No. 15-449

IN THE
Supreme Court of the United States

JOHNSON & JOHNSON AND MCNEIL-PPC, INC.

Petitioners,

v.

LISA RECKIS AND RICHARD RECKIS,

Respondents.

On Petition for a Writ of Certiorari
to the Supreme Judicial Court of Massachusetts

BRIEF OF THE BIOTECHNOLOGY INDUSTRY ORGANIZATION, THE CONSUMER HEALTHCARE PRODUCTS ASSOCIATION, AND THE PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA AS AMICI CURIAE SUPPORTING PETITIONERS

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INTERESTS OF AMICI CURIAE[1]

The Biotechnology Industry Organization (BIO) is the world's largest biotechnology trade association, representing approximately 1,000 members worldwide. BIO members research and develop healthcare, agricultural, environmental, and industrial biotechnology products. BIO promotes biomedical research and development by advocating for public policies that support the interests of its members that focus on human health.

The Consumer Healthcare Products Association (CHPA) is a nonprofit association that represents the makers of over-the-counter (OTC) medicines and nutritional supplements. CHPA members provide millions of Americans with safe, effective, and affordable therapies to treat many common ailments. CHPA is committed to promoting the vital role of OTC medicines and nutritional supplements in America's healthcare system through science, education, and advocacy.

The Pharmaceutical Research and Manufacturers of America (PhRMA) is a voluntary, nonprofit association representing the country's

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[1] Pursuant to this Court's Rule 37.6, *amici* affirm that no counsel for a party authored this brief in whole or in part, and that no person other than *amici*, their members, or their counsel made any monetary contributions intended to fund the preparation or submission of this brief. Counsel of record for all parties received timely notice of the intent to file this brief, and consent letters have been submitted to the Clerk.

leading research-based pharmaceutical and biotechnology companies. PhRMA members produce innovative medicines, treatments, and vaccines that save and improve the lives of countless individuals every day. PhRMA advocates in support of public policies that encourage the discovery of life-saving and life-enhancing new medicines.

This case presents a question of critical importance for BIO, CHPA, and PhRMA members: whether the manufacturer of a medicine can be held liable under state tort law for failing to add a warning that the Food and Drug Administration (FDA) has directly rejected. BIO, CHPA, and PhRMA members share a vital interest in having clear warning standards and in preventing conflicts between state law obligations and federal law. BIO, CHPA, and PhRMA support Petitioners' position that Respondents' failure-to-warn claim is preempted.

STATEMENT

The state court's decision in this case presents a square challenge to the federal Food and Drug Administration's exercise of its regulatory authority. The Respondents recovered a massive verdict by arguing that the Petitioners were required by state law to make a labeling change that FDA specifically considered and rejected after making other warning modifications that FDA deemed appropriate. The verdict thus second-guesses a scientific judgment that FDA made in the exercise of its congressionally-delegated authority.

In *Wyeth v. Levine*, 555 U.S. 555 (2009), this Court explained that a state-law failure-to-warn claim against the manufacturer of an FDA-approved medicine is preempted where there is "clear evidence" that FDA would not have approved the plaintiff's proposed "adequate" labeling. The manufacturer in that case, Wyeth, argued that the plaintiff's state failure-to-warn claim was preempted because Wyeth could not have changed its labeling in the way plaintiff alleged without violating its federal labeling duties. *Id.* at 568. This Court rejected Wyeth's argument, finding in that case that Wyeth could have revised its labeling under the narrow "changes being effected" (CBE) regulation, which allows pharmaceutical manufacturers to make certain changes to their labeling without prior FDA approval in response to "newly acquired information." *See* 21 C.F.R. § 314.70(c)(6)(iii)-(7). The Court noted that FDA can reject changes made through the CBE process but that "absent clear evidence that the FDA would not have approved a change," the Court would not conclude it was impossible for Wyeth to comply with both federal and state requirements. *Wyeth*, 555 U.S. at 571.

