In the

United States Court of Appeals

For the Seventh Circuit

No. 17-3030

WENDY B. DOLIN, Individually and as Independent Executor of the Estate of STEWART DOLIN, Deceased,

Plaintiff-Appellee,

v.

GLAXOSMITHKLINE LLC,
Formerly Known as SMITHKLINE BEECHAM CORP.,

Defendant-Appellant.

Appeal from the United States District Court for the
For the Northern District of Illinois, Eastern Division.
No. 12-CV-6403 — **William T. Hart**, *Judge.*

ARGUED MAY 30, 2018 — DECIDED AUGUST 22, 2018

Before WOOD, *Chief Judge*, and SYKES and HAMILTON, *Circuit Judges*.

HAMILTON, *Circuit Judge*. Defendant GlaxoSmithKline LLC (GSK) appeals from a jury verdict awarding $3 million to plaintiff Wendy Dolin for the death of her husband, Stewart Dolin. Mrs. Dolin alleges that GSK's negligent omissions in the drug label for Paxil caused her husband's death. Stewart

did not actually take Paxil. In 2010, a doctor prescribed Paxil, the brand-name version of paroxetine, to treat Stewart's depression and anxiety. But his prescription was filled with generic paroxetine manufactured by another company (one that is no longer a defendant). Six days later, Stewart committed suicide. Blood tests showed that paroxetine was in his system. He was 57 years old.

At the time of Stewart's death, GSK manufactured brand-name Paxil and was responsible under federal law for the content of the drug's label. When Stewart died, the labels for paroxetine and similar antidepressant drugs warned that they were associated with suicide in patients under the age of 24. The labels did not warn about any association between the drugs and an increased risk of suicide in older adults.

The current state of federal law makes it virtually impossible to sue generic drug manufacturers on a state-law theory for failure to warn. In response to this legal landscape, plaintiffs have advanced a new theory of liability and have sued brand-name manufacturers, who have more control over drug labels, for injuries caused by taking the generic drugs. Mrs. Dolin followed this recent trend here, suing GSK on the theory that it negligently failed to include warnings that paroxetine was associated with suicide in patients older than 24.

Throughout the lawsuit, GSK has maintained that it is not liable under Illinois law simply because Stewart Dolin did not consume a drug that GSK manufactured. Mrs. Dolin responds that the relevant harm was caused by the incomplete label, not the drug, and that under federal law, only GSK could change the label. GSK also argued that federal law preempted Illinois law from requiring the warning that Mrs. Dolin claims was

negligently omitted because the FDA had rejected GSK's attempts to add just such a warning. The district court disagreed with GSK's various arguments, and the case proceeded to trial and a verdict for Mrs. Dolin.

In this appeal, GSK challenges the district court's conclusions about liability under Illinois law and preemption. GSK also argues that the evidence at trial did not support the jury's verdict. We agree with GSK that federal law prevented GSK from adding a warning about the alleged association between paroxetine and suicides in adults. On that basis of federal preemption, we reverse the judgment. The case must be dismissed.

I. *Legal and Factual Background*

A. *Regulation of Drug Labels*

We start with the regulatory background that explains why the parties make the arguments they do. The Food, Drug, and Cosmetic Act bars pharmaceutical companies from manufacturing new drugs unless the Food and Drug Administration approves a "new drug application." 21 U.S.C. § 355(a). The new drug application must show that the drug is safe and effective, which requires an extensive series of clinical trials. *Guilbeau v. Pfizer, Inc.*, 880 F.3d 304, 307 (7th Cir. 2018); see also 21 U.S.C. §§ 355(b) & (d). The application must also include "the labeling proposed to be used for such drug." § 355(b)(1)(F); 21 C.F.R. § 314.50(c)(2)(i).

The label contains a lot more than the drug's name. It must disclose, among other things, warnings and precautions related to the drug's effects. The FDA reviews the proposed label to determine whether it is "false or misleading." 21 U.S.C.

§ 355(d)(7); 21 C.F.R. § 314.125(b)(6). Once the new drug application is approved, the manufacturer must distribute the drug using the FDA-approved label. Otherwise, the drug is misbranded and may not be distributed in the United States. See 21 U.S.C. §§ 331(a), 333(a), & 352(a), (c). In 1992, the FDA approved GSK's new drug application for paroxetine, including a label.

