No. _____

In the
Supreme Court of the United States

JOSEPH C. COLACICCO, INDIVIDUALLY
AND AS EXECUTOR OF THE ESTATE OF
LOIS ANN COLACICCO, DECEASED,
AND
BETH ANN MCNELLIS, ON BEHALF OF THE ESTATE OF
THEODORE DEANGELIS, DECEASED,
AND IN HER OWN RIGHT,
Petitioners,

v.

APOTEX, INC.; APOTEX CORP.,
A SUBSIDIARY OF APOTEX, INC.;
SMITHKLINE BEECHAM D/B/A GLAXOSMITHKLINE;
AND PFIZER, INC.
Respondents.

On Petition for a Writ of Certiorari
to the United States Court of Appeals
for the Third Circuit

PETITION FOR A WRIT OF CERTIORARI

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QUESTION PRESENTED

Whether prior approval of a pharmaceutical label by the Food and Drug Administration ("FDA") preempts state-law failure-to-warn claims where FDA made no authoritative determination requiring or prohibiting a warning prior to the injury, but subsequently allowed warnings that parallel the state-law duty.

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PETITION FOR A WRIT OF CERTIORARI

Petitioners Joseph Colacicco and Beth Ann McNellis respectfully petition for a writ of certiorari to review the judgment of the court of appeals in this case.

INTRODUCTION

This case raises an issue of recurring importance in which the decision of the Third Circuit directly conflicts with that of the Vermont Supreme Court. This Court now has before it that conflicting case, *Wyeth v. Levine*. In this case, a divided panel erroneously held that the patients' claims for failure to provide adequate warnings were preempted by the Food and Drug Administration's approval of the label for the antidepressant drugs Paxil and Zoloft. Because the Court's resolution of *Wyeth v. Levine* is likely to provide needed guidance to the courts below on how to assess a preemption defense in this context, the petition should be held for the Court's disposition of *Wyeth v. Levine*, and then the case vacated and remanded for further proceedings in the Third Circuit.

Even independent of the Court's resolution of *Levine*, the petition here should be granted because this case raises important questions that are not likely to be resolved in *Levine*. In this case, unlike in *Levine*, FDA had given its attention to the issue involved in the patient's injury – the likelihood that antidepressants would paradoxically increase suicidal thoughts and behaviors, especially early in treatment -- before the patients were injured. Nonetheless, as of 2003 – when Lois Colacicco and Theodore DeAngelis committed suicide while taking Paxil and Zoloft, respectively – FDA had made no authoritative federal determination with respect to this risk, neither requiring nor

prohibiting a warning. The Third Circuit failed to recognize that this Court's opinion in *Sprietsma v. Mercury Marine*, 537 U.S. 51 (2002) controls the analysis and outcome of this case.

Furthermore, FDA was in the process of reanalyzing the risk of increased suicidality in 2003 when Paxil and Zoloft were prescribed to Ms. Colacicco and Mr. DeAngelis, and began to request warnings of this risk the following year. While FDA was engaged in its review, two antidepressant manufacturers exercised their power pursuant to 21 C.F.R. § 201.80(e) and § 314.70(c)(6)(iii)(A), adding warnings of increased suicidality without prior FDA approval. Both warnings were based on reanalyses of data that predated the prescriptions to Ms. Colacicco and Mr. DeAngelis. FDA did not claim that the added warnings were "false or misleading" and that the drugs were thus misbranded. Instead, FDA allowed the added warnings to stand for seven months in one instance and a full year in the other, until FDA began to require additional class-wide warnings for all antidepressants. Significantly, the second was an added warning issued by GlaxoSmithKline ("GSK"), the maker of Paxil, that Paxil posed more than six-fold increase in risk to adult patients – like Lois Colacicco – two and a half years after her death.

The Third Circuit below erroneously accepted the drug companies' arguments that both claims should be preempted by the 2003 labels, which FDA's subsequent regulatory actions and GSK's specific admission had demonstrated to be inadequate. The basis for the supposed conflict between state and federal law was that, if the drug companies had added a warning of

increased suicidality before FDA began to request it, the added warnings would have misbranded their drugs. That holding defies common sense and raises issues of surpassing importance that will not be addressed in *Wyeth v. Levine:* whether misbranding is a valid basis for conflict preemption when drug companies add warnings of the increased risk at issue without prior FDA approval and FDA does not pursue misbranding, and when FDA itself subsequently requests warnings of the increased risk -- but only after the patients' death or injury. Because federal regulation of prescription drugs expressly anticipates that risks will be reevaluated and warnings added as the drugs perform in the market, these issues arise with respect to many prescription drugs. Thus, this petition presents questions that are significant in their own right, and the Court should grant the petition irrespective of its handling of *Wyeth v. Levine*.

OPINIONS BELOW

The judgments of the court of appeals, in which *Colacicco v. Apotex, Inc., et al.* and *McNellis v. Pfizer, Inc.* were consolidated, are reprinted at App. 1-6. Its opinion is reported at 521 F.3d 253 (3d Cir. 2008) and is reprinted at App. 7-78.

The opinion and order of the district court in *Colacicco,* granting the defendants' motion to dismiss based on federal preemption, is reported at 432 F. Supp. 2d 514 (E.D. Pa. 2006) and reprinted at App. 79-162.

The original, unpublished opinion of the district court in *McNellis* denying summary judgment based on preemption is available at 2005 WL 3752269 and is

reprinted at App. 163-93. The subsequent order denying Pfizer's motion to vacate and certifying the summary judgment order for interlocutory appeal is reprinted at App. 194-96; and the court's unpublished opinion supporting that order is available at 2006 WL 2819046 and reprinted at App. 197-228.

JURISDICTION

The court of appeals entered its judgments on April 8, 2008, *see* App. 1-6, and denied Petitioners' timely petition for rehearing *en banc* on May 5, 2008, *see* App. 229-31. On July 24, 2008, Justice Souter extended the time for filing a petition for certiorari to and including October 2, 2008. This Court has jurisdiction under 28 U.S.C. § 1254(1).

CONSTITUTIONAL AND REGULATORY PROVISIONS INVOLVED

The Supremacy Clause of the United States Constitution is reprinted at App. 232. Section 201.80(e) of FDA's regulations, 21 C.F.R. § 201.80(e), which provides that a drug's label "shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved," is reprinted at App. 236-37. Section 314.70(c)(6)(iii)(A) of FDA's regulations, 21 C.F.R. § 314.70(c)(6)(iii)(A), which provides that a drug manufacturer may add or strengthen a warning without prior FDA approval, is reprinted at App. 238-41.

STATEMENT

A. Operative Facts. On October 6, 2003, Lois Colacicco's physician prescribed Paxil for her depression, and her prescription was filled with its generic equivalent. Three weeks later, at the age of 55, she killed herself. *See* App. 8-9.