Here, the court failed to find "clear evidence" and refused to apply preemption where the record demonstrated not only that FDA would have rejected the change Respondents requested, but that FDA actually *did* reject that precise change. Respondents, Lisa and Richard Reckis, brought a failure-to-warn claim against Petitioners, Johnson & Johnson and McNeil-PPC, Inc. They alleged that the labeling on Petitioners' OTC ibuprofen product, Children's

Motrin®, failed to provide an adequate warning of the danger of toxic epidermal necrolysis (TEN), which their daughter contracted after taking Children's Motrin® in 2003. They claimed that the labeling should have included explicit warnings about TEN, Stevens-Johnson Syndrome (SJS, a similar disease), and the possibility that specific symptoms could be a "pathway" to a "life-threatening disease." Pet. App. 16a, n.23.

The undisputed regulatory record demonstrates that FDA rejected the precise language that Respondents claim Petitioners should have had on their labeling. In 2005, FDA conducted a comprehensive review of the risks and benefits of the class of drugs that includes ibuprofen, non-steroidal anti-inflammatory drugs (NSAIDs). During this review, FDA received a citizen petition requesting that FDA add warnings about SJS and TEN to all ibuprofen labeling, and specifically requesting a warning on OTC labeling that early symptoms could progress to "potentially life-threatening diseases, including Erythema Multiforme, Stevens Johnson Syndrome and Toxic Epidermal Necrolysis." Pet. App. 142a.

FDA granted the petition's proposal in part and denied it in part. It directed that labeling intended for medical professionals for prescription-strength ibuprofen include the warning that NSAIDs "can cause serious skin adverse events such as exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN)." Pet. App. 158a. It also added a requirement that

prescription ibuprofen come with a Medication Guide listing "life-threatening skin reactions" as one serious side effect. *Id.* at 160a. In contrast, for non-prescription OTC medicines, FDA concluded that the symptoms associated with these conditions, rather than the technical names for the conditions, should be included on the patient-directed OTC labeling. FDA explained its regulatory rationale, concluding that it was not "useful to include the specific terms *SJS*, *TEN* . . . *Stevens-Johnson syndrome*, and *toxic epidermal necrolysis* in the OTC label because most consumers are unfamiliar with these terms." *Id.* at 162a. Rather, FDA explained that a description of symptoms more appropriately "communicates warning information in a manner that consumers can quickly and easily identify and understand." *Id.*

Petitioners argued below that FDA's explicit rejection of the language sought in the 2005 citizen petition constituted "clear evidence" under *Wyeth v. Levine* that FDA would have rejected the same language in 2003. The trial court disagreed and allowed the lawsuit to proceed. Respondents obtained one of the largest verdicts in Massachusetts history, premised on the absence of the very information that FDA had determined should not be in the OTC labeling. Petitioners appealed to the Massachusetts Supreme Judicial Court (SJC), which affirmed the judgment against Petitioners. The SJC acknowledged that FDA's "explicit rejection" of the proposal to name SJS and TEN constituted "clear evidence" FDA would have rejected the same proposal if raised again. Pet. App. 20a. But the SJC held that FDA's explicit rejection of the term "life-

threatening diseases" was not specific enough to support preemption. *Id.* at 23a-24a.

SUMMARY OF THE ARGUMENT

The SJC's decision disregards the extensive expert oversight that FDA brings to bear in balancing the potential benefits of medicines with their potential adverse effects to create medically-warranted labeling appropriate for the audience and class of medicine. The state court's decision is a direct attack on FDA's exercise of its authority to regulate medicines to protect the public health and exemplifies the substantial confusion surrounding the "clear evidence" standard.

FDA undertakes rigorous review to evaluate and regulate the safety of prescription and OTC medicines. The approval process for new medicines is exacting. Among many other aspects, it involves meticulous review of multi-stage animal testing and human clinical trials. The safety and efficacy information derived from that extensive testing is communicated through labeling designed to provide audience-appropriate, medically accurate information for users of the medicines. After approval, FDA continues to evaluate the safety of medicines, including by monitoring new data and reports of adverse events associated with medicines after they enter the market. Throughout this process, FDA undertakes extensive and ongoing evaluation of labeling, including medicine-specific and sometimes class-wide analysis for prescription medicines and detailed rulemaking processes for OTC products. FDA's general and medicine-specific

labeling requirements embody the agency's expert judgment on how best to convey important safety and use information to health care providers and consumers.

