2019 IL App (1st) 171969

No. 1-17-1969 & 1-17-1970 (cons.)

Opinion filed January 23, 2019

THIRD DIVISION

IN THE
APPELLATE COURT OF ILLINOIS
FIRST DISTRICT

DANITTA RINDER, Individually and as Special Administrator of the Estate of Gregg Rinder, GAY LYNNE BRINKLEY, Individually and as Executor of the Estate of Myra Jo Brinkley, and ALAN C. PAPROCKI, Individually and as Executor of the Estate of Carolyn J. Paprocki, Plaintiffs-Appellees, v. MERCK SHARP & DOHME CORP., Defendant-Appellant.	)	Appeal from the Circuit Court of Cook County Nos. 13 L 3244 and 13 L 10283 The Honorable Daniel T. Gillespie, Judge Presiding.
SALLY DONZELLI, Individually and as Special Administrator of the Estate of George Donzelli, Plaintiff-Appellee, v. MERCK SHARP & DHOME CORP., Defendant-Appellant.	)	

PRESIDING JUSTICE FITZGERALD SMITH delivered the judgment of the court, with opinion.

Justices Howse and Cobbs concurred in the judgment and opinion.

OPINION

¶ 1 This consolidated appeal involves two pharmaceutical product liability lawsuits concerning the drug Januvia, which is manufactured and marketed by the defendant, Merck Sharp & Dhome Corp. (Merck). The two lawsuits involve four plaintiffs, who allege their family members died of pancreatic cancer caused by their use of Januvia. The plaintiffs allege that, as of the time their family members were taking Januvia, Merck knew that use of Januvia caused or increased the risk of developing pancreatic cancer and it failed to warn of this risk in the drug's labeling. The four plaintiffs' decedents used Januvia at various times between 2007 and 2012. It is undisputed that Januvia's labeling did not contain any mention of pancreatic cancer.

¶ 2 Januvia was approved by the United States Food and Drug Administration (FDA) in 2006 as a drug to treat type 2 diabetes, a disease that results in chronically elevated blood-sugar levels. If left untreated, type 2 diabetes can lead to various significant health complications. Januvia is one of two classes of drugs sometimes referred to as "incretin-based therapies." Incretins are gastrointestinal hormones that cause an increase in the amount of insulin released from cells in the body after eating. Incretin-based therapies essentially prolong the effect of an incretin hormone that stimulates the production of insulin and in turn lowers blood sugar.

¶ 3 Merck filed a motion for summary judgment, arguing that the plaintiffs' failure-to-warn claims were preempted by federal law. Specifically, Merck argued that federal law made it impossible for Merck to satisfy its duties under state tort law (*i.e.*, by providing the warnings on Januvia's label that the plaintiffs alleged were necessary) because, according to the federal statutes and regulations that controlled the labeling of pharmaceutical drugs, the FDA would have rejected any attempt by Merck to add that warning to Januvia's label. This appeal addresses the specific question of whether Merck's affirmative defense presents a question to be resolved by the judge or by a jury. The trial court ruled that the question presented a factual inquiry that a

jury should decide, and it denied Merck's motion for summary judgment. In doing so, however, it certified to this court the following question of law pursuant to Illinois Supreme Court Rule 308 (eff. July 1, 2017):

> " 'Under *Wyeth v. Levine*, 555 U.S. 555 (2009), federal law preempts state-law failure to warn claims related to use of a prescription drug if there is ' "clear evidence" ' that the FDA would not permit the manufacturer to include the plaintiff's requested warning in the drug's labeling. Is the question whether the defendant has presented the necessary ' "clear evidence" ' one for resolution by the court or jury?' "

For the reasons set forth below, our answer to the certified question is that the issue should be resolved by the jury.

¶ 4 BACKGROUND

¶ 5 To provide the necessary context for the parties' arguments, we first set forth an explanation of the federal statutory and regulatory framework that governs the labeling of prescription drugs. We must then briefly discuss the "clear evidence" test that the Supreme Court set forth in *Wyeth*, 555 U.S. at 571, which addressed when a state law failure-to-warn claim is preempted by those federal drug-labeling regulations. Against this background, we will address the nature of the dispute raised by Merck's motion for summary judgment about whether "clear evidence" exists that the FDA would not have permitted it to add a pancreatic cancer warning to Januvia's labeling. This will then allow us to proceed with our analysis of the certified question, whether the issue presented in the "clear evidence" test is to be decided by the judge or jury.

¶ 6 Federal Drug Labeling Statutes and Regulations

¶ 7 The Federal Food, Drug, and Cosmetic Act governs the marketing and sale of prescription drugs in the United States. 21 U.S.C. § 301 *et seq.* (2012). It prohibits any drug from being

introduced into interstate commerce unless the FDA approves an application in which the manufacturer shows that the drug is safe and effective. *Id.* § 355. The application must also include "the labeling proposed to be used for such drug." *Id.* § 355(b)(1)(F); 21 C.F.R. § 314.50(c)(2)(i) (2012).

¶ 8 All prescription drug labeling must include certain information, including among other things a "warnings and precautions" section and an "adverse reactions" section. 21 C.F.R. § 201.57(a)(10)-(11) (2012). The "warnings and precautions" section must "describe clinically significant adverse reactions," including "any that are potentially fatal" or "are serious even if infrequent." *Id.* § 201.57(c)(6)(i). The "adverse reactions" section is broader than the warnings and precautions section and describes the overall adverse reaction profile of the drug. *Id.* § 201.57(c)(7). An adverse reaction is defined as "an undesirable effect, reasonably associated with use of a drug, that may occur as part of the pharmacological action of the drug or may be unpredictable in its occurrence." *Id.* It includes "only those adverse events for which there is some basis to believe there is a causal relationship between the drug and the occurrence of the adverse event." *Id.*

¶ 9 The Supreme Court has explained that it is a "central premise of federal drug regulation that the manufacturer bears responsibility for the content of its label at all times." *Wyeth*, 555 U.S. at 570-71. The drug's manufacturer "is charged both with crafting an adequate label and with ensuring that its warnings remain adequate as long as the drug is on the market." *Id.* at 571; see also 21 U.S.C. § 355(o)(4)(I) (2012).

¶ 10 Fulfilling this latter responsibility may involve revising the drug's label following its initial approval, and the FDA regulations provide drug manufacturers with two options for doing so. The first and more common option, which is not the one generally involved in cases applying the

Wyeth inquiry, requires the manufacturer to submit an application and obtain the FDA's approval for the label change prior to making changes.[1] 21 C.F.R. § 314.70(b)(2)(v)(A), (b)(3) (2012).

¶ 11 The second option, which is the one generally involved in cases applying the *Wyeth* "clear evidence" inquiry, is known as the "changes being effected" or "CBE" regulation. The CBE regulation provides for several situations in which a manufacturer is allowed to change a drug's label without obtaining prior approval from the FDA. *Id.* § 314.70(c)(6)(iii); *Wyeth*, 555 U.S. at 568. One of those situations is a label change "to reflect newly acquired information"[2] to "add or strengthen a contraindication, warning, precaution, or adverse reaction for which the evidence of a causal association satisfies the standard for inclusion in the labeling under [21 C.F.R.] § 201.57(c)." 21 C.F.R. § 314.70(c)(6)(iii)(A) (2012). The standard for inclusion set forth in 21 C.F.R. § 201.57(c) provides in part that "labeling must be revised to include a warning about a clinically significant hazard as soon as there is reasonable evidence of a causal association with a drug; a causal relationship need not have been definitely established." *Id.* § 201.57(c)(6)(i). In its notice of the final rule concerning 21 C.F.R. § 314, the FDA explained this standard further:

> "If new safety information meets the requirements of § 201.57(c)(6), it is appropriate for inclusion in the labeling of a drug or biologic and a sponsor must update its labeling 'as soon as' such information becomes available. That section states that causation need not

[1]This option is known as the "Prior Approval Supplement" or "PAS." In cases involving the *Wyeth* inquiry, the PAS procedure is generally not involved because the FDA regulations provide that prior FDA approval is not required for a label change to "add or strengthen a contraindication, warning, precaution, or adverse reaction," which is the kind of label change usually at issue in cases involving the *Wyeth* inquiry. 21 C.F.R. § 314.70(b)(2)(v)(A), (c)(6)(iii)(A) (2012). As discussed below, such a change can be made by the manufacturer through the CBE regulation without requiring prior FDA approval. The PAS option may be involved in cases involving the *Wyeth* inquiry where the manufacturer submitted a PAS application.