Plaintiff's theory of liability is based on GSK's ability to change the paroxetine label after the FDA approved it in 1992. There were two ways relevant to this lawsuit for GSK to change the label without running afoul of federal law. First, GSK could have asked the FDA for permission to change the label. 21 C.F.R. § 314.70(b)(2)(v)(A). This is the default rule for most substantive changes to drug labels. Second, in narrow circumstances GSK could unilaterally change the label under what is called the "changes being effected" or CBE regulation. The CBE regulation is an exception to the general rule that changes require advance FDA permission. It allows manufacturers to change a label to "reflect newly acquired information" if, as relevant here, the changes "add or strengthen a … warning" for which there is "evidence of a causal association … ." 21 C.F.R. § 314.70(c)(6)(iii)(A). In other words, GSK needed FDA permission to change the paroxetine label unless three things were true: (1) GSK had newly acquired information about paroxetine (2) that showed a causal association (3) between the drug and an effect that warranted a new or stronger warning. The FDA reviews CBE submissions and can reject label changes even after the manufacturer has made them. See 21 C.F.R. § 314.70(c)(6), (7).

The new drug approval process is "onerous and lengthy." *Mutual Pharmaceutical Co., Inc. v. Bartlett*, 570 U.S. 472, 476

(2013). Generic manufacturers can avoid much of this costly process, but they have little influence on the contents of drug labels. Under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as the Hatch-Waxman Act, a manufacturer can file an "abbreviated new drug application" for approval to distribute a generic drug. See 21 U.S.C. § 355(j). The Supreme Court summarized the requirements for generics:

> First, the proposed generic drug must be chemically equivalent to the approved brand-name drug: It must have the same "active ingredient" or "active ingredients," "route of administration," "dosage form," and "strength" as its brand-name counterpart. 21 U.S.C. §§ 355(j)(2)(A)(ii) and (iii). Second, a proposed generic must be "bioequivalent" to an approved brand-name drug. § 355(j)(2)(A)(iv). That is, it must have the same "rate and extent of absorption" as the brand-name drug. § 355(j)(8)(B). Third, the generic drug manufacturer must show that "the labeling proposed for the new drug is the same as the labeling approved for the [approved brand-name] drug." § 355(j)(2)(A)(v).

Bartlett, 570 U.S. at 477. "This allows manufacturers to develop generic drugs inexpensively, without duplicating the clinical trials already performed on the equivalent brand-name drug." *PLIVA, Inc. v. Mensing*, 564 U.S. 604, 612 (2011).

In sum, "brand-name and generic drug manufacturers have different federal drug labeling duties." *Mensing*, 564 U.S.

at 613. "A brand-name manufacturer seeking new drug approval is responsible for the accuracy and adequacy of its label." *Id.*; see also 21 U.S.C. § 355(b)(1), (d); *Wyeth v. Levine*, 555 U.S. 555, 570–71 (2009). "A manufacturer seeking generic drug approval, on the other hand, is responsible for ensuring that its warning label is the same as the brand name's." *Mensing*, 564 U.S. at 613; see also 21 U.S.C. §§ 355(j)(2)(A)(v) & (j)(4)(G); 21 C.F.R. §§ 314.94(a)(8) & 314.127(a)(7). Thus, from 1992 to 2014, when GSK sold the right to distribute brand-name Paxil, GSK was responsible for the "accuracy and adequacy" of the drug's label. To change the label, GSK needed either FDA permission or newly acquired information that supported a strengthened warning under the CBE regulation.

B. *The History of Paroxetine's Label*

Paroxetine is a selective serotonin reuptake inhibitor, one of a class of antidepressants commonly called SSRIs. For decades, the FDA has scrutinized data on the relationship between SSRIs and suicidal behavior. The FDA's analysis of that relationship is central to the preemption question in this appeal.

1. *The New Drug Application Approval*

GSK's predecessor, SmithKline Beecham Corporation, submitted a new drug application for paroxetine in 1989. Around that time, the FDA began investigating a potential relationship between suicidal behavior and SSRIs. The FDA requested GSK to submit a supplemental analysis of data related to suicide. GSK submitted the additional analysis in May 1991. In June 1991, the FDA safety reviewer for GSK's paroxetine application reported: "there is no signal in this large data base that paroxetine exposes a subset of depressed

patients to additional risk for suicide, suicide attempts or suicidal ideation."

The FDA continued its investigation of the risk of suicide. In September 1991, the agency convened an independent committee of experts to review whether SSRIs were associated with suicide. The FDA also asked the committee to evaluate data specific to paroxetine. The committee "unanimously agreed that there is no credible evidence of a causal link between the use of antidepressant drugs … and suicidality or violent behavior." The committee also found that paroxetine was safe and effective for treating adult depression.