In *Wyeth v. Levine*, the Court found that the FDA gave only "passing attention" to the risk at issue. In this case, in contrast, FDA carefully analyzed the appropriate way to warn about the relevant risks of ibuprofen, including the precise risk at issue here. Respondents should not be permitted to pursue a state-law claim when there is no reasonable dispute that FDA would have rejected the labeling formulation upon which Respondents hinged their claims.

If *Wyeth v. Levine*'s "clear evidence" standard is not satisfied here, then it is difficult to envision any situation in which it would apply. The SJC's rationale for not finding "clear evidence" sufficient to support preemption – the theoretical possibility that, if asked the right way by the right person, FDA might have allowed language it otherwise rejected – cannot withstand even cursory scrutiny. There is no dispute that FDA independently exercised its authority to review ibuprofen labeling to ensure it was appropriate in light of current scientific data, conducted additional review in response to a 2005 proposal to add precisely the warning pressed before the jury below, and, after that extensive, careful, detailed review, directly rejected that proposal. That rejection embodies FDA's regulatory judgments about how to describe this established risk to various audiences. The SJC's decision fundamentally

undermines FDA's expert authority to determine how best to communicate safety information to medical professionals and consumers. Not only does the decision add to the substantial confusion over the meaning of "clear evidence," but if taken at face value it would result in "an approach to pre-emption that renders conflict pre-emption all but meaningless." *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2579 (2011). The Court should grant the petition for certiorari.

ARGUMENT

I. The SJC's opinion disregards the extensive review and analysis FDA conducts to establish and monitor appropriate labeling.

Congress has tasked FDA with advancing the public health by ensuring the availability of safe and effective medicines. *See* 21 U.S.C. § 393(b). FDA carries out that statutory responsibility through an extensive regulatory structure designed to monitor and evaluate the safety and efficacy of all of the medicines it oversees, from pre-approval testing throughout the time they remain on the market. FDA's oversight of ibuprofen provides a model example of the agency exercising its statutory authority to make informed judgments on how best to communicate safety information about the medicines it regulates. This lawsuit represents a frontal assault on that authority.

A. The comprehensive FDA regulatory regime ensures that expert medical and regulatory judgment is brought to bear on labeling decisions.

Labeling is the primary risk communication tool for medicines that FDA regulates. Labeling must convey a wealth of information necessary for safe and effective use, including information on ingredients, dosages, usage, contraindications, adverse reactions, warnings, precautions, interactions, use in specific populations, and abuse and dependence. And it must provide all this information in a way that diverse users can effectively understand. If labeling is too lengthy, many users will not read it or will not be able to find the information they need. If labeling contains too many warnings, users may miss the ones most relevant to them or choose to discontinue use of a medicine that would benefit them.[2]

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[2] Congress, FDA, and courts have long recognized the dangers of overwarning. *See, e.g.*, *Robinson v. McNeil Consumer Healthcare*, 615 F.3d 861, 869 (7th Cir. 2010) ("The resulting information overload [from describing every remote risk] would make label warnings worthless to consumers."); *Hood v. Ryobi Am. Corp.*, 181 F.3d 608, 611 (4th Cir. 1999) ("[T]he proliferation of label detail threatens to undermine the effectiveness of warnings altogether . . . Well-meaning attempts to warn of every possible accident lead over time to voluminous yet impenetrable labels-too prolix to read and too technical to understand."); H.R. Rep. No. 86-1861 (1960), *reprinted in* 1960 U.S.C.C.A.N. 2833, 2837 (noting overwarning leads consumers "more and more to disregard label warnings, thus inviting (...continued)