[2]"Newly acquired information" is defined as "data, analyses, or other information not previously submitted to [FDA], which may include (but are not limited to) data derived from new clinical studies, reports of adverse events, or new analyses of previously submitted data (*e.g.*, meta-analyses) if the studies, events or analyses reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA." 21 C.F.R. § 314.3(b) (2012).

> have been 'definitely established' for a warning to be required to appear in labeling, but rather that there need only be 'reasonable' evidence of a causal association with the drug, a standard that could be met by a wide range of evidence. A CBE submission may be made when the evidence meets the standard set forth in this rule, even if that evidence would not also support a higher evidentiary standard, such as a finding that there is a 'preponderance' of evidence that a product actually causes a particular kind of adverse event. A sponsor's submission or FDA's acceptance of a CBE supplement does not necessarily mean that a drug product actually has caused any particular adverse event or type of adverse event." Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices, 73 Fed. Reg. 49,603, 49,604 (Aug. 22, 2008).

Significantly, however, the FDA does review all submissions pursuant to the CBE regulation and can reject or rescind label changes after the manufacturer has made them. 21 C.F.R. § 314.70(c)(6), (c)(7) (2012). The CBE regulation's requirements ensure that "only scientifically justified information is provided in the labeling for an approved product." Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices, 73 Fed. Reg. 2848, 2851 (Jan. 16, 2008). Thus, the FDA would not allow a change to labeling to add a warning in the absence of reasonable evidence of an association between the product and an adverse event. *Id.*

¶ 12 *Wyeth* and the "Clear Evidence" Test

¶ 13 In *Wyeth*, 555 U.S. at 568-73, the Supreme Court addressed the regulatory framework set forth above in considering a drug manufacturer's argument that, under principles of federal preemption, a plaintiff's failure-to-warn claim under state law was barred because it was

impossible for the drug manufacturer to comply with a state-law duty to modify a drug's labeling without violating federal drug labeling laws. The Supreme Court held that state-law claims based on deficiencies in a drug's labeling are not preempted by federal law if the drug manufacturer could have added the warning under the CBE regulation, which did not require prior FDA approval. *Id.* at 573. However, it recognized that the FDA retained authority to reject labeling changes that a manufacturer made through the CBE regulation. *Id.* at 571. It went on to hold that, "absent clear evidence that the FDA would not have approved a change to [the drug's] label, we will not conclude that it was impossible for Wyeth to comply with both federal and state requirements." *Id.*

¶ 14 This statement has developed into a standard that is often referred to as the "clear evidence" test or the "*Wyeth* inquiry." Beyond this sentence, however, the Supreme Court did not elaborate on how lower courts should apply this standard,[3] and "lower courts have struggled to make it readily administrable." *In re Fosamax (Alendronate Sodium) Products Liability Litigation*, 852 F.3d 268, 282 (3d Cir. 2017), *cert. granted sub nom. Merck Sharp & Dohme Corp. v. Albrecht*, ___ U.S. ___, 138 S. Ct. 2705 (2018). As discussed in detail below, one aspect of this test about which lower courts have not agreed is whether it presents a question to be decided by a judge or by a jury.

¶ 15 Merck's Motion for Summary Judgment

¶ 16 The *Wyeth* inquiry arose in this case when Merck filed a motion for summary judgment, arguing that "clear evidence" existed that the FDA would not have approved a warning for

[3] In a footnote in a later case, the Supreme Court described the "clear evidence" test it had set forth in *Wyeth* as follows: "The FDA, however, retained the authority to eventually rescind Wyeth's unilateral CBE changes. Accordingly, the Court noted that Wyeth could have attempted to show, by 'clear evidence,' that the FDA would have rescinded any change in the label and thereby demonstrate that it would in fact have been impossible to do under federal law what state law required." *PLIVA, Inc. v. Mensing*, 564 U.S. 604, 624 n.8 (2011) (citing *Wyeth*, 555 U.S. at 571).

pancreatic cancer if it had tried to add one to Januvia's labeling. In support of its motion, Merck submitted medical journal articles, various forms of FDA correspondence, memoranda, documentation, and communications involving Januvia and other drugs, part of the FDA staff manual, and expert deposition transcripts. Merck argued that, to decide this inquiry, the trial court "should compare the facts concerning FDA's evaluation of incretin drugs and pancreatic-cancer risk with the facts" that had been held insufficient in *Wyeth*, 555 U.S. at 573, and *Mason v. SmithKline Beecham Corp.*, 596 F.3d 387, 396 (7th Cir. 2010), and the trial court should conclude that the "evidence that was missing" in those cases was present in this case. Specifically, Merck argued that its evidence showed that since at least 2009, the FDA had been investigating the pancreatic safety of incretin-based medications, it had conducted a serious scientific study of the issue, and it made an affirmative scientific decision that the evidence did not warrant a change in labeling.

¶ 17 First, Merck submitted two FDA memoranda showing that in 2009, the FDA had reviewed its adverse event reporting databases for incidents of pancreatic cancer associated with use of Januvia and Bayetta, a similar drug. One memorandum stated that "little inference for risk [could be] appreciated from review of spontaneous reports of pancreatic cancer in adult recipients" of the drugs, as pancreatic cancer is relatively common in adults. In response, the plaintiffs argued that more recent statements by the FDA indicated a greater level concern that a causal association exists between pancreatic cancer and use of Januvia.

¶ 18 Second, Merck argued that in 2009, the FDA required the manufacturer of Bayetta to conduct pancreatic safety studies of that drug to assess the relative risk of pancreatic cancer and patients using metformin or glyburide. In response, the plaintiffs argued this fact supported their contention that the FDA would recognize the existence of "some basis to believe there is a causal

relationship" between incretin-based drugs and pancreatic cancer, which would have satisfied the standard for Merck to have added pancreatic cancer as an "adverse reaction" to Januvia's label through the CBE regulation. See 21 C.F.R. §§ 201.57(c)(7), 314.70(c)(6)(iii)(A) (2012).

¶ 19 Third, Merck relied on a 2013 communication issued by the FDA titled, "FDA Drug Safety Communication: FDA investigating reports of possible increased risk of pancreatitis and pre-cancerous findings of the pancreas from incretin mimetic drugs for type 2 diabetes" (2013 Drug Safety Communication). Food & Drug Admin., FDA Drug Safety Communication: FDA Investigating Reports of Possible Increased Risk of Pancreatitis and Pre-Cancerous Findings of the Pancreas From Incretin Mimetic Drugs for Type 2 Diabetes (Mar. 14, 2013), https://www.fda.gov/Drugs/DrugSafety/ucm343187.htm [https://perma.cc/ZNG2-AUVV]. The plaintiffs also relied on this same communication as significant evidence supporting their position. The 2013 Drug Safety Communication was apparently prompted by the findings of Dr. Peter Butler and his colleagues, who conducted a study that concluded that the use of Januvia increased the odds of developing pancreatitis and pancreatic cancer. Because the 2013 Drug Safety Communication is significant to an understanding of both parties' arguments, its pertinent text is set forth as follows:

> "The U.S. Food and Drug Administration (FDA) is evaluating unpublished new findings by a group of academic researchers that suggest an increased risk of pancreatitis, or inflammation of the pancreas, and pre-cancerous cellular changes called pancreatic duct metaplasia in patients with type 2 diabetes treated with a class of drugs called incretin mimetics. These findings were based on examination of a small number of pancreatic tissue specimens taken from patients after they died from unspecified causes. FDA has asked the researchers to provide the methodology used to collect and study

these specimens and to provide the tissue samples so the Agency can *further investigate potential pancreatic toxicity associated with the incretin mimetics*.