In December 1992, the FDA approved the new drug application for paroxetine, which allowed GSK to market the drug as Paxil. The original label did not contain any paroxetine-specific warning about suicidality. Instead, the FDA required that the label contain the same warning as all other antidepressants at the time: "The possibility of a suicide attempt is inherent in depression and may persist until significant remission occurs. Close supervision of high-risk patients should accompany initial drug therapy."

Throughout the late 1990s and early 2000s, GSK submitted additional data on paroxetine to the FDA. The FDA continued to reject any link between paroxetine and suicidality. In January 2004, the FDA summarized its findings as follows:

> FDA has done several analyses on completed suicides for adult data sets provided to us in response to a request for patient level data sets for all relevant studies involving 20 antidepressant drugs studied in 234 randomized controlled trials with [major depressive disorder].

> Based on our initial analyses of these data, we have reached a similar conclusion, i.e., that there does not appear to be an increased risk of completed suicide associated with assignment to either active drug or placebo in adults with [major depressive disorder].

2. *The FDA's 2004 Pediatric Suicide Warning*

Later in 2004, however, the FDA found an association between SSRIs and suicide in pediatric patients. The FDA convened an advisory committee to review data on nine antidepressant drugs, including paroxetine and other SSRIs, in pediatric patients. The committee unanimously agreed that the "data in aggregate indicate an increased risk of suicidality" in "pediatric patients." As a result, the FDA required that the labels for paroxetine and other SSRIs be changed to include a warning that antidepressants "increase the risk of suicidal thinking and behavior (suicidality) in children and adolescents with major depressive disorder (MDD) and other psychiatric disorders."

The FDA required that this appear as a "black-box" warning, meaning that it "should be added to the beginning" of the label "with bolded font and enclosed in a black box." The FDA also required new language in the "WARNINGS—Clinical Worsening and Suicide Risk" section of the previous label applicable to all SSRIs. The new language warned that patients "with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior … whether or not they are taking antidepressant medication," and that a "causal role for antidepressants in inducing suicidality has been established in pediatric patients." The FDA did

not require a warning about any association between antidepressants and suicidality in adults.

3. *GSK's 2006 Adult Suicide Warning*

After finding that SSRIs were associated with suicide in pediatric patients, the FDA began a similar analysis of suicide in adults. The FDA requested more data from manufacturers of antidepressants, including data from GSK on paroxetine. The FDA limited its data request to "completed, double-blind, randomized, placebo-controlled trials." GSK submitted data to the FDA.

At the same time, GSK conducted its own re-analysis of data on adult suicidality and paroxetine. In the re-analysis, GSK looked for an association between paroxetine use with suicidal ideation and increased suicide attempts. GSK found no statistically significant difference when looking at suicidal ideation, but it found "evidence of an increase in suicide attempts in adults with [major depressive disorder] treated with paroxetine compared with placebo." GSK submitted its findings to the FDA, explaining that its data showed a 6.7-fold increase in suicide attempts in adults treated with paroxetine compared to a placebo. GSK cautioned the FDA that "these data should be interpreted with caution" because "the absolute number and incidence of events" were "very small."

After completing the re-analysis, GSK acted unilaterally to change paroxetine labeling on April 27, 2006. It did so under the CBE regulation, i.e., without advance FDA approval. GSK removed language that described the risk of suicide in adults as "unknown" and added the following:

> In adults with [major depressive disorder] (all ages), there was a statistically significant increase in the frequency of suicidal behavior in patients treated with paroxetine compared with placebo (11/3,455 [0.32%] versus 1/1,978 [0.05%]); all of the events were suicide attempts. However, the majority of these attempts for paroxetine (8 of 11) were in younger adults aged 18-30 years. These [major depressive disorder] data suggest that the higher frequency observed in the younger adult population across psychiatric disorders may extend beyond the age of 24.

GSK also sent a letter to doctors nationwide, attaching the new paroxetine label and explaining the "important changes to the Clinical Worsening and Suicide Risk subsection of the Warnings section."