In the prescription context, the health care professionals who read the labeling need to be able to quickly identify information on patient-specific concerns and risks from complex, detailed warnings. FDA's current prescription labeling rule was developed to address concerns that the ever-growing length and complexity of prescription labeling made it difficult for health care providers to use labeling effectively. Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922, 3922-23 (Jan. 24, 2006). FDA identified a number of factors that contributed to this problem, including the constantly growing body of available information and concern about including "virtually all known adverse event information, regardless of its importance or its plausible relationship to the drug." Requirements on Content and Format of Labeling for Human Prescription Drugs and Biologics; Requirements for Prescription Drug Product Labels, 65 Fed. Reg. 81,082, 81,083 (Dec. 22, 2000). The current rule

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indifference to cautionary statements on packages of substances presenting a real hazard of substantial injury or illness"); 73 Fed. Reg. 49,603, 49,605-606 (Aug. 22, 2008) (stating that "overwarning" in labeling "may deter appropriate use of medical products" and "overshadow more important warnings") 73 Fed. Reg. 2,848, 2,851 (Jan. 16, 2008) (explaining excessive warnings in labeling "could discourage appropriate use of a beneficial drug" and "decrease the usefulness and accessibility of important information by diluting or obscuring it"); *id.* ("Overwarning has the effect of not warning at all. The reader stops paying attention to excess warnings." (quotation marks omitted)).

seeks to streamline and standardize information to enable health care providers to effectively advise their patients about proper use and potential risks.

Similar considerations apply to an even greater degree in the OTC context. OTC medicines present the additional concern that patient-directed information must be readable and understandable by widely diverse users, with elderly and low-literacy patients often presenting particular challenges. FDA works with manufacturers, advisory committees, and the public at large to weigh these challenges and carefully evaluate effective labeling practices. FDA then applies its expertise to design appropriate labeling to ensure labeling effectively conveys essential information to all users.

FDA supervision of medicine labeling begins with the approval process. New medicines must pass multi-stage safety and effectiveness testing before a manufacturer can submit a New Drug Application (NDA). The NDA process also involves intense review, including evaluation of consumer label comprehension, consumer behavior, clinical trial results, and other scientific data. *See* Ctr. for Drug Evaluation & Research, MAPP 6020.5, Good Review Practice: OND Review Management of INDs and NDAs for Nonprescription Drug Products (2007). FDA may require additional studies, including label

comprehension studies,[3] before approving a medicine.

FDA scrutinizes labeling throughout the life of a medicine. Manufacturers have to provide proposed labeling, which FDA must approve before a medicine is marketed. *See* 21 U.S.C. § 355(b); 21 C.F.R. § 314.105. FDA regulations provide detailed labeling requirements, dictating required categories, precise information each category should include, and, in many cases, exact formatting standards. *See* 21 C.F.R. §§ 201.56-57, 201.66, 201.80. Consistency and uniformity in regulation and labeling are particularly critical. *See* S. Rep. No. 105-43, at 63 (1997) ("An essential element of a nationwide marketplace is a national uniform system of regulation. It is 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 . . . .").

FDA uses a standardized format for OTC labeling, the "Drug Facts" label, which was designed to make information uniform, readable, and understandable by the average consumer. *See* 21

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[3] *See* FDA, Guidance for Industry, Label Comprehension Studies for Nonprescription Drug Products (2010). Label comprehension studies serve to "assess whether literate and low literate individuals can understand a drug product label." *Id.* at 2. FDA can also require label comprehension studies after a medicine enters the market to respond to circumstances such as new indications or proposed labeling changes. *Id*. at 2-3.

C.F.R. § 201.66; FDA, OTC Drug Facts Label, www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143551.htm. In addition, OTC labeling often reflects standards developed through the OTC monograph process. OTC monographs are regulations that establish standards for permissible ingredients, uses, doses, formulations, labeling, and testing for therapeutic categories of medicines, which are separated based on their active ingredients. OTC monographs are developed through OTC Drug Review, a three-phase public rulemaking process. *See* 21 C.F.R. § 330. In phases one and two, expert advisory review panels and FDA hold public meetings and evaluate data submitted by industry, healthcare professionals, and consumers to evaluate the safety and efficacy of class ingredients and existing labeling. The results of these reviews are published for public comment. In phase three, FDA considers comments and new data received before publishing a final monograph.[4]

Once a final monograph is published, OTC medicines in that category can enter the market without undergoing an individual NDA so long as they comply with the precise monograph requirements. *See* 21 C.F.R. §§ 330.1, 330.10. OTC monographs reflect careful review and ensure consistent labeling across products, which aids

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[4] *See* FDA, Over-the-Counter (OTC) Drug Monograph Process, http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ucm317137.htm.

consumers in selecting and properly using appropriate medicines.