On January 22, 2003, Theodore DeAngelis's physician prescribed Zoloft for his depression. He killed himself eight days later, at the age of 64. *See* App. 10.

B. The Evolution of Drug Labeling. FDA approves drugs based on a limited number of clinical trials, which are simply incapable of detecting many adverse reactions to the drug, or of providing adequate information about the drug's risks and benefits in a much broader population of people who are not typically as healthy or as carefully monitored as subjects in pre-marketing clinical trials.[1] Adverse reactions and side effects of approved drugs inevitably appear as the drug performs in the marketplace.[2] And this is where FDA is particularly lacking. FDA simply does not have

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[1] *E.g.*, FDA, *Clinical Therapeutics and the Recognition of Drug-Induced Disease* (June 1995) ("When a drug goes to market, we know everything about its safety . . . Wrong."), *available at* http://www.fda.gov/medwatch/articles/dig/ceart.pdf. "Clinical trials seldom detect, or define the frequency of, all important adverse effects." *Id*.

[2] According to a 1990 General Accounting Office report, for example, serious post-approval risks surfaced in more than one-half of the 198 drugs approved by FDA between 1976 and 1985, "as evidenced by labeling changes or withdrawal from the market." GAO, *FDA Drug Review, Post-Approval Risks 1976-85,* at 3 (1990), *available at* http://archive.gao.gov/d24t8/141456.pdf.

sufficient resources comprehensively to review and analyze all approved drugs in the post-marketing phase.[3] Thus, there is much information that is not submitted to FDA, both by statutory design and by omission.

The responsibility to review and analyze all safety information as a drug performs in the marketplace does not fall on FDA, but on drug manufacturers themselves. *See* 21 C.F.R. § 314.80(b). Because drug manufacturers will always have far superior knowledge of their drugs' safety issues, they must add warnings "as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved." *Id*. § 201.80(e). Significantly, drug manufacturers have the power and the duty to add warnings without prior FDA approval. *See id*. § 314.70(c)(6)(iii)(A).

C. FDA Consideration of Antidepressants and Increased Suicidality. Prozac, the first of the modern antidepressants, was approved for treatment of depression in adults in 1987. The label submitted by Eli Lilly and approved by FDA mentioned suicide only as being inherent in depression. There was no indication that the drug could be a part of the problem rather than a part of the cure, or that taking an antidepressant might actually increase the risk of suicide early in treatment.

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[3] *See generally* David A. Kessler & David C. Vladeck, *A Critical Examination of the FDA's Efforts to Preempt Failure-to-Warn Claims,* 96 GEO. L.J. 461, 486-91 (2008).

Following the publication of a study suggesting such an increased risk, however, two citizen petitions were filed with FDA in 1990 and 1991 seeking withdrawal of Prozac or a warning that Prozac caused increased suicidal thoughts and behaviors. In response, FDA convened an advisory committee, which concluded that it had insufficient data to require a warning that Prozac caused suicide. Nevertheless, FDA observed that "nobody in the agency dismisses the possibility that antidepressants in general or fluoxetine [Prozac] in particular may have – and I emphasize 'may' – the capacity to cause untoward injurious behaviors, acts, and/or intensify them."[4]

When FDA approved Paxil and Zoloft, their manufacturers proposed, and FDA approved, "inherent in [depression]" language similar to the Prozac label, and this language was still in place in 2003. App. 9-10. Until August 2003 (as discussed in section D below), no antidepressant manufacturer proposed the addition of any warning of an association between its drug and increased suicidality. Until 2004, FDA neither required nor prohibited a warning of this association to patients of any age.

In 2002, however, FDA's regulatory view began to change. On October 7, 2002, an FDA reviewer noted "numerous adverse events coded with terms such as hostility and emotional lability" in an application

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[4] PSYCHOPHARMACOLOGICAL DRUGS ADVISORY COMMITTEE, FDA (Rockville, Maryland) (Sept. 20, 1991)("1991 PDAC"), Hearing Tr. at 126. The full committee minutes are available at http://www.fda.gov/ohrms/dockets/ac/prozac/2443T1.PDF.

seeking approval of Paxil to treat pediatric patients.[5] On October 10, 2002, FDA requested that GSK "reanalyze its data and better characterize the adverse events identified under the term emotional lability."[6] When GSK submitted its response in May 2003, FDA learned that "almost all of these events [labeled 'emotional lability'] related to suicidality."[7] On June 3, 2003, FDA's Dr. Russell Katz wrote that GSK "has not proposed labeling changes, and makes a feeble attempt to dismiss the finding."[8] FDA then expanded the scope of its investigation and requested a reanalysis of pediatric data from other antidepressant manufacturers.[9]

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[5] Clinical Review of Pediatric Exclusivity Supplement for Paxil, FDA (Oct. 7, 2002) at 6, *available at* http://www.fda.gov/cder/foi/esum/2004/20031s037_paxil_Clincal_BPCA_FIN.pdf.

[6] *Amicus* Brief for the United States at 16-17, *Kallas v. Pfizer, Inc.*, Case No. 2:04CV0998 (D. Utah filed Sept. 15, 2005)("U.S. *Kallas Amicus* Br."), available at https://ecf.utd.uscourts.gov/doc1/1831186593.

[7] *FDA's Role in Protecting the Public Health: Examining FDA's Review of Safety and Efficacy Concerns in Anti-Depressant Use by Children: Hearings Before the Subcomm. on Oversight and Investigations of the H. Comm. on Energy and Commerce,* 108th Cong., 2nd Sess., Hearing Tr. at 135 (Sept. 23, 2004)("Sept. 23, 2004 Cong. Hearing Tr."), *available at* http://www.access.gpo.gov/congress/house/pdf/108hrg/96099.pdf.

[8] *Id.* at 136.

[9] U.S. *Kallas Amicus* Br. at 17.

FDA pooled the data it subsequently received from all antidepressant manufacturers and considered the effects of antidepressants as a class. When FDA's advisory committee convened to examine the reanalyzed pediatric data in February 2004, the chairman of the committee observed that "we do not believe that this data until now has been provided to us in a way that would permit us to interpret it fully."[10] After finally analyzing the pediatric data, FDA concluded that "[a] causal role for antidepressants in inducing suicidality has been established in pediatric patients" and began to require that warnings of increased suicidality be placed in a "black box."[11] A boxed warning is the strongest warning FDA regulations allow, short of contraindicating the use altogether. *See* 21 C.F.R. § 201.80(e), App. 237. FDA also requested that drug companies warn patients directly – rather than only through their physicians – via a Patient Medication Guide.[12] FDA subsequently requested that antidepressant manufacturers reanalyze their data concerning adult patients, as they had with the pediatric data.