4. *FDA's Meta-Analysis & the 2007 Class-Wide Label Change*

About seven months later, in November 2006, the FDA completed a meta-analysis—that is, a statistical analysis of a large group of similar studies—to study the risk of suicide in adults who use antidepressants. The meta-analysis considered 372 placebo-controlled clinical trials and involved nearly 100,000 adult patients, including data on paroxetine submitted by GSK. The FDA found "an elevated risk for suicidality and suicidal behavior among adults younger than 25," but concluded that the "net effect appears to be neutral on suicidal behavior but possibly protective for suicidality for adults between the ages of 25 and 64 and to reduce the risk of both suicidality and suicidal behavior in subjects aged 65 years and older."

The FDA's meta-analysis analyzed the data for each drug. For paroxetine, the FDA data showed a statistically-significant 2.76-fold increase in suicidal behavior compared with adults treated with placebo. The FDA noted this result, but concluded that "the significance of those findings must be discounted for the large number of comparisons being made."

In response to these findings, in 2007, the FDA took action that is central to GSK's preemption defense in this case. The agency ordered that all SSRI labels be updated based on the results of the meta-analysis. Critically, the FDA decided to order that warnings be uniform for all SSRIs. On May 1, 2007, the FDA directed GSK to revise the paroxetine labeling "to ensure standardized labeling pertaining to adult suicidality with all of the drugs to treat major depressive disorder." Def. Ex. 122. The SSRI labels were to warn of a suicidality risk in patients 24 years old or under, and to state that "studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction with antidepressants compared to placebo in adults aged 65 and older." The FDA required all SSRI labels to include this language "verbatim." This action had the effect of rejecting GSK's unilateral change to the paroxetine label in 2006 using the CBE regulation to warn of increased risk among older adults.

5. *Later Attempts to Add a Paroxetine-Specific Warning*

After the FDA ordered uniform warnings for all SSRIs, GSK asked the FDA several times for permission to maintain a paroxetine-specific suicide warning. Within a week of the FDA's announcement, GSK emailed the FDA to "clarify" whether it could retain the paroxetine-specific warning it had

added in 2006 under the CBE regulation. The FDA immediately said no. It replied that GSK should "replace the previous warning section with the new language" that the FDA had circulated. Def. Ex. 124.

Four days later, on May 11, GSK more formally asked the FDA to maintain the paroxetine-specific warning. In a letter to the FDA, GSK proposed keeping the paroxetine-specific language and argued that it "would complement the class labeling" and "could help physicians." The FDA advised GSK to submit the paroxetine-specific warning as a separate CBE supplement and explained that the FDA would "be discussing all" manufacturers' "proposals during the last week of May." GSK submitted the CBE supplement that the FDA requested.

On June 21, 2007, the FDA finalized the new class-wide warnings. The FDA stressed that "it is critical that the labeling be consistent for all" SSRIs. This final version omitted GSK's paroxetine-specific warning. The next day, GSK again followed up with the FDA to clarify whether the FDA had rejected its most recent CBE supplement adding a paroxetine-specific warning. It had. The FDA responded that it was rejecting product-specific warning language:

> [T]he Agency has reviewed your proposed changes, and we do not believe that your product specific analysis should be included in class labeling revisions since the labeling is targeted at the class of drugs. If you would like to discuss this matter further, please submit a formal meeting request.

Def. Ex. 129. GSK did not pursue the matter any further.

On June 25, 2007, GSK implemented the new class-wide warning that the FDA ordered. GSK continued to assert to the FDA that "the paroxetine specific language" would "be useful for prescribers." On August 2, 2007, the FDA approved GSK's supplement—and thus the new paroxetine label—containing *only* the class-wide SSRI suicide warning. GSK continued to market paroxetine under the Paxil brand name in the United States using the FDA-approved label through 2014, when GSK sold the right to sell Paxil to another manufacturer. The paroxetine label maintains the FDA's class-wide warning today. It does not warn of any association with an increased risk of suicide in adults older than 24.

C. *This Lawsuit*

Mrs. Dolin sued GSK in state court, alleging that paroxetine increases the risk of suicide in adults; that GSK negligently failed to update the paroxetine label to reflect that risk; and that GSK's negligence caused Stewart's death. GSK removed to the Northern District of Illinois, asserting diversity jurisdiction under 28 U.S.C. § 1332(a)(1). Mrs. Dolin is a citizen of Illinois. GSK is a limited liability company organized under Delaware law, and its sole member is GlaxoSmithKline Holdings (Americas) Inc., a Delaware corporation with its principal place of business in Delaware. The amount in controversy exceeds $75,000.[1]

[1] Mrs. Dolin also sued Mylan, Inc., the company that manufactured the generic paroxetine that Stewart Dolin actually took. Mylan moved to dismiss on preemption grounds under *Mensing*, 564 U.S. 604, and *Bartlett*, 570 U.S. 472. The district court granted Mylan's motion, and Mrs. Dolin has not appealed that decision.