***

FDA has not reached any new conclusions about safety risks with incretin mimetic drugs. This early communication is intended only to inform the public and health care professionals that the Agency intends to obtain and evaluate this new information. *FDA will communicate its final conclusions and recommendations when its review is complete or when the Agency has additional information to report.*

*** FDA has not previously communicated about the potential risk of pre-cancerous findings of the pancreas with incretin mimetics. Further, FDA has not concluded these drugs may cause or contribute to the development of pancreatic cancer.

***

*FDA is continuing to evaluate all available data to further understand this potential safety issue. ****" (Emphases added.) *Id.*

¶ 20 The parties disputed the scope of what the FDA actually evaluated after it announced it was conducting an evaluation in the 2013 Drug Safety Communication. According to Merck, the FDA was announcing it would "conduct a comprehensive evaluation of a possible association between incretin-based medications and pancreatic cancer," and that it would consider the entire body of scientific research and data available to date, as well as the Agency's own " 'further investigat[ion] [into the] potential pancreatic toxicity associated with the incretin mimetrics.' " (Brackets used by Merck.) The plaintiffs, by contrast, argued that the study the FDA undertook was merely "a 'comprehensive' evaluation of the Butler group's findings, not of the 'totality of available scientific data.' "

¶ 21 The plaintiffs argued that the 2013 Drug Safety Communication was the most significant statement of the FDA's position relevant to the issue of whether "clear evidence" existed that the FDA would have rejected an attempt by Merck to add a pancreatic cancer warning to Januvia's label through the CBE regulation. They pointed to its statements that the FDA was continuing to evaluate all available data to understand the issue and would communicate its final conclusions and recommendations when the review was complete or when it had additional information to report. They further cited the requirement of the FDA's Guidance on Drug Safety Information that a document such as the 2013 Drug Safety Communication was to be updated if "data become available that provide sufficient evidence that a drug is not associated with the safety concern previously described by the Agency as an emerging drug safety issue," and they pointed out that the FDA had not updated the 2013 Drug Safety Communication through any of its official methods for doing so as of the as of the time of the summary judgment briefing in 2017.

¶ 22 Fourth, Merck argued that the 2013 Drug Safety Communication was followed by a publication by Dr. Amy G. Egan, *et al.*, in the February 27, 2014, issue of the *New England Journal of Medicine* titled, "Pancreatic Safety of Incretin-Based Drugs—FDA and EMA Assessment" (Egan article). See Amy G. Egan *et al., Pancreatic Safety of Incretin-Based Drugs—FDA and EMA Assessment*, 370 New Eng. J. Med. 794 (2014). (The "EMA" is the European Medicines Agency.) The significance of the Egan article was a major point of disagreement between the parties.

¶ 23 Merck argued that the Egan article constituted "an official statement of FDA," in which the "FDA stated that (i) the scientific data do not support a causal association between the medications and pancreatic cancer, (ii) there is no evidence to support a change to the existing labeling, and (iii) the current warnings are adequate." Merck pointed to the article's statements

that the FDA performed its own pancreatic toxicology studies with exenatide (Bayetta) using three rodent models of disease and a non-diseased control. Data from two of the models did not identify exenatide-related pancreatic injury, and the third showed minimal-to-moderate exacerbations of background findings after 12 weeks of treatment meriting further investigation. Merck pointed to the article's statement that the FDA reevaluated more than 250 toxicology studies conducted in nearly 18,000 healthy animals, which yielded no findings of overt pancreatic toxic effects or pancreatitis. Merck also pointed to a similar EMA review showing drug-induced pancreatic tumors were absent in rats and mice that had been treated up to 2 years with incretin-based drugs, even at doses that greatly exceeded the level of human clinical exposure. Merck pointed to the article's statement that the FDA had required sponsors of marketed incretin-based drugs to conduct 3-month pancreatic toxicity studies in a rodent model of diabetes, of which three had been submitted reporting no treatment-related adverse effects on the pancreas. Also, three FDA pathologists conducted independent and blinded examinations of approximately 120 histopathology slides from one of the three studies, and those examinations were "generally concordant with the sponsor's report." Merck also cited the statement in the report that a pooled analysis of data from 14,611 patients with type 2 diabetes from 25 clinical trials in the sitagliptin (Januvia and Janumet) database provided no compelling evidence of an increased risk of pancreatitis or pancreatic cancer.

¶ 24 Merck argued that, based on the results of the study reported in the Egan article, the FDA made an affirmative decision that the scientific evidence did not warrant a change in Januvia's labeling, a fact that indicated it would have rejected an attempted change through the CBE regulation. Merck relied on the following passage from the Egan article:

> "Both agencies [*i.e.*, FDA and EMA] agree that assertions concerning a causal association between incretin-based drugs and pancreatitis or pancreatic cancer, as expressed recently in the scientific literature and in the media, are inconsistent with the current data. The FDA and the EMA have not reached a final conclusion at this time regarding such a causal relationship. *** The FDA and the EMA believe that the current knowledge is adequately reflected in the product information or labeling, and further harmonization among products is planned in Europe."

¶ 25 The plaintiffs, by contrast, argued that, for purposes of determining whether "clear evidence" exists that the FDA would have rejected an attempt by Merck to add a pancreatic cancer warning to Januvia's label through the CBE regulation, the second sentence from the above passage is significant, in which the article states the FDA had "not reached a final conclusion at this time regarding such a causal relationship." The plaintiffs pointed to various other statements in the Egan article indicating that the issue of whether a causal association exists between increin-based drugs and pancreatic cancer is the subject of ongoing review within the FDA. Thus, the plaintiffs argued that the statements in the Egan article cannot amount to an "affirmative decision" by the FDA that it would have rescinded an attempt by Merck to amend its label under the CBE regulation, pending the outcome of that review. Instead, they argued that the mere fact that the FDA considers its investigation ongoing, when combined with the existing scientific data, indicates there exists "some basis to believe there is a causal relationship" between use of Januvia and pancreatic cancer, which satisfies the standard for adding it as an "adverse reaction" to Januvia's label. 21 C.F.R. § 201.57(c)(7) (2012). They argued it also satisfies the standard for adding a warning, which does not require causation to be "definitely established" (*id.* § 201.57(c)(6)(i)), but only that there be " 'reasonable' evidence of a causal

association with the drug," which can be met by "a wide range of evidence." Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices, 73 Fed. Reg. at 49,604.

¶ 26 The plaintiffs further argued that the evaluation undertaken by the FDA as reported in the Egan article was not nearly as comprehensive as Merck suggested. The plaintiffs argued the study was merely a review of the findings of Dr. Butler's group, and it did not amount to a rejection by the FDA of any causal connection between incretin-based drugs and pancreatic cancer. The plaintiffs proffered the testimony of a controlled expert witness in FDA labeling, Dr. Alexander Fleming, who testified that the Egan article should be interpreted as an effort to respond to the findings of Dr. Butler's group and to make a "clear statement that this particular assertion, again, by a particular investigator, are not supported by the data [the FDA] reviewed."

¶ 27 The parties also disputed whether the Egan article constituted an "official statement" of the FDA. The parties agreed it constituted an "FDA-Assigned article" under the FDA staff manual. Merck argued that an FDA-Assigned article represents the official position of the FDA, as the absence of a disclaimer on the Egan article stating that it was not an official statement of the FDA means it was an official statement. Merck pointed out that the article states it is by "the Office of New Drugs, Center for Drug Evaluation and Research, Food and Drug Administration" and argued that it is "replete with statements about the 'FDA's' position on the issues." The plaintiffs, by contrast, argued the absence of a disclaimer does not mean the article was an official statement. Rather, they argued that, based on how it was published, under the staff manual and regulations, it amounts merely to "an informal communication that *** does not necessarily represent the formal position of FDA, and does not bind or otherwise obligate or commit the agency to the views expressed." 21 C.F.R. § 10.85(k) (2012). The plaintiffs

contended that only the document pertinent to this case that constitutes an "official statement" of the FDA under its staff manual is the 2013 Drug Safety Communication.