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[10] PSYCHOPHARMACOLOGIC DRUGS ADVISORY COMMITTEE WITH THE PEDIATRIC SUBCOMMITTEE OF THE ANTI-INFECTIVE DRUGS ADVISORY COMMITTEE, FDA (Bethesda, Maryland) (Feb. 2, 2004)("Feb. 2004 PDAC"), Hearing Tr. at 24. The full committee minutes are *available at* http://www.fda.gov/ohrms/dockets/ac/04/transcripts/4006T1.pdf.

[11] FDA, Labeling Change Request Letter for Antidepressant Medication (Oct. 15, 2004), *available at* http://www.fda.gov/cder/drug/antidepressants/SSRIlabelChange.htm.

[12] *Ibid*.

On March 22, 2004, while reanalysis of the pediatric data was still ongoing, FDA issued a public health advisory warning of the risk of increased suicidality to adult patients, "especially at the beginning of therapy."[13] In May 2004, GSK sent a "Dear Doctor" letter warning "both adult and pediatric" patients in conformance with the March 22, 2004 Public Health Advisory.[14] On June 30, 2005, FDA issued a second public heath advisory, warning that adults being treated with antidepressants, "particularly those being treated for depression," should be closely watched for increasing suicidal thoughts or behavior, especially "early in treatment."[15]

In 2007, FDA revised the class-wide portion of the label for all antidepressants, based on its reanalysis of the pooled adult data. Although the pooled data did not show a class-wide, increased risk in patients treated with antidepressants as compared to placebo beyond age 24, the black box (in the class-wide section of the label) was revised to warn that "[p]atients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for

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[13] FDA Public Health Advisory, *Worsening Depression and Suicidality in Patients Being Treated with Antidepressant [sic]* (Mar. 22, 2004), *available at* http://www.fda.gov/cder/drug/antidepressants/AntidepressanstPHA.htm.

[14] *See* "Dear Healthcare Professional" Letter from GSK (May 2004), *available at* http://www.fda.gov/medwatch/SAFETY/2004/Paxil_hcp.pdf.

[15] FDA Public Health Advisory, *Suicidality in Adults Being Treated with Antidepressant Medications* (June 30, 2005), *available at* http://www.fda.gov/cder/drug/advisory/SSRI200507.htm.

clinical worsening, suicidality, or unusual changes in behavior."[16]

D. The Two Warnings Added by Antidepressant Manufacturers Without Prior FDA Approval. On two occasions, antidepressant manufacturers have added warnings of increased suicidality associated with their drugs without prior FDA approval. On August 22, 2003, Wyeth sent out a "Dear Doctor" letter in which it warned of "increased reports among [pediatric patients] of hostility and suicide-related adverse events." The letter went on to state that Wyeth had "updated the prescribing information for Effexor" to warn of those increased reports of suicide risk.[17] FDA did not pursue misbranding against Wyeth for changing its label without prior approval. Instead, FDA emphasized that Wyeth's action was specifically permitted: "[i]t should be noted that sponsors have the authority to make changes of this nature, *i.e.*, that are perceived to strengthen labeling from the standpoint of safety, without prior approval by FDA."[18] FDA's Director of the

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[16] FDA, Revisions to Product Labeling (May 2, 2007), *available at* http://www.fda.gov/cder/drug/antidepressants/antidepressants_label_change_2007.pdf.

[17] "Dear Healthcare Professional" Letter from Wyeth (Aug. 22, 2003), *available at* http://www.antidepressantsfacts.com/2003-08-22-Wyeth-Effexor-kids.pdf.

[18] Memorandum, Background Comments for February 2, 2004 Meeting of PDAC and Peds AC, FDA, at 11 (Jan.5, 2005), *available at* http://www.fda.gov/ohrms/dockets/ac/04/briefing/4006B1_03_Background%20Memo%2001-05-04.pdf.

Office of Drug Evaluation confirmed in his testimony to Congress that FDA had allowed Wyeth's added precaution to stand, unaltered, for seven months, until it began to require even stronger class-wide warnings for all antidepressants in 2004.[19]

In May 2006, while the reanalysis of the adult data was ongoing, GSK issued its own warning pursuant to 21 C.F.R. § 314.70(c)(6)(iii)(A). Without prior FDA approval, it sent a "Dear Doctor" letter to alert physicians of its label change and to warn that "in the analysis of adults with [major depressive disorder](all ages), the frequency of suicidal behavior was higher in patients treated with [Paxil] compared with placebo," and that the difference was "statistically significant."[20] GSK's data demonstrated that patients taking Paxil were more than six times as likely to experience increased suicidal behavior as patients taking placebo and emphasized that "the higher frequency observed in the younger adult population across psychiatric disorders may extend beyond the age of 24."[21] This dramatic increase in risk was "not based

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[19] Sept. 23, 2004 Cong. Hearing Tr. at 85.

[20] "Dear Healthcare Professional" Letter from GSK (May 2006)("GSK May 2006 Warning"), *available at* http://www.fda.gov/MedWatch/safety/2006/paroxetineDHCPMay06.pdf.

[21] *Ibid.* *Compare* the actual wording of the added warning to the court of appeals' implication that it applied only to "young adults." App. 49 n.18.

on new data," but on a reanalysis of old data.[22] Again, FDA did not pursue a misbranding action (or any other type of enforcement proceeding) against the manufacturer. GSK's added warning stood unchanged for a full year, until FDA again requested that all antidepressant labeling be revised to contain certain warnings in a class-wide portion of the drug's label, uniform for all antidepressants.

Other than these two instances, no antidepressant manufacturer has ever proposed or added a warning of increased suicidality until FDA has requested it to do so. FDA has never rejected any strengthened warning of increased suicidality proposed by any antidepressant manufacturer.

E. Proceedings Below.

1. The defendants in *Colacicco* moved to dismiss the claims against them pursuant to Federal Rule of Civil Procedure 12(b)(6), based on federal preemption. They claimed that if they had added a warning of increased suicidality before FDA requested it, the added warning would have misbranded the drug. On May 25, 2006, the district court granted that motion. *See* App. 162. Significantly, the district court noted that "it is not in dispute that the FDA's position is a hypothetical," App. 104, but believed it was required to give conclusive deference to FDA's new litigation position that the claims were preempted rather than follow the many "forceful" opinions failing

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[22] Report of Joseph Glenmullen, M.D. at 58 (Aug. 10, 2007)("Glenmullen Report"), *available at* http://finance.senate.gov/press/Gpress/2008/prg061208a.pdf.

to find preemption of antidepressant cases, App. 120. The court "concluded not that [the] analysis [in those opinions] is wrong, but that it is improper for a federal district judge to engage in this analysis in the first place." App. 120.