Once in federal court, GSK made two arguments that are relevant to this appeal. First, GSK argued that it did not owe Stewart—who consumed paroxetine made by another company—a duty of care under Illinois law. Second, GSK argued that plaintiff's claim was preempted under *Wyeth v. Levine*, 555 U.S. 555 (2009), because the FDA had rejected the paroxetine-specific warning that, according to plaintiff, Illinois law required. The district court denied GSK's motions for summary judgment, and the case proceeded to trial.

GSK moved for judgment as a matter of law during and after trial. GSK argued that plaintiff had failed to provide evidence that paroxetine causes suicide and that the paroxetine labeling caused Stewart's suicide. GSK also renewed its arguments that it was not liable both because it did not owe Stewart a duty under Illinois law and because federal law preempted the failure-to-warn claim. The district court denied GSK's motions and entered final judgment in favor of Mrs. Dolin.

II. *Preemption*

The Supremacy Clause was at the core of the Framers' effort to provide a national government with the powers needed to govern the new Republic effectively. It provides: "This Constitution, and the Laws of the United States which shall be made in Pursuance thereof; and all Treaties made, or which shall be made, under the Authority of the United States, shall be the supreme Law of the Land; and the Judges in every State shall be bound thereby, any Thing in the Constitution or Laws of any State to the Contrary notwithstanding." U.S. Const. art. VI, cl. 2. The Supremacy Clause "invalidates state laws that 'interfere with, or are contrary to,' federal law." *Hillsborough County v. Automated Med. Labs., Inc.*, 471 U.S. 707,

712 (1985), quoting *Gibbons v. Ogden*, 22 U.S. 1, 211 (1824). State law includes duties imposed by court decisions applying state tort law. E.g., *Mensing*, 564 U.S. 604 (invalidating state laws imposing duty on generic manufacturers to change drug labels).

"Preemption comes in three forms." *Mason v. Smithkline Beecham Corp.*, 596 F.3d 387, 390 (7th Cir. 2010). First is express preemption, "which occurs when Congress clearly declares its intention to preempt state law." *Id.* Second is implied preemption, "which occurs when the 'structure and purpose' of federal law shows Congress's intent to preempt state law." *Id.* This case involves the third form, called conflict or impossibility preemption. Conflict preemption occurs when there is "an actual conflict between state and federal law such that it is impossible for a person to obey both." *Guilbeau v. Pfizer, Inc.*, 880 F.3d 304, 310 (7th Cir. 2018), quoting *Mason*, 596 F.3d at 390. When that is true, "federal law controls and the state-law tort claims must be dismissed." *Id.*

In *Wyeth v. Levine*, the Supreme Court addressed how conflict preemption applies to state-law claims against brand-name drug manufacturers. The Court held that state-law claims based on labeling deficiencies are not preempted if the manufacturer could have added the warning unilaterally under the CBE regulation. 555 U.S. at 573 (finding that defendant had "failed to demonstrate that it was impossible for it to comply with both federal and state requirements" when the "CBE regulation permitted" defendant "to unilaterally strengthen its warning" on its brand-name drug). In a later case addressing how *Levine* would apply to claims against manufacturers of generic drugs, the Court reiterated that the "question for 'impossibility' is whether the private party

could independently do under federal law what state law requires of it." *Mensing*, 564 U.S. at 620, citing *Levine*, 555 U.S. at 573. As a general rule, then, state law can hold a brand-name manufacturer liable for failing to use its powers under the CBE regulation to add a new warning to a drug label.

There is one final part to this standard, and it is decisive here. Recall that the FDA can reject CBE submissions and require manufacturers to revert to the prior version of the label. *Levine* acknowledged that the FDA retains this authority, and "held that there could be preemption if the manufacturer met the stringent standard of proving that there was *clear evidence* the FDA would have rejected the proposed change in the drug's label." *Mason*, 596 F.3d at 391, citing *Levine*, 555 U.S. at 571. The evidence here meets that standard.