¶ 28 Fifth, Merck relied on the FDA's denial in 2014 of a petition submitted in 2012 by the Public Citizen's Health Research Group (Public Citizen), requesting that the FDA remove the drug Victoza (liraglutide) from the market. The parties disputed the extent to which the risk of pancreatic cancer was an issue in the Public Citizen's petition, as only two paragraphs of the FDA's 37-page response were dedicated to discussing pancreatic cancer. Merck pointed out that the FDA's response does state that "[a]ny causal association between exposure to Victoza and pancreatic cancer is indeterminate at this time." The response further states,

> "In our review of 49 unique cases recovered from [the FDA's adverse event database] we found no new evidence regarding the risk of pancreatic carcinoma in association with the use of Victoza that would support any changes to the current approved labeling. Therefore, any suspicion of causal association between exposure to Victoza and pancreatic cancer is indeterminate at this time."

¶ 29 The plaintiffs, by contrast, pointed out that Public Citizen's petition did not request a pancreatic cancer warning for Victoza. They argued the FDA's decision not to mandate the addition of a warning is not the same as determining that it would reject a warning the manufacturer attempted to add through the CBE regulation. The plaintiffs cited the testimony of their regulatory expert, Dr. Fleming, that the FDA's denial of the Public Citizen petition does not support the conclusion that FDA found that adverse events reports do not support changes to the current approved labeling for Victoza. They pointed out that, for purposes of assessing clear evidence that the FDA would have rejected an attempted label change by Merck, Dr. Fleming testified it was more significant that the FDA stated it was "indeterminate" whether any causal

association existed between Victoza and pancreatic cancer.

¶ 30 Sixth, Merck relied on a 2014 "FDA Briefing Document" concerning the drug Saxenda (liraglutide). Merck pointed to two statements by FDA reviewers in that document. The first states, "Risk for pancreatic cancer has more recently emerged as a concern with GLP-1-based therapies, including liraglutide. *** However, animal, observational, and clinical trial data reviewed by FDA to date have not supported a causal association." The second states,

> "To date, studies have been inconclusive in evaluating the risk of pancreatic cancer with incretin mimetric use. Both FDA and the [EMA] have explored multiple data streams to evaluate pancreatic toxicity as a potential drug safety signal, which to date, do not support pancreatic cancer as an incretin mimetic-mediated event."

¶ 31 The plaintiffs pointed out that the FDA Briefing Document contained a disclaimer, which Merck did not include in its submission to the trial court, stating the assessments, conclusions, and recommendations therein "do not necessarily represent the final position of the individual reviewers, nor do they necessarily represent the final position of the Review Division or Office." The plaintiffs pointed to other statements in the FDA Briefing Document that, they argued, support their contention that the FDA would not have rejected an attempted label change by Merck through the CBE regulation. For example, they point out that the document confirms "a disproportionate number of liraglutide associated thyroid and pancreatic cancers" and "the medical literature offers inconclusive data to determine the role that liraglutide may play in these malignancies."

¶ 32 Finally, the plaintiffs responded to Merck's overall reliance on the above evidence by arguing that the evidence demonstrated Merck also had "new safety information" that it could have provided to the FDA to substantiate the need for a change to Januvia's label under the CBE

regulation. See Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices, 73 Fed. Reg. at 49,604-05. The plaintiffs argued this "new safety information" included a comprehensive signal assessment provided to Merck in 2013 by Health Canada that found the "use of Januvia may be associated with an increased risk of cancer of the pancreas." The plaintiffs cited testimony by Dr. Fleming giving the opinion that this study by Health Canada outlines both the biological plausibility and disproportionate spontaneous adverse event reports, which would amount to "reasonable evidence of a causal association" between use of Januvia and pancreatic cancer. 21 C.F.R. § 201.57(c)(6)(i) (2012). The plaintiffs also argued that Merck could have provided the FDA with "new safety information" that clinical trials had shown an imbalance of pancreatic cancer cases in users of incretin based drugs. The plaintiffs argued that Merck's regulatory expert admitted in his deposition that an imbalance in clinical trials could affect FDA's assessment.

¶ 33 The trial court issued a written order reviewing the above evidence and the parties' dispute about whether the "clear evidence" test should be decided by the judge or by the jury. The trial court noted that the case was not one in which Merck was able to supply evidence of its own attempts to change Januvia's label and FDA's actual responses to that request. Rather, Merck had submitted circumstantial evidence of how the FDA would have responded if it had tried to do so, in the form of clinical studies, FDA correspondence, clinical data, expert depositions, periodicals, and expert reports. The plaintiffs had submitted similar evidence in opposition to the motion. The trial court stated that, whether the issue of "clear evidence" was decided by a judge or jury, the decision required weighing the evidence, drawing inferences from the facts presented, comparing evidence that is not similar, and assessing the credibility of that evidence. The trial court recognized that under both Illinois and federal law, these responsibilities are

traditionally the function of a jury, not a judge. The trial court stated that the dispute before it "involves extremely complex scientific issues that require explanation and context from the parties' witnesses," and thus the decision would be best made after a full trial in which all evidence is presented. Thus, the trial court concluded the "clear evidence" inquiry should be resolved by the jury. It found that genuine issues of material fact prevented it from granting summary judgment in favor of Merck on its affirmative defense that the plaintiffs' failure-to-warn claims were preempted by federal law. At Merck's request, the trial court certified the question of law to this court as set forth above.

¶ 34 ANALYSIS

¶ 35 The certified question requires us to determine whether it is for a judge or jury to decide in a pharmaceutical product liability case whether a drug manufacture has shown "clear evidence" that the FDA would not have permitted it to include the plaintiffs' requested warning in the labeling of the drug at issue. In most reported cases where this issue has arisen, the question of whether that standard has been satisfied has been resolved by the judge. See, *e.g.*, *In re Depakote*, 87 F. Supp. 3d 916, 921-24 (S.D. Ill. 2015) (granting defendant's motion *in limine* to bar argument it could have changed label through CBE regulation); *Cross v. Forest Laboratories*, 102 F. Supp. 3d 896, 899-901 (N.D. Miss. 2015) (ruling on defendant's motion for summary judgment that plaintiff's failure to warn claim was not preempted); but see *Maya v. Johnson & Johnson*, 97 A.3d 1203, 1222 (Pa. Super. Ct. 2014) (discussing jury instruction on clear evidence test). However, almost universally, this has been done without analysis or discussion of whether the question is one for the judge or jury. The few reported cases that have specifically addressed this issue are not in agreement about who the decision maker should be. The Third Circuit has held it should be decided by a jury. *Fosamax*, 852 F.3d at 282. A federal

district court in California held it should be a question for the judge, although the Ninth Circuit vacated that decision on other grounds. *In re Incretin-Based Therapies Products Liability Litigation*, 142 F. Supp. 3d 1108, 1114 (S.D. Cal. 2015), *vacated*, 721 F. App'x 580 (9th Cir. 2017).[4]

¶ 36 In this case, the trial court concluded the question was one for the jury. Merck argues on appeal that it should be decided by a judge. The plaintiffs argue it should be decided by a jury. The certified question itself presents an issue of law, which we review *de novo*. *De Bouse v. Bayer AG*, 235 Ill. 2d 544, 550 (2009).