2. Pfizer, the defendant in *McNellis*, moved for summary judgment, likewise claiming preemption based on misbranding. On December 29, 2005, the court denied Pfizer's motion. *See* App. 193. The district court based its decision on its finding that FDA regulations expressly envisioned that the approved labeling would evolve as the drug performed in the marketplace. *See* App. 172, 175-76.

Pfizer moved the court to vacate its decision in light of subsequent statements by FDA and the district court decision in *Colacicco*. On September 29, 2006, the district court denied the motion to vacate, disagreeing with the deference the district court in *Colacicco* had given to FDA's position, *see* App. 194-96, 221, and commenting that "the abrupt rejection of the agency's own prior interpretation (while the regulations themselves are unchanged) suggests a degree of informality yielding an interpretation unhinged from the text and original intent of the regulations themselves," App. 218. The court did certify for interlocutory appeal the following question: "Whether that the United States Food and Drug Administration's requirements for the form and content of the labeling for the prescription antidepressant Zoloft preempted New Jersey's failure-to-warn law, under the doctrine of conflict preemption, where the FDA's regulations at 21 C.F.R. 201.57(e) and 314.70(c)(6)(iii) permit a manufacturer to unilaterally enhance its warning when

the manufacturer has reasonable evidence of an association of a serious hazard with a drug." App. 196.

3. The Third Circuit consolidated the two cases on appeal. On April 8, 2008, in a divided opinion, the court of appeals wrote that "[t]he scarcity of actual conflict cases has led the Justices to pose hypothetical conflicts" as the basis for conflict preemption. App. 32. The court viewed it as immaterial that FDA had never actually rejected a warning of increased suicidality added by an antidepressant manufacturer, App. 47, but focused on FDA's failure to require a warning as of 2003. The court wrongfully equated FDA's failure to require a warning with a prohibition of the warning, finding preemption in "circumstances in which the FDA has publicly rejected the need for a warning that plaintiffs argue state law requires," App. 46. The majority affirmed *Colacicco* and reversed *McNellis*.

Judge Ambro dissented, emphasizing FDA's "180-degree reversal" of its historical position on preemption, App. 65 (citation omitted), and observing that "[n]one of the drug manufacturers in these cases attempted to enhance a warning and received an FDA sanction in response," App. 70. Because "[d]rug manufacturers have the best information about the safety of their products," he found it logical that they had the power under the regulations to add warnings without prior FDA approval, App. 71. Judge Ambro was unwilling to find preemption under these circumstances.

4. Petitioners sought rehearing *en banc*, which was denied. *See* App. 229-31.

REASONS FOR GRANTING THE PETITION

I. THE COURT SHOULD HOLD THIS PETITION PENDING ITS OPINION IN *WYETH V. LEVINE*.

Because the Court's resolution of *Levine* likely will provide needed guidance to the courts below, the Court should hold this petition and then vacate and remand for further proceedings in light of *Levine*.

A. There Are Express Conflicts Between the Court of Appeals' Opinion in This Case and the Vermont Supreme Court's Opinion in *Levine*. The court of appeals' decision in this case directly conflicts with the Vermont Supreme Court's decision in several respects.

1. Hypothetical Conflicts. The asserted basis for conflict preemption in this case is that if the drug manufacturers had added a warning of increased suicidality in 2003, before FDA requested such warnings, they would have misbranded their drugs.[23] Because no antidepressant manufacturer actually proposed or added any such warning with respect to adult patients prior to the prescriptions to Ms. Colacicco and Mr. DeAngelis, however, "it is not in dispute that the FDA's position is a hypothetical," App. 104. This Court has instructed that "[t]he existence of a

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[23] Conflict preemption based on hypothetical misbranding is before this Court in *Levine*. *See* Brief for the United States as *Amicus Curiae* Supporting Petitioner at 21, *Wyeth v. Levine,* No. 06-1249 (U.S. filed June 2, 2008)("U.S. *Levine Amicus* Br."); Brief for Respondent Diana Levine at 34, *Wyeth v. Levine,* No. 06-1249 (U.S. filed August 7, 2008)("Resp. *Levine* Br.").

hypothetical or potential conflict is insufficient to warrant the preemption of" state law. *Rice v. Norman Williams Co.*, 458 U.S. 654, 659 (1982).

The Vermont Supreme Court correctly rejected hypothetical misbranding as a basis for conflict preemption. 944 A.2d at 189 n.3. In contrast, the Third Circuit held that a hypothetical conflict can form the basis for conflict preemption, noting that "[t]he scarcity of actual conflict cases has led the Justices to pose hypothetical conflicts." App. 32. With due respect to the court of appeals, it has misunderstood the opinions of this Court. It is true that this Court has sometimes posed hypotheticals in its analysis of conflict issues. It is not true that the Court has held that a hypothetical conflict can form the basis for conflict preemption. *See, e.g., Rice,* 458 U.S. at 664 (Hypothesizing scenarios that might result in a conflict "ignore[s] the teaching of this Court's decisions which enjoin seeking out conflicts between state and federal regulation when none clearly exists."). Such a holding would be particularly inappropriate in the prescription drug context, where Congress has disclaimed preemption absent a "direct and positive conflict" with state law. Drug Amendments of 1962, Pub. L. No. 87-781 § 202, 76 Stat. 793, App. 232.

The court of appeals used the example of this Court's opinion in *Florida Lime & Avocado Growers, Inc. V. Paul*, 373 U.S. 132, 142-43 (1963), writing that "the Supreme Court hypothesized the existence of an impossibility conflict." App. 32. What the Court actually observed in *Paul* is that there might be an impossibility conflict if the state and federal statutes were written so that it was impossible to comply with

both. But they were not. "No such impossibility of dual compliance is presented on this record, however." *Paul*, 373 U.S. at 143.[24]

If any antidepressant manufacturer had attempted to give an appropriate warning prior to January or October 2003, FDA could have evaluated the added warning. If FDA had considered the added warning to be "false or misleading," it could have pursued a case for misbranding in federal court. *See* 21 U.S.C. § 321(n), §§ 331(a-b), 332, 333, 352(a). Unless FDA actually takes appropriate legal action, however, "misbranding" remains a speculative concept.[25]

2. The Federal Regulation Allowing a Drug Manufacturer To Add or Strengthen a Warning Without Prior FDA Approval. The court of appeals in this case acknowledged that drug manufacturers have the power to add a warning without prior FDA approval pursuant to § 314.70(c)(6)(iii)(A), but found conflict preemption in the face of this acknowledged power. App. 38, 56. The

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[24] In the other example cited by the Third Circuit, the Court found that there was an "irreconcilable conflict" between state and federal statutes where "the Federal Statute authorizes national banks to engage in activities that the State Statute expressly forbids." *Barnett Bank of Marion County, N.A. v. Nelson*, 517 U.S. 25, 31 (1996). The conflict that the Court found was not hypothetical, but an actual conflict grounded in the language of the statutes.