In sum, Dolin's state-law claim against GSK is preempted if GSK could not have added the adult-suicidality warning using the CBE regulation. See *In re Celexa & Lexapro Marketing & Sales Practices Litigation*, 779 F.3d 34, 41 (1st Cir. 2015) (finding that plaintiff must allege a label deficiency that defendant "could have corrected using the CBE regulation."). To add a warning through the CBE regulation, GSK needed newly acquired information about paroxetine that would allow it to add a warning about suicide risk in adults. And even if GSK had newly acquired information along these lines, GSK can still succeed on its preemption defense if there is clear evidence that the FDA would have rejected the adult-suicidality warning that plaintiff argues was tortiously omitted. Based on the evidence in this case, we conclude that, as a matter of law, (1) there is clear evidence that the FDA would have rejected

the warning in 2007, and (2) GSK lacked new information after 2007 that would have allowed it to add an adult-suicidality warning under the CBE regulation.[2]

A. *Standard of Review*

Before we can reach the merits of GSK's preemption defense, we must address a threshold issue. Plaintiff argues that we must review the district court's preemption finding for clear error. In the district court, both plaintiff and GSK maintained that preemption under *Levine* was a question of law. The district court initially found that *Levine* preemption was a question of fact to be submitted to the jury. GSK objected to the wording of the court's proposed jury instructions and continued to argue that the issue was a legal one. The district court ultimately omitted the instruction and did not submit the question of preemption to the jury.

Our cases have analyzed preemption under *Levine* as a legal question. In *Guilbeau*, we wrote that "preemption is a legal question for determination by the courts … ." 880 F.3d at 318, quoting *Watters v. Wachovia Bank, N.A.*, 550 U.S. 1, 20 (2007); see *Mason*, 596 F.3d at 390, 393–96 (referring to preemption issue as "a legal one" and analyzing preemption as a matter of law). Recently, the Third Circuit determined that "the ultimate question of whether the FDA would have rejected a label change is a question of fact for the jury rather than for the

[2] Judge Zagel denied GSK's motion for summary judgment on the preemption defense, finding that the FDA's invitation to request a meeting after the fourth denial of a paroxetine-specific warning defeated the *Levine* preemption defense. App. 28. We respectfully disagree with our colleague's finding on this point, though our decision is based on the trial record rather than the summary judgment record. The case was later reassigned from Judge Zagel to Judge Hart for trial.

court." *In re Fosamax Products Liability Litig.*, 852 F.3d 268, 282 (3d Cir. 2017). The district court in this case relied on the Third Circuit's decision when it proposed submitting the preemption defense to the jury.

The Third Circuit noted that other circuits treat the *Levine* "test" as "a legal question." *Id.* at 287 & nn.103–105 (collecting cases). To reach a contrary conclusion, the Third Circuit relied in part on *Boyle v. United Technologies Corp.*, 487 U.S. 500 (1988), which addressed conflict preemption for products liability claims against manufacturers of military equipment whose products must comply with military specifications. The Court stated that "whether the facts establish the conditions for the [government specification] defense is a question for the jury." *Id.* at 514. The Supreme Court has granted certiorari to review the Third Circuit's decision on this issue. *Merck Sharp & Dohme Corp. v. Albrecht*, 138 S. Ct. 2705 (2018).

We need not determine in this case whether preemption under *Levine* involves a factual question for the jury. As the Third Circuit noted, "when no reasonable jury applying the clear-evidence standard" could "conclude that the FDA would have approved a label change," then "the manufacturer will be entitled to judgment as a matter of law." *In re Fosamax*, 852 F.3d at 282. That is the case here. As we explain next, given the facts in this case, no reasonable jury could find that the FDA would have approved an adult-suicidality warning for Paxil under the CBE regulation between 2007 and Stewart Dolin's suicide in 2010.

B. *Clear Evidence of Rejection?*

GSK has provided undisputed evidence that the FDA rejected any adult-suicidality warning in 2007 when the agency

required all SSRIs to adopt the same class-wide warnings. By 2000, a potential association between SSRIs and suicide was a high-profile controversy at the center of the FDA's attention. As part of its response to that controversy, the agency reviewed data on suicidal behavior in patients taking paroxetine. In 2007, after completing that review, the FDA ordered GSK to remove a paroxetine-specific warning of increased suicide risk in adults from the paroxetine label. It is hard to imagine clearer evidence that, considering the data available in 2007, "the FDA would not have approved a change" to the paroxetine label at that time. *Levine*, 555 U.S. at 571. No reasonable jury could find otherwise.