¶ 37 The ultimate legal effect of this inquiry involves the federal preemption of state law, something Congress has the power to do under the supremacy clause of the United States Constitution. U.S. Const., art. VI, cl. 2. Three types of federal preemption exist: (1) express preemption, shown by a clear expression of congressional intent to preempt state law; (2) field preemption, shown by comprehensive legislation demonstrating a clear congressional intent to occupy the entire regulatory field; and (3) conflict preemption, shown by a conflict between state and federal law. *City of Chicago v. Comcast Cable Holdings, L.L.C.*, 231 Ill. 2d 399, 404 (2008). This case involves only the third category, conflict preemption, which occurs when it is impossible for a private party to comply with both state and federal requirements. *Kinkel v. Cingular Wireless, LLC*, 223 Ill. 2d 1, 18 (2006); *PLIVA*, 564 U.S. at 618. This includes duties imposed by court decisions applying state tort law. *PLIVA*, 564 U.S. at 608-09. The party raising the defense of conflict preemption must "demonstrate that it was impossible for it to comply with both federal and state requirements." *Wyeth*, 555 U.S. at 573. The Supreme Court has described

[4]Both the Seventh Circuit and the Tenth Circuit have acknowledged the decision reached by the Third Circuit in the *Fosamax* case, but neither court needed to resolve the issue to decide the case before it. *Dolin v. GlaxoSmithKline LLC*, 901 F.3d 803, 812-13 (7th Cir. 2018); *Cerveny v. Aventis, Inc.*, 855 F.3d 1091, 1098, 1103 n.11 (10th Cir. 2017)

impossibility preemption as a "demanding defense." *Id.* In the pharmaceutical labeling context, the Supreme Court has also recognized the importance of state law failure-to-warn cases as a complement to federal drug regulation, as a mechanism for enforcing the requirement that drug manufacturers, not the FDA, bear primary responsibility for the adequacy of their drug's labeling at all times. *Id.* at 578-79.

¶ 38 Merck's first argument on appeal is that, because the question is ultimately one of federal preemption, it should be considered a question of law to be decided by a judge. Merck cites various cases from the Illinois Supreme Court that have stated that federal preemption presents a question of law. See, *e.g.*, *Comcast Cable Holdings*, 231 Ill. 2d at 404 ("Because federal preemption presents a question of law, it is subject to *de novo* review."). Merck goes on to argue that cases considering preemption as a question of law "are consistent with *Wyeth*, which requires primarily legal, not factual, analysis and thus presents a question of law for resolution by the court." Merck argues that the "clear evidence" test requires the decision maker to review agency action, the evidence of which can be found entirely in the public record, and determine whether that action demonstrates that the agency reached a certain conclusion in light of the agency's complex regulatory regime.

¶ 39 This court has acknowledged in the past that, in some instances, determining whether a particular issue presents a question of law to be decided by a judge or a question of fact to be decided by a jury can be difficult. *Kujbida v. Horizon Insurance Agency, Inc.*, 260 Ill. App. 3d 1001, 1004 (1994) (citing *Pullman-Standard v. Swint*, 456 U.S. 273, 288 (1982) (noting the absence of any "rule or principle that will unerringly distinguish a factual finding from a legal conclusion")). In most cases, questions of federal preemption present the types of inquiries judges can resolve as a purely legal issue. Often the inquiry is merely one involving statutory

interpretation, which is a traditionally the function of a judge. For example, the inquiry may involve determining whether Congress clearly expressed an intent to preempt state law (see *Moskowitz v. Washington Mutual Bank, F.A.*, 329 Ill. App. 3d 144, 147 (2002)), whether Congress has legislated in such a comprehensive way as to demonstrate an attempt to occupy an entire regulatory field (see *Kellerman v. MCI Telecommunications Corp.*, 112 Ill. 2d 428, 438-44 (1986)), or whether a federal statute or regulation conflicts with a state one (see *Carter v. SSC Odin Operating Co.*, 237 Ill. 2d 30, 39-50 (2010)).

¶ 40 However, it is also clear that the ultimate legal question of whether a claim under state law qualifies for preemption by federal law may depend on the existence of an underlying question of fact. See *Fosamax*, 852 F.3d at 288 (citing *Boyle v. United Technologies Corp.*, 487 U.S. 500, 514 (1988)); *Brown v. Earthboard Sports USA, Inc.*, 481 F.3d 901, 913 (6th Cir. 2007); *Norfolk Southern Ry. Co. v. Box*, No. 06 C 0641, 2007 WL 1030320, at *14 (N.D. Ill. Mar. 30, 2007); *Uphold v. Illinois Workers' Compensation Comm'n*, 385 Ill. App. 3d 567, 571 (2008). Facts which determine the outcome of litigation often necessitate the simultaneous interpretation of a legal standard and the application of that standard to factual material from which factual inferences must be drawn, giving rise to what is characterized as a mixed question of law and fact. *Kujbida*, 260 Ill. App. 3d at 1004 (citing *Tucker v. Spalding*, 80 U.S. (13 Wall.) 453, 455 (1872); *Baumgartner v. United States*, 322 U.S. 665, 671 (1944)). We believe that the correct characterization of the "clear evidence" inquiry under *Wyeth* is that it is a mixed question of law and fact.

¶ 41 We disagree with Merck's contention that the *Wyeth* inquiry "requires primarily legal, not factual, analysis." Above we set forth in detail the nature of the parties' dispute on this issue to demonstrate that it is substantively a dispute about the state of scientific and medical knowledge

linking the use of Januvia to pancreatic cancer at various points in time and what inferences should be drawn from that knowledge about how the FDA would have responded if Merck had attempted to change Januvia's label. The FDA's regulations provide the legal standards of causation and proof through which that dispute must be analyzed, but the substantive question to be resolved is whether enough was shown through scientific, medical, or other evidence to allow the decision maker to draw a clear conclusion that if Merck had attempted through the CBE regulation to add a pancreatic cancer warning to Januvia's labeling, the FDA would have rescinded that change. See *Wyeth*, 555 U.S. at 571; *PLIVA*, 564 U.S. at 624 n.8. Within this broader dispute are various subsidiary disputes, such as the scope of what the FDA studied scientifically concerning the link between incretin-based drugs and pancreatic cancer and what scientific and medical conclusions it drew from its examination of those issues. Another subsidiary dispute is how the FDA's actions concerning other incretin-based drugs, such as Bayetta, Victoza, and Saxenda, support the conclusion of how it would have viewed an attempted change to Januvia's label. Yet another example is the question of whether Merck had other "new safety information" available that it could have used to substantiate to the FDA that a causal association existed between the use of Januvia and pancreatic cancer and how this would have affected the FDA's decision to allow Merck to change Januvia's label through the CBE regulation. We do not believe these kinds of issues can be classified as questions of law.

¶ 42 As the parties framed their dispute in the trial court, it does not present a case where the issue can be resolved solely by applying the language of FDA regulations to undisputed facts that allow for only one interpretation. Although Merck argues to the contrary, we do not believe this case presents a situation in which the issue can be resolved simply by looking at documentary evidence in light of those regulations. We agree with the trial court that far more

context and explanation would be necessary to appropriately answer this question. Both the plaintiffs and Merck have proffered expert witnesses to testify about how the FDA actually makes drug-labeling decisions, what the FDA has studied or done with respect to the link between various incretin-based drugs and pancreatic cancer, what inferences can fairly be drawn from public or internal statements by FDA employees, and ultimately what conclusions should be drawn from the evidence about how the FDA actually would have responded if faced with an attempt by Merck to add a pancreatic cancer warning to Januvia's labeling. Regardless of whether the decision maker is the judge or jury, we do not believe that the decision could be made without hearing all of the testimony by and cross-examination of all the expert witnesses on all scientific, medical, and regulatory issues in the case.