Once a medicine is approved and enters the market, FDA tracks adverse event reports and other research conducted on the medicine to ensure the medicine continues to remain safe and effective for its labeled uses.[5] *See* 21 C.F.R. § 314.80. FDA must be notified of, and generally must approve, all labeling changes before they become publicly available.[6] *See* 21 C.F.R. § 314.70(b)(2)(v). FDA suggests and rejects labeling changes based in part on its monitoring of adverse event reports.

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[5] Manufacturers must report "serious and unexpected" adverse events to FDA within 15 days of receipt of that information and are required to regularly report all adverse events to FDA for the life of the medicine. *See* 21 C.F.R. § 314.80. Manufacturers face severe consequences if they fail to meet these requirements. *See, e.g.*, 21 U.S.C. §§ 332-34. FDA also receives adverse event reports through a voluntary event reporting system, MedWatch. FDA compiles all the reports it receives in a database, the Adverse Event Reporting System (AERS), which it uses to monitor potential issues with medicines throughout their lifecycle on the market.

[6] Manufacturers can make some minor changes without prior approval. *See* 21 C.F.R. § 314.70(d)(ix)-(x). They can also, in some circumstances, add or strengthen a warning, precaution, contraindication, or adverse reaction without pre-approval to reflect "newly acquired information." They still must submit changes to FDA before distributing the new labeling, and FDA can reject those changes and require the manufacturer to stop distributing products that include the change. *See id.* § 314.70(c)(6)(iii)-(7).

FDA engages in such extensive regulation of labeling because all medicines have unavoidable risks, and providing medically-appropriate labeling to ensure the safe and effective use of medicines requires careful weighing of a host of considerations. FDA is uniquely positioned to do this balancing and decide what labeling best serves to protect all consumers. Decisions that contravene FDA's expert judgments can benefit individual plaintiffs, but they may do so at the expense of the broader population's health and safety.[7]

B. FDA carefully evaluated the safety of OTC ibuprofen and determined what labeling best balanced the risks for consumers.

In accordance with these regulations, FDA has closely scrutinized the risks and benefits of OTC ibuprofen. FDA has monitored the safety of ibuprofen since it entered the U.S. prescription market in 1974 and the OTC market in 1984. *See, e.g.*, Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for Over-the-Counter Human Use, 67 Fed. Reg. 54,139 (Aug. 21, 2002); FDA, Rulemaking History for OTC Internal Analgesic Drug Products, http://www.fda.gov/Drugs/

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[7] *Cf. Riegel v. Medtronic, Inc.*, 552 U.S. 312, 325 (2008) (noting that in the medical device context, a jury does not conduct the cost-benefit analysis "applied by the experts at the FDA" but rather "sees only the cost of a more dangerous design, and is not concerned with its benefits; the patients who reaped those benefits are not represented in court.").

DevelopmentApprovalProcess/DevelopmentResources/Over-the-CounterOTCDrugs/StatusofOTCRulemakings/ucm070484.htm.

Indeed, FDA has conducted additional, particularized review of OTC ibuprofen in relation to the risks at issue in this case. In 2005, FDA undertook a comprehensive review of the risk and benefit profile of all NSAIDs, including ibuprofen. Pet. App. 148a. FDA reviewed the regulatory histories and new drug application databases of the various NSAIDs and a number of materials from a February 2005 joint meeting of FDA's Arthritis and Drug Safety and Risk Management Advisory Committees, including FDA and sponsor background documents, material and data submitted by other stakeholders, presentations made at the joint meeting, and the specific votes and recommendations made by the joint Committee. *See* FDA, COX-2 Selective (includes Bextra, Celebrex, and Vioxx) and Non-Selective Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) (2005), http://www.fda.gov/Drugs/DrugSafety/ PostmarketDrugSafetyInformationforPatientsandProviders/ucm429364.htm. FDA's review also included an evaluation of clinical trials and adverse event reports of SJS and TEN in association with the use of ibuprofen products. Pet. App. 149a-152a.