[25] The government inadvertently emphasized the extreme unlikelihood of misbranding at oral argument, when FDA's counsel admitted that she knew of no instances in which FDA had claimed misbranding as a result of a drug manufacturer's strengthening a warning. App. 71.

court of appeals attempted to distinguish *Levine*, claiming that the evidence in this case showed FDA's intention to prohibit a warning of increased suicidality. App. 46 n.17. As Petitioners discuss *infra*, the court of appeals wrongfully equated FDA's failure to require a warning with a prohibition of the warning.

In contrast, the Vermont Supreme Court cited a drug manufacturer's power to add a warning without prior FDA approval under 21 C.F.R. § 314.70(c)(6)(iii)(A) to demonstrate that it is not impossible to comply with federal labeling requirements and concurrently to give an adequate warning under state law. 944 A.2d at 188-89. The dissenting judge in the court of appeals understood this regulation in the same manner: "to avoid discouraging the party with the best safety information from coming forward, 21 C.F.R. § 314.70 permits a manufacturer to alter a drug label before the FDA has evaluated and approved the change." App. 71. Both parties in Levine have briefed this issue,[26] and the Court's interpretation of the regulation in *Levine* will impact the resolution of these cases.

3. Deference to FDA's Changed Position Regarding Preemption. The dissenting judge in the court of appeals reviewed FDA's historical position on preemption, concluding that "FDA has for over three-quarters of a century viewed state tort law as complementary to its warning regulations. Only for the last two years has it claimed otherwise." App. 78. He

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[26] *See* Brief for Petitioner Wyeth at 10, 34-40, *Wyeth v. Levine*, No. 06-1249 (U.S. filed May 27, 2008)("Pet. *Levine* Br."); Resp. *Levine* Br.. at 7, 37-38.

ultimately concluded that FDA's new position on preemption deserves little deference. App. 66. The Vermont Supreme Court was more blunt, according FDA's position "no deference." 944 A.2d at 193. Although the majority of the court of appeals was unwilling to defer its entire preemption analysis to FDA as the district court in *Colacicco* had done, App. 120, the majority found that "FDA's view is entitled to some degree of deference," App. 55. *Levine* also involves the level of deference to be accorded to FDA's litigation position,[27] and the Court's opinion will be instructive in these cases.

B. The Parties in *Levine* Have Raised Other Issues That Will Provide Guidance in These Cases. In addition to the express conflicts between the court of appeals' decision and *Levine*, there are other issues before the Court in *Levine* that could affect – and might well be dispositive of – this case. One such issue is whether misbranding under the federal statutes parallels failure to warn claims under state law, which has been raised and briefed in *Levine*.[28] Federal law does not preempt state actions that parallel federal law. *Riegel v. Medtronic, Inc.*, 128 S. Ct. 999, 1011 (2008); *Bates v. Dow AgroSciences LLC,* 544 U.S. 431, 447-49 (2005). A drug is misbranded if it "fails to reveal facts . . . material with respect to consequences which may result from the use of the article," 21 U.S.C. § 321(n). *Cf. Bates,* 544 U.S. at 438. When Paxil was prescribed to Lois Colacicco in October 2003, there was no warning

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[27] *See* Pet. *Levine* Br. at 39, 43; Resp. *Levine* Br. at 39, 55-56.

[28] *See* Resp. *Levine* Br. at 26-27, 33, 45, 50.

that the drug itself was associated with increased suicidality. Two and a half years later, GSK issued its Dear Doctor letter, warning of a more than six-fold increase in suicidal thoughts and behaviors in adult patients treated with Paxil as compared to those treated with placebo.[29] GSK's added warning demonstrated that Paxil was misbranded by omission when it was prescribed to Lois Colacicco because the 2003 label for Paxil failed to adequately warn of its risks. As such, Petitioners' failure-to-warn claims do not conflict with federal misbranding standards at all. They parallel them. The likely effect of the Court's holding in *Levine* on this issue is yet another reason to hold this petition, and then to grant, vacate and remand for further proceedings in light of *Levine*.

II. NO MATTER HOW THE COURT DECIDES *LEVINE*, THIS CASE PROVIDES AN IDEAL VEHICLE TO FURTHER DEFINE IMPORTANT CONTOURS OF PREEMPTION ANALYSIS IN PRESCRIPTION DRUG CASES.

There are several issues of substantial importance in these cases which are not involved, or only tangentially involved, in *Levine*. In general, these issues arise from the nature of federal regulation of prescription drugs. The federal regulations expressly anticipate that risks will be reevaluated and warnings added as the drugs perform in the market. *See* 21 C.F.R. § 201.80(e) and § 314.70(c)(6)(iii)(A). Because the nature of the system is that warnings will be periodically added or strengthened, prescription drug

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[29] GSK May 2006 Warning.

labels necessarily evolve over time. Given that evolution, there are significant difficulties with attempts to "freeze" an ongoing process and to determine whether the FDA-approved label at a particular point in time should be preemptive.

As this Court has observed with respect to industries in which warning labels "evolve over time," "tort suits can serve as a catalyst" in the evolution. *Bates,* 544 U.S. at 449. This also underscores the wisdom of Congress in foreclosing preemption absent a "direct and positive conflict" with state law. 1962 Amendments § 202, 76 Stat. 793, App. 232. The issues identified below are important to many prescription drug cases, and this case presents an ideal vehicle for their consideration, irrespective of the decision in *Levine*.

A. The Court of Appeals Failed To Recognize That *Sprietsma* Controls the Disposition of This Case. This Court's decision in *Sprietsma* squarely addresses the situation regarding antidepressants and increased suicidality prior to 2004.[30] In *Sprietsma*, the Court acknowledged that "a federal decision to forgo regulation in a given area may imply an authoritative federal determination that the area is best left *un*regulated, and in that event would have as much pre-emptive force as a decision *to* regulate." *Id.* at 66 (citation and internal quotations

[30] *Sprietsma* was briefed in *Levine* as well, *see* Resp. *Levine* Br. at 53. In *Levine*, however, there is no evidence that FDA ever focused its attention on the administration of Phenergan by IV - push, whereas these cases present a scenario in which *Sprietsma* is more directly applicable.

omitted, italics in original). But the Court will not imply an authoritative federal determination against regulation simply because an agency has given some attention to a particular subject. Even where the agency "carefully consider[s]" an issue and consciously refuses to require action under federal law, its decision is not preemptive unless the decision rises to the level of an authoritative federal determination that prohibits action on the state level. *Id.* at 67.