¶ 43 We believe that Merck overstates the extent to which an understanding of the FDA's "complex regulatory regime" plays the determinative role in the *Wyeth* inquiry. We find the FDA regulations cited to us by both parties, as well as those discussed in the pertinent case law (see, *e.g.*, *Wyeth*, 555 U.S. at 568-73), to be similar to the kinds of legal standards of causation and burdens of proof that juries regularly apply when making decisions in tort cases. For example, the regulations at issue provide that a manufacturer must revise a drug's labeling to include a warning about a clinically significant hazard as soon as there is "reasonable evidence of a causal association with a drug," although a causal relationship need not have been definitely established. 21 C.F.R. §§ 201.57(c)(6)(i), 314.70(c)(6)(iii)(A) (2012). The comments to the final rule elaborate that a manufacturer may revise a label under the CBE regulation "even if that evidence would not also support a higher evidentiary standard, such as a finding that there is a 'preponderance' of evidence that a product actually causes a particular kind of adverse event." Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and

Medical Devices, 73 Fed. Reg. at 49,604. These concepts of "reasonable evidence," "causal association," and evidentiary standards or proof are the same kinds of concepts that we entrust to properly-instructed juries to resolve in almost every tort case. See Illinois Pattern Jury Instructions, Civil, No. 15.01 (2011) (hereinafter IPI Civil No. 15.01) (defining "proximate cause"); IPI Civil No. 21.01 (defining burden of proof in civil cases). We see no reason why a different practice would be required with the *Wyeth* inquiry.

¶ 44 Rather, we find that the issue presented by the *Wyeth* inquiry is simply a particular application of the task juries regularly perform in tort cases, determining what the evidence shows probably would have happened if the allegedly wrongful conduct had not occurred. In this case, the allegedly wrongful conduct is the failure to add a pancreatic cancer warning to the labeling for Januvia. The *Wyeth* inquiry asks whether, if this had not occurred, and Merck did in fact add such a warning through the CBE regulation, there is nevertheless clear evidence that the FDA would have rescinded it. Juries are commonly given the task of resolving questions of what probably would have happened absent allegedly wrongful conduct. See, *e.g.*, *Lee v. Chicago Transit Authority*, 152 Ill. 2d 432, 455 (1992) (cause-in-fact aspect of proximate cause inquiry requires jury to determine whether, absent defendant's conduct, injury still would have occurred); *Clark v. Children's Memorial Hospital*, 2011 IL 108656, ¶ 29 (determining compensatory damages requires jury to determine "the position [the injured party] would have occupied if the wrong had not been committed"); *Buck v. Charletta*, 2013 IL App (1st) 122144, ¶¶ 68-73 (in medical negligence cases involving failure to communicate medical information, jury determines whether plaintiff would have received the same medical treatment if communication had occurred); *Nelson v. Quarles & Brady, LLP*, 2013 IL App (1st) 123122, ¶¶ 71-73 (in legal malpractice cases, jury determines what the outcome of underlying litigation

would have been if the alleged malpractice had not occurred); *Adams v. Family Planning Associates Medical Group, Inc.*, 315 Ill. App. 3d 533, 544-46 (2000) (jury applying doctrine of *res ipsa loquitur* determines if injury would ordinarily have occurred in absence of negligence).

¶ 45 Despite the fact that the ultimate legal effect of the *Wyeth* inquiry involves federal preemption, we believe that its factual underpinnings require it to be classified not as a pure question of law, but as a mixed question of fact and law. Where mixed questions are presented, their resolution can involve an allocation of function between judge and jury. *Kujbida*, 260 Ill. App. 3d at 1004. However, where a jury is the trier of fact, the usual procedure is that the trial judge instructs the jury as to the legal standard which should govern, and the jury then determines the ultimate fact by applying that legal standard to the evidence presented. *Id.* (citing *Tucker*, 80 U.S. (13 Wall.) at 455); see also *United States v. Gaudin*, 515 U.S. 506, 512 (1995) ("the application-of-legal-standard-to-fact sort of question ***, commonly called a 'mixed question of law and fact,' has typically been resolved by juries"). We believe that is the proper procedure to be employed in answering the *Wyeth* inquiry presented in this case.

¶ 46 Merck points out that courts faced with motions involving preemption under the *Wyeth* inquiry "overwhelmingly have accepted or rejected the defense themselves with no involvement from the jury." We have reviewed the many cases cited to us by Merck, and we do agree that it appears that in most (although not all) of the reported cases involving the *Wyeth* inquiry, the inquiry has been decided by the trial judge or by the reviewing court.

¶ 47 In *Fosamax*, which is the only federal court of appeals case to have specifically analyzed the issue of whether a judge or jury should decide the *Wyeth* inquiry, the Third Circuit rejected this as a persuasive reason for holding that the issue should be decided by the judge and not the jury. *Fosamax*, 852 F.3d at 286-88. The Third Circuit noted that while *Wyeth* itself did not

indicate whether the "clear evidence" test involved a legal or factual question, and it was not possible to divine a clear answer from the Supreme Court's application of the test in *Wyeth* itself, the Supreme Court did decide that the evidence presented in *Wyeth* was not sufficient to satisfy the test. *Id.* at 286-87. The Third Circuit recognized that given this fact, "many federal courts that have applied the *Wyeth* preemption test have simply compared the evidence presented in their cases to the evidence presented in *Wyeth*." *Id.* at 287. As an example of a case where this occurred, the Third Circuit discussed the Seventh Circuit's opinion in *Mason*, noting that in that case the court "walked through the record evidence and concluded that, 'in light of the extensive showing required by [*Wyeth*],' the manufacturer 'did not meet its burden of demonstrating by clear evidence that the FDA would have rejected a label change.' " *Id.* (quoting *Mason*, 596 F.3d at 396). It noted that in *Mason*, the Seventh Circuit "did not explain why the *Wyeth* test should be resolved by the court in the first instance." *Id.* It then went on to state:

> "We do not lightly discount the wisdom of our sister circuits and the district courts that have grappled with these issues. But there is a difference between rejecting another court's considered judgment, on the one hand, and taking up an issue that has not been thoroughly analyzed, on the other. Furthermore, the approach taken by our sister circuits would be entirely consistent with our decision that the 'clear evidence' test is a fact question that is ultimately for a jury to decide. After all, by comparing the evidence presented in these cases with the evidence presented in *Wyeth*, these circuits are in fact engaging in a summary judgment analysis, even if they do not name it." *Id.* at 287-88.

We agree with this assessment by the Third Circuit. We do not believe that the fact that the issue has been decided by the trial judge in most cases is a valid reason for us to hold that this fact-specific decision should be resolved by the trial judge in all cases.

¶ 48 After reviewing the cases cited to us by Merck, we have several observations. First, numerous cases where the district judges have resolved the issue contain statements to the effect that "application of the clear evidence standard is necessarily fact specific." *Dobbs v. Wyeth Pharmaceuticals*, 797 F. Supp. 2d 1264, 1270 (W.D. Okla. 2011); *In re Depakote*, 87 F. Supp. 3d at 922 (same); *In re Incretin-Based Therapies*, 142 F. Supp. 3d at 1115-16 (same); *Koho v. Forest Laboratories, Inc.*, 17 F. Supp. 3d 1109, 1118 (W.D. Wash. 2014) ("the clear evidence standard is a fact based inquiry that depends on the express type of warning at issue and the particular facts of each case"); *Seufert v. Merck Sharp & Dohme Corp.*, 187 F. Supp. 3d 1163, 1170 (S.D. Cal. 2016) (it is a "fact specific inquiry dependent on the particular warning at issue in each case"); *Lofton v. McNeil Consumer & Specialty Pharmaceuticals*, 682 F. Supp. 2d 662, 677 (N.D. Tex. 2010) (court must "determine if there is a material question of fact whether 'the FDA would not have approved a change' to [the drug's] label" (quoting *Wyeth*, 555 U.S. at 571)). As discussed above, we concur with the statements by these courts that this is a fact-specific inquiry.

