, or overshadow more important warnings." *See also Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices*, 73 Fed. Reg. 49,603, 49,605–06 (Aug. 22, 2008).

These guiding principles support a finding of preemption here. The FDA concluded that consumer health and safety is best protected by cautioning pregnant or nursing acetaminophen users to "ask a health professional before use," rather than by crowding the label with lists of potential risks and benefits. Recognizing that "warnings must be used judiciously so that they do not lose their effectiveness," 47 Fed. Reg. at 54,753, the FDA long ago concluded that "a single national pregnancy-nursing warning . . . is necessary to ensure that OTC drugs are used safely and for their intended purposes," *id.* at 54,756.

The second problem stemming from the district court's decision is non-uniformity: just as labels should not have too much information, the FDA also recognizes that OTC labels should be consistent across the country. As the FDA put it, "[d]iffering [s]tate requirements could conflict with the Federal warning, cause confusion to consumers, and otherwise weaken the Federal warning." *Id.* A regime in which it is left to state juries to decide how companies should warn pregnant and nursing women about the risks of OTC drugs would disrupt the FDA's effort to "ensure that consumers receive clear, unambiguous, and consistent information on the labeling of OTC drugs concerning use by

pregnant or nursing women." *Id.* Yet that is precisely the regime that the district court's ruling embraces. Instead of prompting a proliferation of confusing warnings on commonplace products like Tylenol®, a finding of preemption "ensure[s] that OTC drugs are used safely and for their intended purposes." *Id.*

These information-overload and non-uniformity concerns are only heightened for pregnant consumers of OTC drugs. Even the authors of one of Plaintiffs' cited papers recognize that, "[d]uring pregnancy, the use of [acetaminophen] is important for the treatment of high fever and severe pain." Ann Z. Bauer et al., *Paracetamol Use During Pregnancy—A Call For Precautionary Action*, 17 Nature Revs. Endocrinology 757, 758 (2021). Fever during pregnancy can pose severe risks to the fetus, including potential neurological problems. *See id.* ("Fever is a well-accepted risk factor for multiple disorders."). And "[s]evere and persistent pain that is not effectively treated during pregnancy can result in depression, anxiety, and high blood pressure in the mother." *FDA Drug Safety Communication*.[3] If unfounded or unjustified warnings on

[3] FDA, *supra* note 3.

acetaminophen deter consumers from using the drug to treat fever and pain, those consumers would be exposed to these well-established risks.

The same pregnant consumers would also suffer trickle-down effects from asking companies to comply with a fifty-state patchwork of warning requirements. As one court noted in the medical-device context, for example, "[r]equiring manufacturers to comply with fifty states' warning requirements . . . on top of existing federal . . . requirements, might introduce sufficient uncertainty and cost that manufacturers would delay or abandon at least some number of lifesaving innovations." *Caplinger v. Medtronic, Inc.*, 784 F.3d 1335, 1346 (10th Cir. 2015) (Gorsuch, J.). Retailers who market their own versions of common OTC products might simply choose not to offer certain products. Not to mention the broader negative effects like "increased costs and risks of doing business in an area," "disincentives for innovations which promote consumer welfare," and "deterrence of economic development and job creation initiatives" The Perryman Group, *Economic Benefits of Tort Reform* at 4 (2021).[4] The appropriate application of preemption would avoid all of this.

[4] https://tinyurl.com/3a3suved.

## CONCLUSION

The Court should reject the district court's attempt to impose liability on manufacturers and retailers of OTC drugs who fail to supplement the pregnancy-related warnings required and approved by the FDA. There is simply no place for state law to mandate additions to the FDA's clear and unambiguous warning, and doing so would risk drastic consequences for manufacturers, retailers, and pregnant and nursing consumers.

November 14, 2024

Respectfully submitted,

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## CERTIFICATE OF COMPLIANCE

This document complies with the word limit of Local Rule 32.1(a)(4)(A) because, excluding the parts of the document exempted by Fed. R. App. P. 32(f), this document contains 2,882 words.

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## CERTIFICATE OF SERVICE

I hereby certify that, on November 14, 2024, an electronic copy of the foregoing Brief for *Amicus Curiae* The Chamber of Commerce of the United States of America in Support of Defendants-Appellees was filed with the Clerk of Court using the ECF system and thereby served upon all counsel appearing in this case.

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