When deciding preemption in this context, "*Levine* is our intellectual anchor." *Mason*, 596 F.3d at 392. We "look at the long and fairly extensive administrative history" for the drug in *Levine* "and compare it to the administrative history of Paxil." *Id.* In *Levine*, the Court found four key facts critical when it found no preemption: (1) there was "no evidence … that either the FDA or the manufacturer gave more than passing attention" to the risk at issue; (2) the manufacturer had not "supplied the FDA with an evaluation or analysis" of the risk; (3) the manufacturer never "attempted to give the kind of warning required" under state law; and (4) the FDA "had not made an affirmative decision" to reject the warning. *Id.* at 572–73.

All four of those evidentiary gaps in *Levine* were filled here. In 2006, GSK re-analyzed the placebo-controlled data on paroxetine and found a link between paroxetine and suicide in adults. It then made a unilateral change to the label, using the CBE regulation and adding a warning "that the higher fre-

quency" of suicidality "observed in the younger adult population … may extend beyond the age of 24." GSK submitted that data to the FDA. But within a year, the FDA completed its own analysis of the same data and ordered GSK to remove that warning. The FDA notified manufacturers that all SSRIs needed to contain the same warning, saying there was a risk of suicide in patients under 24 but that "studies did not show an increase in the risk of suicidality … in adults beyond age 24."

After the FDA effectively told it to remove the paroxetine-specific warning, GSK followed up with four requests to reconsider and to allow that warning. Each time, the FDA told GSK not to add the paroxetine-specific warning. These requests by GSK and the responses are clearly documented. They are not subject to reasonable dispute. This is clear evidence that, as of 2007, the FDA rejected an adult-suicidality warning for paroxetine.

To avoid the consequences of this evidence, plaintiff raises two arguments. Neither argument undermines the preemptive effect of the FDA's actions or decisions. First, plaintiff argues that the FDA rejected the paroxetine-specific warning only because GSK proposed adding it to the wrong spot on the label. GSK proposed warning about the risks of paroxetine in the middle of the class-wide SSRI warning, which FDA wanted to maintain as a uniform warning for all SSRIs. Because GSK never proposed adding the warning elsewhere in the label, plaintiff argues, there is no "clear evidence" that the FDA would have rejected a proposal along those lines.

This is an unreasonable interpretation of the discussions between the FDA and GSK. When the FDA rejected GSK's

paroxetine-specific warning, the relationship between suicide, age, and SSRI use was at the forefront of the agency's attention. The FDA had just completed two lengthy meta-analyses on the topic. In its analyses, the FDA observed a statistically significant association between paroxetine and suicidal behavior in adults, but decided to discount that result in favor of uniform SSRI labeling. That labeling affirmatively stated that SSRIs' "net effect appears to be neutral on suicidal behavior but possibly protective for suicidality for adults between the ages of 25 and 64." Plaintiff asks us to believe that the FDA—after deciding against an adult-suicidality warning based on its own analysis—rejected GSK's warning only because GSK proposed putting it in the wrong place. That is unreasonable.

Second, plaintiff argues that GSK could have followed up with a formal meeting with the FDA to discuss the paroxetine-specific warning. According to plaintiff, GSK lacks clear evidence that the FDA would have rejected the warning after such a meeting. This misunderstands the preemption standard. State laws requiring a label change are preempted unless the manufacturer could unilaterally add the new warning under the CBE regulation. *Levine*, 555 U.S. at 573; see also *Mensing,* 564 U.S. at 620.

The Supreme Court has rejected a very similar preemption argument in *Mensing*, where the Court held that federal law preempts state laws that require generic drug manufacturers to change a drug's label. In reaching that conclusion, the Court rejected the plaintiff's argument that the generic manufacturer could have asked the FDA to change the brand-name label. 564 U.S. at 619–20. The Court explained: "when a

party cannot satisfy its state duties without the Federal Government's special permission and assistance, which is dependent on the exercise of judgment by a federal agency, that party cannot independently satisfy those state duties for preemption purposes." *Id.* at 623–24. That is what plaintiff's second argument amounts to. The preemption analysis asks only whether GSK could have added the adult-suicidality warning through the CBE regulation, not whether GSK might have been able to persuade the FDA to change its mind in a formal meeting—and certainly not whether GSK could have persuaded the FDA after already asking four times to include that warning and being told no four times.[3]