¶ 49 Second, we believe the cases cited to us by Merck fall into several categories. The minority of cases have involved the proverbial "smoking gun" evidence of an actual rejection by the FDA of the proposed warning at issue. In such cases, the court can determine that no reasonable decision maker applying the "clear evidence" standard could ever conclude that the FDA would have approved the label change. See *Dolin*, 901 F.3d at 813 (manufacturer changed drug label to add warning under CBE regulation and FDA ordered manufacturer to remove the warning); *Cerveny*, 855 F.3d at 1103 n.11 (FDA's multiple rejections of citizen's petition seeking to add virtually identical warning to drug at issue "would foreclose any reasonable juror from finding that the FDA would have approved warnings" proposed by plaintiff); *Rheinfrank v. Abbott*

Laboratories, Inc., 680 F. App'x 369, 386 (6th Cir. 2017) (several years after injury at issue, manufacturer sought FDA approval to add warning and FDA responded that the warning should not be added to label); *In re Depakote*, 87 F. Supp. 3d at 921-23 (same); *Christison v. Biogen Idec Inc.*, 199 F. Supp. 3d 1315, 1347-48 (D. Utah 2016) (manufacturer met with FDA regulators twice to discuss potential labeling change at issue, and FDA rejected the proposed labeling changes); *Amos v. Biogen Idec Inc.*, 249 F. Supp. 3d 690, 699-700 (W.D.N.Y. 2017) (same); *Reckis v. Johnson & Johnson*, 28 N.E.3d 445, 457-58 (Mass. 2015) (FDA's rejection of citizen's petition proposing specific mention of two medical conditions on label because most consumers were unfamiliar with the conditions constituted clear evidence it would have rejected proposed labeling change adding names of conditions).

¶ 50 The majority of the cases cited to us by Merck have involved situations in which the courts reviewed the drug manufacturer's evidence and found that it was inadequate to support the affirmative defense of conflict preemption. *Mason*, 596 F.3d at 393-96; *Gaeta v. Perrigo Pharmaceuticals Co.*, 630 F.3d 1225, 1237 (9th Cir. 2011), *vacated on other grounds*, 565 U.S. 973 (2011); *McWilliams v. Novartis AG*, No. 2:17-CV-14302, 2018 WL 3369655, at *3-5 (S.D. Fla. July 9, 2018); *In re Testosterone Replacement Therapy Products Liability Litigation Coordinated Pretrial Proceedings*, No. 14 C 1748, 2017 WL 1836435, at *7-11 (N.D. Ill. May 8, 2017); *Batoh v. McNeil-PPC, Inc.*, 167 F. Supp. 3d 296, 318-20 (D. Conn. 2016); *Cross*, 102 F. Supp. 3d at 899-901; *Muzichuck v. Forest Laboratories, Inc.*, No. 1:07CV16, 2015 WL 235226, at *6-8 (N.D. W. Va. Jan. 16, 2015); *Koho*, 17 F. Supp. 3d at 1116-19; *Wells v. Allergan, Inc.*, 2013 WL 389147, at *6-7 (W.D. Okla. Jan. 31, 2013); *Newman v. McNeil Consumer Healthcare*, No. 10-CV-01541, 2012 WL 39793, at *5-11 (N.D. Ill. Jan. 9, 2012); *Dorsett v. Sandoz, Inc.*, 699 F. Supp. 2d 1142, 1156-60 (C.D. Cal. 2010); *Baumgardner v. Wyeth Pharmaceuticals*, No.

06-2518, 2010 WL 3431671, at *1-2 (E.D. Pa. Aug. 31, 2010); *Aaron v. Wyeth*, No. 2:07cv927, 2010 WL 653984, at *3-6 (W.D. Pa. Feb. 19, 2010); *Forst v. SmithKline Beecham Corp.*, 639 F. Supp. 2d 948, 953-54 (E.D. Wis. 2009); *Hayes v. SmithKline Beecham Corp.*, No. 07-CV-0682-CVE-TLW, 2009 WL 4912178, at *4 (N.D. Okla. Dec. 14, 2009). We believe it is significant that, in these cases where the issue was decided by the judge, the conclusion was that the evidence was insufficient to support the affirmative defense, on which the defendant would have the burden of proof at trial. Generally speaking, when a trial court can decide on the merits that, regardless of whether the facts are disputed, the defendant's best evidence is not of the quantum or quality of proof necessary to support the affirmative defense pled, this is a proper basis for determining that the defense as insufficient as a matter of law. When that occurs, there is no need for a trial on the merits of the defense. But that is not the same thing as saying that a trial court can just as easily decide on the merits that, despite the existence of genuine issues of material fact, the defendant should be entitled to judgment as a matter of law on the defense. The former is usually proper, but the latter normally requires that the issue be submitted to the jury for a decision on the merits. We believe these cases above fall into the former category, and we do not read them to stand for the proposition that the latter procedure is appropriate where the question involved is the *Wyeth* inquiry.

¶ 51 Of the reported decisions cited to us by Merck, it appears that only in *Dobbs*, 797 F. Supp. 2d at 1271-80, *In re Incretin-Based Therapies*, 142 F. Supp. 3d at 1120-32, and *Seufert*, 187 F. Supp. 3d at 1170-78, did the district judge resolve disputed facts in favor of the drug manufacturer and grant summary judgment on the preemption defense in the defendant's favor.[5]

[5]Merck cites a California state trial court order in which the trial judge granted summary judgment for the drug manufacturer on the *Wyeth* inquiry despite the existence of disputed facts, after concluding that the issue should be decided the trial judge. The California Court of Appeal reversed the trial court's judgment on other grounds, and in doing so it declined to address the issue of whether the

Of these three cases, the only one in which the court addressed whether the issue presented a decision for the judge or jury was *In re Incretin-Based Therapies*, 142 F. Supp. 3d at 1114, which was vacated on other grounds. *Seufert* was decided by the same district judge as *In re Incretin-Based Therapies*, and it did incorporate by reference part of the discussion from *In re Incretin-Based Therapies*. *Seufert*, 187 F. Supp. 3d at 1169 n.10. In *Dobbs*, the court did not address or mention the issue, and we note that the reasoning of *Dobbs* has been questioned by later courts. See *Muzichuck*, 2015 WL 235226 at *8.

¶ 52 In the court's analysis of the issue in *In re Incretin-Based Therapies*, the district judge stated only that he had considered the parties' arguments, the relevant authority, and the pending cross-motions and was "satisfied that preemption presents purely a question of law appropriate for resolution by summary judgment." *In re Incretin Based Therapies*, 142 F. Supp. 3d at 1114. The only supporting citations were to *Dobbs* (which, as mentioned, did not discuss this issue) and to *Bank of America v. City & County of San Francisco*, 309 F.3d 551, 566 (9th Cir. 2002), which involved the preemption by a federal statute of certain municipal ordinances pertaining to ATM fees and did not discuss whether the jury or judge should decide the question. *In re Incretin Based Therapies*, 142 F. Supp. 3d at 1114. The court further stated in a footnote that its "fact-intensive analysis" was suitable for determination by the judge through summary judgment because "[t]he factual inquiry is limited to what the FDA has done, if anything, in addressing the need for a warning on a particular drug," in contrast "to considering the specific data relied upon by the FDA." *Id.* at 1115 n.5. We do not find persuasive reasoning in the *In re Incretin Based*

Wyeth inquiry presents a question to be decided by a judge or jury. *Rotondo v. Amylin Pharmaceuticals, Inc.*, No. B275314, 2018 WL 5800780, at *9 (Cal. Ct. App. Nov. 6, 2018) (unpublished opinion). Because of this, and because the decisions of out-of-state trial courts are not precedential (*In re A.C.*, 2016 IL App (1st) 153047, ¶ 47), we decline to specifically discuss this order. We note that the reasons cited by the California trial judge are largely the same as those advanced by Merck in this case that we have addressed and rejected elsewhere in our analysis.

Therapies decision or any of the other cases cited to us by Merck as to why this primarily factual issue should be decided by the trial judge and not the jury in this case. Furthermore, the district judge in the *In re Incretin Based Therapies* case relied on the fact that the plaintiffs had filed a cross-motion for summary judgment on the affirmative defense and found that fact "supports the Court's conclusion that summary judgment is appropriate for resolution of Defendants' conflict preemption defense." *Id.* at 1114-15. That situation is not present in this case.