FDA's report on this review made clear it considered and responded to SJS/TEN risks. *See* Pet. App. 71a-110a. FDA further detailed its review and analysis of the association between ibuprofen and SJS and TEN in its formal response to the 2005

citizen petition. *See* Pet. App. 146a-164a. In that response, FDA explained its decision to add SJS and TEN and "life-threatening skin reactions" to prescription labeling as well as its decision to omit those terms from OTC labeling. *Id.* at 158a-163a. FDA explained that "effective OTC labeling communicates warning information in a manner that consumers can quickly and easily identify and understand" and thus that "a description of symptoms" is a more effective way to communicate risks on OTC labeling than the terms the petition proposed. *Id.* at 162a.

FDA's view on effective OTC communication of SJS/TEN risks has not changed. In 2013, FDA explained that there is a link between acetaminophen and serious skin reactions, including SJS and TEN. FDA concluded OTC acetaminophen products should be labeled with the same type of symptom warnings FDA added to the OTC ibuprofen labeling template. FDA again explained that this warning helps consumers "recognize and react quickly to the initial symptoms of these rare but serious side effects." FDA, Consumer Health Information, FDA Warns of Rare Acetaminophen Risk (2013), http://www.fda.gov/downloads/ForConsumers/ConsumerUpdates/UCM363067.pdf.

II. The record provides "clear evidence" that FDA would reject a proposal to add "life-threatening diseases" to OTC ibuprofen labeling to warn of the risks of SJS and TEN.

Under established conflict preemption principles, state-law claims are preempted where "it is impossible for a private party to comply with both state and federal requirements." *Mensing*, 131 S. Ct. at 2577 (internal quotation marks omitted). Conflict preemption applies to Respondents' failure-to-warn claim because Respondents seek to hold Petitioners liable under state law for failing to make changes to OTC ibuprofen labeling that FDA would not have allowed Petitioners to make.

A. The *Wyeth* "clear evidence" standard.

This Court articulated the "clear evidence" standard in *Wyeth v. Levine*, 555 U.S. 555 (2009). The manufacturer in that case, Wyeth, argued that a state-law failure-to-warn claim based on its labeling of an injectable antihistamine, Phenergan, was preempted by federal law. The plaintiff claimed Phenergan's labeling was defective because it did not instruct clinicians to use the IV-drip method to administer Phenergan instead of the higher risk IV-push method. *Id.* at 559-60.

This Court concluded Wyeth could have used the CBE process to strengthen its warning. *Id.* at 568-69. The Court noted that FDA "retains authority to reject labeling changes made pursuant to the CBE

regulation" but held that plaintiff's claim would not be preempted "absent clear evidence that the FDA would not have approved a change to Phenergan's label." *Id.* at 571. The Court determined that Wyeth had not offered this "clear evidence," noting the lower courts' findings that neither FDA nor Wyeth "gave more than passing attention" to this issue and that FDA did not make an affirmative decision to reject the change in question. *Id.* at 572. The Court concluded that the record did not show FDA prohibited or intended to prohibit the "kind of warning" the plaintiff sought and that "the mere fact that the FDA approved Phenergan's label does not establish that it would have prohibited such a change." *Id.* at 572-73.