As the government explained in its *amicus* brief in *Sprietsma*, "[e]ven where a federal agency has focused its attention on a particular subject matter within its jurisdiction, it may have various reasons for concluding that federal regulation is inappropriate. The agency may believe that the available evidence is too inconclusive to warrant the imposition of a prescriptive standard under the criteria set forth in the relevant federal statute."[31] FDA's failure to require a warning of increased suicidality associated with antidepressants prior to 2004 reflected only that FDA had not required a warning based on the evidence then before it – not an authoritative federal determination prohibiting one.

While FDA found that the Prozac data it examined in 1991 were not sufficient to require a warning of increased suicidality,[32] FDA's official spokesman confirmed that there was no authoritative

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[31] Brief for the United States as *Amicus Curiae* Supporting Petitioner at *17, *Sprietsma v. Mercury Marine*, 537 U.S. 51 (2002)(No. 01-706), 2002 WL 500643 ("U.S. *Sprietsma Amicus* Br.").

[32] The court of appeals discussed the 1991 PDAC, but overstated its conclusion. *See* App. 41.

determination prohibiting such a warning: "[N]obody in the agency dismisses the possibility that antidepressants in general or fluoxetine [Prozac] in particular may have – and I emphasize 'may' – the capacity to cause untoward injurious behaviors, acts, and/or intensify them."[33]

Furthermore, in response to the 1991 citizen petition, FDA wrote that "an actual court finding of a causal relationship" would be significant.[34] "In that event, the agency would be able to evaluate the scientific basis for the court's conclusion, and consider whether the court's conclusion warranted a modification of its own position."[35] If FDA had considered its action in refusing to require a warning to be an "authoritative federal determination" prohibiting a manufacturer's addition of such a warning pursuant to 21 C.F.R. § 314.70(c)(6)(iii)(A), court cases would of course be preempted and there could not be an "actual court finding."

FDA's response to the Prozac petitions is analogous to the Coast Guard's decision not to require propeller guards in its 1990 letter, which the Court discussed in *Sprietsma.* Although the Coast Guard did not require guards, it emphasized that it would

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[33] 1991 PDAC at 126.

[34] Letter from Carl C. Peck, M.D. to Sanford Block, Executive Director of Citizens Commission on Human Rights (July 26, 1991), *available at* https://ecf.wyd.uscourts.gov/doc1/2071540001. An "actual court finding" would come 10 years later, *infra* at 30.

[35] *Id*.

"continue to collect and analyze accident data for changes and trends."[36] "The letter thus expressly contemplated continuing federal scrutiny of the propeller guard issue in light of additional information, including information regarding the development of new safety devices."[37] Just as the Coast Guard continued to consider safety data concerning propeller guards after its 1990 letter, FDA continued to consider the relationship between increased suicidality and antidepressants after its denial of the citizen petitions in 1992, and even requested further studies to investigate the phenomenon.[38]

GSK, Pfizer, and other antidepressant manufacturers sought and received FDA approval of various indications over the ensuing years, and FDA denied another citizen petition regarding Prozac in 1997. But until Wyeth issued its Dear Doctor letter in August 2003, no antidepressant manufacturer ever proposed adding, or actually added pursuant to 21 C.F.R. § 314.70(c)(6)(iii)(A), a warning of an association between its drug and increased suicidality. FDA thus never rejected any such warning.

Nonetheless, the court of appeals repeatedly wrote that FDA "rejected" such a warning. *E.g.*, App. 40, 45. While the court acknowledged that "a court could more easily determine the preemption issue if the FDA had formally rejected such a CBE supplement,"

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[36] U.S. *Sprietsma Amicus* Br. at *27-28.

[37] *Id*. at *28.

[38] 1991 PDAC at 128. No further studies were ever done.

App. 47, it wrongly equated FDA's refusal to require a warning with a rejection of any such warning. This appears clearly when the court purports to limit its holding to "circumstances in which the FDA has publicly rejected **the need** for a warning. *Id*. at 33 (boldface added). FDA's rejection of the need for a warning is merely a failure to require the warning.

The court of appeals repeated the mistake made by the Illinois Supreme Court, which had concluded "that the Coast Guard's failure to promulgate a propeller guard requirement here equates to a ruling that no such regulation is appropriate pursuant to the policy of the FBSA." *See Sprietsma,* 537 U.S. at 66 (citation omitted). The Illinois Supreme Court overstated the impact of that failure to require. The Coast Guard had simply concluded, "given the evidence available *at that time*, that affirmative imposition of a federal propeller guard requirement could not be justified under the relevant statutory criteria."[39] Just as the Illinois Supreme Court improperly gave preemptive weight to the Coast Guard's decision not to require propeller guards, the court of appeals did the same regarding FDA's pre-2004 decision not to require warnings of increased suicidality. *Sprietsma,* 537 U.S. at 65 ("It is quite wrong to view that decision as the functional equivalent of a regulation prohibiting all States and their political subdivisions from adopting such a regulation."). Likewise, both courts misread this Court's holding in *Geier v. American Honda Motor Co.,* 529 U.S. 861 (2000), which "does not suggest that common-law suits will be preempted whenever the federal agency has focused its attention upon the

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[39] U.S. *Sprietsma Amicus* Br. at *27 (italics in original).

particular aspect of motor vehicle (or recreational vessel) performance that forms the basis of the plaintiff's claim."[40]

When FDA's advisory committee convened to examine the reanalyzed pediatric data in February 2004, however, it erased any doubt that there had been any prior "authoritative federal determination" on the antidepressant/suicide issue. The chairman observed that "we do not believe that this data until now has been provided to us in a way that would permit us to interpret it fully."[41] In his testimony to Congress later that year, FDA's Director of the Office of Drug Evaluation explained why the FDA had not seen the increased signal earlier: "what we conceivably could have asked but didn't know to ask was a better, more structured, more careful look at events that might or might not represented [sic] suicidality, but we didn't know to do that."[42] FDA did not even request drug manufacturers to reanalyze their data concerning adult patients until after it completed its review of the pediatric data in 2004. Under the holding in *Sprietsma*, therefore, FDA had made no authoritative

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[40] U.S. *Sprietsma Amicus* Br. at *19. In its *amicus* brief in *Levine*, the government opined that, as long as FDA "considered" data concerning a potential side effect of a drug but did not require a warning, that failure to require preempts a state-law claim predicating liability on the failure to warn of that side effect. U.S. *Levine Amicus* Br. at 25. Based on its *amicus* brief in *Sprietsma,* the government would have taken the opposite view six months earlier.

[41] Feb. 2004 PDAC at 24.