C. *Newly Acquired Information?*

The FDA's rejection of the adult-suicidality warning in 2007 does not definitively answer whether GSK could have added the warning between 2007 and 2010, when Stewart Dolin took paroxetine and committed suicide. The CBE regulation allows manufacturers to add or strengthen a warning when they acquire new information about the drug that makes the warning necessary. Plaintiff has failed to offer evidence that GSK acquired new information after 2007, when

[3] In *Mason*, we found that GSK's predecessor had not shown the clear evidence needed for *Levine* preemption for a 23-year-old's suicide that occurred in 2003. 596 F.3d at 395–96. *Mason* thus addressed a suicide by a patient who would have fallen within the scope of the 2004 and 2007 class-wide warnings for pediatric suicide risk, so it does not control the preemption question here. Plaintiff also cites *Tucker v. Smithline Beecham Corp.*, 596 F. Supp. 2d 1225, 1236 (S.D. Ind. 2008), which similarly found that GSK's predecessor had not established a preemption defense for Paxil. *Tucker* addressed a 55-year-old's suicide in 2002, and was decided before *Levine* and *Mensing*, so its analysis does not apply here, to a 2010 suicide with the direction of *Levine* and *Mensing* available to the court.

the FDA rejected its proposal to add an adult-suicidality warning to the paroxetine label that would have justified a change in the label and thus undermine GSK's preemption defense.

Newly acquired information "is data, analyses, or other information not previously submitted to the Agency." 21 C.F.R. § 314.3. Newly acquired information is not limited to new data. It includes new analysis of old data. *Id*. The "rule accounts for the fact that risk information accumulates over time." *Levine*, 555 U.S. at 569.

Plaintiff proposes two ways that GSK had newly acquired information that supported the paroxetine-specific warning. First, plaintiff argues that GSK withheld or manipulated data in its submissions to the FDA. Plaintiff argues that the complete, untainted data showed an association between paroxetine and suicide in adults, and that the FDA never considered this information.

This argument fails because the undisputed evidence shows that the FDA was aware of the nature of the data it received from GSK. Plaintiff argues that GSK improperly attributed suicides that occurred in the "wash-out" phase of drug tests as occurring on the placebo. The wash-out phase refers to the period when patients are given placebos to wash out other drugs in their system before the study begins. By attributing negative incidents that occurred during the wash-out phase to the placebo, Paxil looks better by comparison.

We have already rejected this argument about the same Paxil/paroxetine data in *Mason*. 596 F.3d at 394. As we noted then, "each erroneous datum had a star by it which noted that part of the suicidal behavior occurred during the wash-out

phase." *Id.* The FDA scientist who reviewed the data "understood that the wash-out events were included when he analyzed the data," and his analysis "found no relationship between Paxil and suicidal behavior." *Id.* And in 2002 and 2003, GSK re-analyzed the data while excluding the wash-out phase and submitted that data to the FDA. *Id.*

Plaintiff points to one other possible source of newly acquired information. She offers an article published in 2011 as evidence that GSK conducted a re-analysis in 2008 that found a statistically significant association between adult suicidality and paroxetine. Plaintiff's expert testified, however, that this was not new analysis. He testified that the article was "submitted for publication in 2008 and published in 2011," but "was based on" GSK's "2006 analysis." The article contained the same figures as GSK's 2006 analysis, which GSK submitted to the FDA. There is no basis to conclude that this was a new analysis or that it was "not previously submitted to the Agency." 21 C.F.R. § 314.3.

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GSK asked the FDA for permission to modify the paroxetine label as plaintiff argues was needed. The FDA said no, repeatedly. Federal law thus preempted plaintiff's Illinois-law claim that GSK should have warned of a risk of adult suicidality on the paroxetine label in 2010. GSK added a similar warning in 2006, and the FDA ordered that GSK remove that label and replace it with a class-wide SSRI warning in 2007. As a matter of law, this is what *Levine* called "clear evidence" that the FDA would have rejected the warning that plaintiff seeks under Illinois law. After 2007, GSK lacked newly acquired information that would have allowed it to add an adult-suicidality warning under the CBE regulation.

The parties and amici have briefed extensively whether Illinois law would impose a duty on a brand-name drug manufacturer toward a patient like Stewart Dolin, who took a generic form of the drug manufactured by a different company. The Illinois courts have not yet considered the new theory of liability that plaintiff advances. Because the evidence of federal preemption is decisive, we do not offer for that question of duty a prediction of state law under *Erie Railroad Co. v. Tompkins*, 304 U.S. 64 (1938). We also need not consider GSK's other arguments based on the trial evidence. The judgment of the district court is REVERSED.