Courts have expressed uncertainty about how to apply the "clear evidence" standard. *See, e.g.*, *Mason v. SmithKline Beecham Corp.*, 596 F.3d 387, 391 (7th Cir. 2010) ("The Supreme Court . . . did not clarify what constitutes 'clear evidence.' Therefore, the only thing we know for sure is that the evidence presented in *Levine* did not meet this exacting standard."). This uncertainty has led to a confusing landscape where the meaning of "clear evidence" varies widely from court to court. *Compare, e.g.*, *Mason*, 596 F.3d at 396 (finding the record did not show "clear evidence" FDA would have rejected an enhanced suicidality warning for an SSRI), *with Dobbs v. Wyeth Pharm.*, 797 F. Supp. 2d 1264, 1277-80 (W.D. Okla. 2011) (finding "clear evidence" FDA would have rejected an enhanced suicidality warning for an SSRI and distinguishing SSRI cases with different outcomes). Indeed, in this case, the SJC

considered the same evidence the Seventh Circuit considered in *Robinson v. McNeil Consumer Healthcare*, 615 F.3d 861 (7th Cir. 2010) and drew the opposite conclusion about whether it constituted "clear evidence" under *Wyeth*. *See Robinson*, 615 F.3d at 873.

B. There was "clear evidence" in this case that FDA would not have approved the changes Respondents demand.

The SJC analyzed whether there was clear evidence that FDA would have rejected a proposal to mention SJS and TEN by name or warn that redness, rash, or blisters could be a "pathway" to a "life-threatening disease." Pet. App. 20a-21a. The citizen petition proposed adding SJS, TEN, and "life-threatening diseases" to OTC warning labeling. The SJC found that FDA's "explicit rejection" of the petition's proposal to mention SJS and TEN by name constituted clear evidence that FDA would have rejected this same proposal if raised again. *Id.* at 20a. But the SJC found that FDA's response made it "anybody's guess" as to whether FDA would have rejected a proposal to add a warning that symptoms could lead to "life-threatening diseases" if that term were offered on its own. *Id.* at 23a.

This situation requires no guessing about what FDA would have done, because the record amply establishes what FDA actually did. FDA conducted a comprehensive review of the risks of ibuprofen, paying careful attention to SJS and TEN. FDA considered a proposal to add SJS, TEN, and

"life-threatening diseases" to prescription and OTC labeling. FDA included SJS, TEN, and "life-threatening skin reactions" on prescription labeling, while deciding not to add those terms to OTC labeling, stating consumers would be better protected by a description of symptoms. FDA thus rejected the precise warning Respondents now demand.

If the SJC's interpretation of "clear evidence" is correct, *Wyeth* "renders conflict pre-emption all but meaningless," an approach this Court rejected in *Mensing*. *See* 131 S. Ct. at 2579. A plaintiff could always avoid preemption by suggesting that, had the manufacturer offered language that was ever so slightly different from the rejected language, or pushed harder for that language, the result might have been different. But as the United States recognized in its brief in *Wyeth*: "The agency could not reasonably be expected to *expressly* reject every possible variant of approved labeling as part of its decisional process. Indeed, it would underestimate the post hoc imagination of lawyers to think such an exhaustion of potential variants by the manufacturer or the agency is even possible." Brief for the United States as Amicus Curiae Supporting Petitioner at 25, *Wyeth v. Levine*, 555 U.S. 555 (2009) (No. 06-1249).

Conflict preemption cannot require that FDA expressly reject every word or variant that a shrewd advocate might later conceive. Decisions like the SJC's, together with the substantial uncertainty around the meaning of "clear evidence," leave manufacturers in an impossible position, with no

way to anticipate how to meet their obligations under state law and no way to interpret how to follow FDA direction. Under the SJC's view of "clear evidence," to avoid liability, the manufacturer would have been obligated to decline to implement FDA's final agency decision that came at the end of the exhaustive regulatory process, and instead plead for reconsideration. The law should not require regulated parties to reject the conclusions of federal regulators to protect themselves under state tort law. Indeed, that is the essence of conflict preemption.

In this case, FDA duly carried out its regulatory function, evaluating extensive data, consulting advisory experts, and applying its judgment to determine what labeling best communicates warnings to consumers in a way that actually helps to protect them. As part of this extensive review, FDA rejected the precise warning Respondents demand. If this situation does not satisfy the "clear evidence" standard for application of conflict preemption, then as a practical matter that standard will never be satisfied.

CONCLUSION

For these reasons, as well as the reasons set forth in the petition for a writ of certiorari, the Court should grant the petition.

Respectfully submitted,

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