[42] Sept. 23, 2004 Cong. Hearing Tr. at 113.

determination that could form the basis of conflict preemption at the time of either death involved in this case.

B. When Conflict Preemption Is Based on Misbranding, FDA's Reaction to Warnings That Were Actually Added Is More Persuasive Than Its Hypothetical Reaction to Warnings That Were Not. Although conflict preemption based on hypothetical misbranding is before the Court in *Levine*, the case at bar presents important questions in the analysis that are not involved in *Levine*. Even if the Court allows hypothetical misbranding as a basis for conflict preemption in some instances, the Court should grant certiorari in this case to address how these issues affect the analysis.

Specifically, there are two actual instances in which antidepressant manufacturers added warnings of an association with increased suicidality, without prior FDA approval. In each instance, the manufacturer based the added warning on a reanalysis of long-existing data. In neither instance did FDA pursue misbranding. Petitioners assert that FDA's actual reaction to warnings that were added is far more persuasive than its hypothetical reaction to warnings that were not.

Wyeth added its precaution to pediatric patients on August 22, 2003, six weeks before Paxil was prescribed to Lois Colacicco. It is true that Wyeth's added warning addressed pediatric patients, not adult patients such as Mr. DeAngelis or Ms. Colacicco. But as of 2003, FDA's position regarding adult and pediatric patients was the same: it had neither required nor

prohibited a warning of increased suicidality. Furthermore, FDA would later claim in an *amicus* brief filed on September 15, 2005 that such a warning added in October-November 2002 would have misbranded Zoloft with respect to a pediatric patient.[43] FDA apparently takes the position that an added warning before it required it would have misbranded an antidepressant as to any patient, pediatric or adult.

Of even more significance is the warning added by GSK in May 2006 with respect to the use of Paxil by adult patients. FDA allowed this added warning to stand unchallenged for a full year, and admitted in its *amicus* brief in the court of appeals that it "did not reject the proposed labeling change."[44] FDA as regulator had evaluated a warning added without its prior approval, concerning the same drug, the same side effect and the same patient group, and had not claimed misbranding. FDA as litigator claimed that FDA would have reacted differently to the same warning, with the same scientific support from the manufacturer, three years earlier.[45]

Furthermore, it is important to note that allegations of misbranding are almost always decided by juries. *See* 21 U.S.C. §§ 332, 334(b), 337(a); *cf. Bates,* 544 U.S. at 452. Only one jury has passed on the relationship between Paxil and suicide, and it did so two years **before** the prescriptions to Mr. DeAngelis and Ms. Colacicco. On June 6, 2001, a unanimous

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[43] *See* U.S. *Kallas Amicus* Br. at 38.

[44] U.S. 3d Cir. *Amicus* Brief at 14.

[45] *Id*. at 16, 19.

federal jury in Wyoming found that Paxil "can cause some individuals to commit homicide and/or suicide." *Tobin v. SmithKline Beecham Pharms.*, 164 F. Supp. 2d 1278, 1287-88 (D. Wyo. 2001). The district court found the plaintiffs' evidence "scientifically reliable" and "legally admissible" under *Daubert v. Merrill Dow Pharms,,* 509 U.S. 579 (1993), both before trial and after. 164 F. Supp. 2d at 1283.

The court of appeals cited GSK's added warning in a footnote and mistakenly believed that it applied only to "young adults." App. 49 n.18. The majority opinion did not mention Wyeth's added warning, although the dissenting justice did so. *See* App. 71. Neither opinion cited *Tobin*. If hypothetical misbranding can establish a "direct and positive conflict" in some instances, the Court should clarify that the analysis of that conflict should place significant weight on warnings that were actually added, FDA's reaction to those warnings and actual jury verdicts concerning the warnings.

C. The Court Should Clarify Whether It Is Appropriate To Consider Subsequent Regulatory Events in an Analysis of Conflict Preemption by Misbranding. Courts have struggled to determine whether to "freeze" the misbranding analysis or whether and to what extent they should consider subsequent regulatory events. Misbranding is an allegation that must be proven in court, and there is no misbranding without a judgment. To claim misbranding as the basis for conflict preemption without a trial, however, FDA has attempted to vest itself with more power than it actually has. That is why, in its initial *amicus* brief making this assertion,

FDA characterized misbranding as a "self-executing statutory prohibition."[46] If misbranding were "self executing," analysis of a potential conflict at a certain point in time might be appropriate without a misbranding action. But it is not.

Most courts analyzing the issue have concluded that the subsequent warnings were relevant, at least to some extent.[47] The district court in *McNellis* agreed, concluding that "[i]n recommending label changes that reflect concerns about the association between SSRIs and suicidality, neither the FDA nor Pfizer can now claim, as they had in *Motus,* that no scientific basis exists for a suicide warning." App. 185. But FDA has remained undeterred, to the point that its litigation positions have become untethered to its regulatory activities.

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[46] Brief for the United States as *Amicus Curiae* in Support of the Defendant-Appellee at 19, *Motus v. Pfizer, Inc.*, 358 F.3d 659 (9th Cir. 2004)(Nos. 02-55372, 02-55498), 2002 WL 32303084.

[47] *E.g., Witczak v. Pfizer, Inc.*, 377 F. Supp. 2d 726, 730 (D. Minn. 2005)("[T]he FDA has since distanced itself from the substance of the *Motus* brief by recommending labeling changes that, in fact, reflect concerns about the association between SSRIs and suicidality. Thus, the Court has 'reason to suspect that the [*Motus* brief's] interpretation does not reflect the agency's fair and considered judgment on the matter in question.'"(*quoting Auer v. Robbins*, 519 U.S. 452, 462(1997))); *Cartwright v. Pfizer, Inc.*, 369 F. Supp. 2d 876, 885-86 (E.D. Tex. 2005)("Given the hearings by both Congress and the FDA regarding suicidality, the FDA's PDAC's recent decision to recommend black box warnings regarding suicidality in children and adolescents, and the numerous experts who have concluded that there is a link between SSRIs, like Zoloft, and suicidality, it would be **inconceivable** to this Court to argue that an additional warning regarding suicidality would be false or misleading.")(boldface added).

FDA's *amicus* brief in *Kallas v. Pfizer* provides a clear example. Shyra Kallas was a pediatric patient whose physician prescribed Zoloft on October 8, 2002. She shot herself on November 4, 2002. At the time of her prescription and death, FDA had not yet required the black box warnings to pediatric patients (although it had already seen a signal and had asked GSK to reanalyze its data). By the time the government filed its *amicus* brief on September 15, 2005, however, it had been almost a full year since FDA had requested that a warning of the same side effect that led Shyra Kallas to take her own life be placed in a black box. Nonetheless, FDA claimed preemption because "Shyra Kallas' death preceded FDA's receipt of the May 2003 Paxil report, FDA's request for and receipt of additional information from antidepressant New Drug Application sponsors, Columbia University's reclassification of the sponsors' data, and FDA's preliminary and subsequent analysis of the sponsors' data. Thus, in October/November 2002, FDA did not believe that there was reasonable evidence of an association between Zoloft and an increased risk of suicidality in either adult or pediatric patients."[48] FDA wrongly attempted to equate its own "judgment"to a "self-executing statutory prohibition."[49]

The Third Circuit appeared at first to freeze the analysis in this case: "Our focus is on the period before the two deaths that are the subject of the actions before us." App. 48. The court then proceeded to discuss some of the regulatory events that came in the following years, *see* App. 48-51, ostensibly using the subsequent

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[48] U.S. *Kallas Amicus* Br. at 36.

[49] *E.g.,* U.S. *Kallas Amicus* Br. at 26, 34, 38.

events to bolster misbranding in 2003, *see* App. 50. If subsequent events were not relevant, *Sprietsma* is dispositive. If subsequent events were relevant, surely GSK's admission of a more than six-fold elevation of risk in May 2006 is conclusive evidence against misbranding. The conclusion should be the same in this particular case, but the analysis is very different.

Because risks are always being evaluated and warnings are periodically added to drug labels, the point in time at which to analyze conflict preemption based on misbranding becomes critical. If the Court allows hypothetical misbranding to serve as a basis for conflict preemption, it should clarify the extent to which subsequent regulatory events are relevant to the analysis.

D. *Buckman* Does Not Preclude Consideration or Evidence That a Drug Manufacturer Withheld or Manipulated Data in a Failure-to-Warn Case. The court of appeals refused to consider evidence that GSK had manipulated data it had submitted to FDA concerning Paxil, citing this Court's opinion in *Buckman Co. v. Plaintiffs' Legal Committee,* 531 U.S. 341 (2001). *See* App. 48. This interpretation, which allows a drug company to exclude evidence that it has withheld or manipulated data submitted to FDA and to then successfully claim conflict preemption because the agency has not required a warning, is an incorrect reading of *Buckman.* Although the Third Circuit is not alone in using

Buckman in this manner,[50] its interpretation is no less mistaken.

This Court held in *Buckman* that a claim of fraud on FDA is solely FDA's to pursue and is thus preempted by federal law. The Court differentiated a claim of fraud on FDA from a claim based on "traditional state tort law principles of the duty of care," 531 U.S. at 352, and emphasized in particular that reliance by FDA, absent acts affirmatively showing reliance, is peculiarly within FDA's knowledge, *id*. at 353 (Stevens, J., concurring). The government, appearing as *amicus curiae*, acknowledged the narrowness of the issue: "The fraud claim is preempted, but if there is negligent design, negligent manufacturing, failure to warn, common law malpractice, all of those claims are available." Transcript of Oral Argument at 19, *Buckman Co. v. Plaintiffs' Legal Comm.,* 531 U.S. 341 (2001)(No. 98-1768).

This case illustrates the absurdity of reading *Buckman* as an evidentiary exclusion case. On June 12, 2008, Sen. Grassley (R-Iowa), the ranking member of the Senate Committee on Finance, formally asked FDA to investigate whether GSK had withheld safety information regarding the use of Paxil by adults. In his floor statement, Sen. Grassley alluded to drug

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[50] Two district courts have also held that *Buckman* precluded consideration of the manipulation of the Paxil data, *see Mason v. SmithKline Beecham Corp*., 546 F. Supp. 2d 618, 627 n.5 (C.D. Ill. 2008); *O'Neal v. SmithKline Beecham Corp*., 551 F. Supp. 2d 993, 997 n.8 (E.D. Cal. 2008), while one has reached an opposite conclusion, squarely refusing to read *Buckman* as an evidentiary exclusion case, *see Knipe v. SmithKline Beecham Corp*., No. 06-3024, 2008 WL 4090995 at *23 n.31 (E.D. Pa. Aug. 28, 2008).

companies' "hiding data," then clarified that "I don't mean that they actually hide the data. But they make these numbers so difficult to find that they might as well be invisible."[51] He concluded that, "[e]ssentially, it looks like GlaxoSmithKline bamboozled the FDA."[52]

Sen. Grassley's allegations are based on GSK's improper reporting of suicidal events in adult patients in its initial NDA for Paxil and in follow-up reports to the FDA between 1989 and 1992. The true data "demonstrate[] a causal link between the antidepressant and suicidal behavior. This has been true since 1989 although the 'bad' Paxil numbers obscured the risk for a decade-and-a-half."[53] GSK's manipulation of the data hid the fact that adult patients treated with Paxil are many times as likely to experience increased suicidal thoughts and behavior than patients treated with placebo, until it finally admitted to a more than six-fold increase in the risk in its May 2006 "Dear Doctor"letter – 17 years later.[54] "GlaxoSmithKline's failure to provide the correct data to the FDA in 1991 when the FDA was trying to get to the bottom of this potentially lethal side effect delayed

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[51] Floor Statement of Sen. Chuck Grassley, *Hidden Data on Paxil* (June 11, 2008), *available at* http://finance.senate.gov/press/Gpress/2008/prg061208.pdf.

[52] *Id.*

[53] Glenmullen Report at 74.

[54] GSK May 2006 Warning.

warnings for 15 years and placed countless people at risk."[55]

When the asserted conflict is that an added warning would have been "false or misleading," evidence that demonstrates that the drug manufacturer manipulated data that it submitted to FDA, and that the actual data demonstrate[] that the warning is neither false nor misleading, should be relevant. This reasoning is analogous to the Second Circuit's in *Desiano v. Warner-Lambert & Co.*, 467 F.3d 85 (2d Cir. 2006), *aff'd sub nom. by an equally divided court*, *Warner-Lambert Co. v. Kent*, 128 S. Ct. 1168 (2008). The Sixth Circuit disagreed with the Second Circuit in *Garcia v. Wyeth-Ayerst Labs,* 385 F.3d 961, 966 (6th Cir. 2004), resulting in the conflict that was presented in *Kent*. The Court should grant this petition to clarify that *Buckman* does not allow exclusion of evidence that a drug company withheld or manipulated data, and that consumers in a failure-to-warn case may use such evidence to defeat preemption in a traditional failure to warn case.

CONCLUSION

The petition for writ of certiorari should be held pending the Court's decision in *Wyeth v. Levine*, after which the Court should grant the petition, vacate the judgment below, and remand for reconsideration in light of *Levine*. In the alternative, the Court should grant the petition and schedule the case for briefing and hearing on the merits.

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[55] Glenmullen Report at 14.

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