¶ 53 Merck's next argues that the lower courts and Supreme Court in the *Wyeth* case treated preemption as a matter of law. *Wyeth* involved a failure-to-warn claim under Vermont tort law involving the drug Phenergan, a medication that posed a risk of causing gangrene when administered through "IV push" (direct injection into the vein) as opposed to "IV drip" (slow administration through a hanging intravenous bag). *Wyeth*, 555 U.S. at 558-59. The plaintiff contended IV drip was the only safe way to administer Phenergan, and its labeling should have contraindicated the use of IV push. *Id.* at 559-60. The Supreme Court's opinion reflects that the issue of conflict preemption was first raised in Wyeth's motion for summary judgment, which the trial court denied. *Id.* at 560-61. The Supreme Court noted the trial court, in denying summary judgment, had "reviewed the sparse correspondence between Wyeth and the FDA about Phenergan's labeling and found no evidence that Wyeth had 'earnestly attempted' to strengthen the intra-arterial injection warning or that the FDA had 'specifically disallowed' stronger language." *Id.* at 561. The case then proceeded to trial. The Supreme Court again noted that "[t]he trial record also contains correspondence between Wyeth and the FDA discussing Phenergan's label." *Id.* The most notable aspect of that evidence was the fact that Wyeth had submitted a proposed labeling change related to the risk of arterial exposure to Phenergan, received no response from the FDA for eight years, and then the FDA instructed Wyeth to retain

the verbiage of its current label regarding intra-arterial injection. *Id.* at 561-62.

¶ 54 The jury rendered a verdict for the plaintiff. *Id.* at 562. Wyeth then raised its conflict preemption argument again by filing a posttrial motion seeking judgment as a matter of law on that basis. *Id.* The Supreme Court's opinion noted that the trial judge made "findings of fact based on the trial record." *Id.* It noted that in denying the posttrial motion, "the trial court found 'no evidence in this record that either the FDA or the manufacturer gave more than passing attention to the issue of' IV-push versus IV-drip administration." *Id.* at 572. The Supreme Court of Vermont affirmed the trial court's denial of Wyeth's posttrial motion. *Id.* at 563.

¶ 55 The United States Supreme Court affirmed. As stated above, it held that state-law claims based on the failure to include warnings in a drug's labeling are not federally preempted, provided the drug manufacturer could have added the warning under the CBE regulation. *Id.* at 573. The Court held that it would not conclude that it was impossible for Wyeth to comply with both federal and state requirements "absent clear evidence that the FDA would not have approved a change to Phenergan's label" if Wyeth had tried to make one through the CBE regulation. *Id.* at 571.

¶ 56 Merck argues that we should find significance in the fact that the Supreme Court did not remand the case for a jury to decide whether such "clear evidence" was present. Merck further argues that we should find it significant that "at no time did the *Wyeth* Court indicate that the lower courts had been wrong to treat the question of preemption as one of law for the court," and the Supreme Court treated it the same.

¶ 57 However, we agree with the Third Circuit that it is not "possible to divine a clear answer from the Supreme Court's application of the test in *Wyeth* itself" whether it presents a question to be decided by a judge and not a jury in all instances. *Fosamax*, 852 F.3d at 286. Procedurally,

Wyeth involved the denial of a posttrial motion for judgment as a matter of law. The Supreme Court affirmed the rulings by the lower courts that the evidence presented by Wyeth was insufficient to establish the affirmative defense of preemption. *Wyeth,* 555 U.S. at 572-73. Having ruled that the evidence was insufficient to establish the affirmative defense, there was no need for the Supreme Court to remand the case for a jury to decide whether that evidence amounted to "clear evidence that the FDA would not have approved a change to Phenergan's label." *Id.* at 571. Thus, we reject Merck's argument that, for the purpose of the issue we are deciding, we should find significance in the fact that the Supreme Court did not remand the case. We do not discern any direction from the Supreme Court's application of the test in *Wyeth* that judges and not juries should resolve the "clear evidence" test when doing so would require deciding genuine issues of material fact.

¶ 58 Merck next argues that the *Wyeth* inquiry should be treated as a question for resolution by the judge because determining what conclusion the FDA reached is similar to judicial review of the correctness of administrative agency action. Merck argues that the decision maker in the "clear evidence" determination must discern from the FDA's words and action whether there is "clear evidence" that the agency reached a regulatory conclusion that the available science did not support a warning. It argues that "*Wyeth* preemption is similar to an assessment of whether an agency acted arbitrarily and capriciously," in that both inquiries require courts to "review the administrative record, examine the words and conduct of the relevant agency actors, and decide for themselves."

¶ 59 Although some cases involving the *Wyeth* inquiry may simply require review of an actual FDA decision, we disagree that the dispute Merck and the plaintiffs presented to the trial court in this case was akin to judicial review of administrative agency action. We believe there is a

significant difference between the question presented to the trial court in this case and a typical administrative review case. Put simply, when a court reviews an action or decision by an administrative agency, there exists an actual, specific action taken or decision made by an agency with substantive expertise in the subject matter, which a court reviews for compliance with certain legal standards. In almost all such cases, the court employs a standard of review that gives substantial deference to the agency's action or decision, by ensuring it was not arbitrary and capricious or contrary to the manifest weight of the evidence. See *Greer v. Illinois Housing Development Authority*, 122 Ill. 2d 462, 496 (1988). The court does not substitute its own reasoning or judgment for that of the agency. *Id.* at 506. The substantive correctness of the decision or action is usually not as significant as ensuring that the agency complied with the law in reaching that decision or taking that action.

¶ 60 Here, Merck is not pointing to an actual FDA action or decision to be reviewed (*i.e.*, an actual rejection by the FDA of an attempt to add the warning at issue to the label by the manufacturer). Instead, the decision maker is being asked to extrapolate from other evidence whether it is clear what the FDA's action or decision *would have been* if Merck had attempted to change Januvia's label through the CBE regulation to add the warning that the plaintiffs allege was necessary. The decision maker is being asked to ascertain the substantive answer to this question. Doing so requires the decision maker—whether judge or jury, normally has no expertise in the substantive subject matter—to discern from the totality of evidence presented by the parties whether it is clear what the FDA's substantive action would have been in the first instance. The substance of the FDA's decision is what matters, not the FDA's compliance with the law in reaching that decision. Thus, we perceive these inquiries to be different and believe that the *Wyeth* inquiry presents a question for the jury in this case.

¶ 61 Merck next argues that, assuming the "clear evidence" inquiry involves both legal and factual elements, the trial judge should nevertheless make those factual determinations as a matter of institutional competence, as judges have training in interpreting statutes, regulations, and other legal texts, as well as in assessing agency action in light those statutes and regulations. It further argues that consistent application of the "clear evidence" standard is crucial in pharmaceutical product liability litigation, and judges are more likely than juries to apply the standard consistently from case to case.

¶ 62 Merck relies principally on the case of *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 372 (1996), in which the Supreme Court held that the construction of patent claims (the portion of the patent document that defines the scope of the patentee's rights) is an issue to be resolved by a judge rather than by a jury. The question at issue in that case was whether assigning the resolution of that issue to the trial judge infringed upon the seventh amendment right to trial by jury, and the Supreme Court noted that "history and precedent provide no clear answers" to this question. *Id.* at 388. The Court thus looked to "functional considerations" and an evaluation of whether " 'as a matter of the sound administration of justice, one judicial actor is better positioned than another to decide the issue in question.' " *Id.* (quoting *Miller v. Fenton*, 474 U.S. 104, 114 (1985)). The Supreme Court recognized that the construction of written instruments was a task judges often perform, and judges were likely to perform this task better than untrained jurors. *Id.* It further recognized the importance of uniformity in the treatment of a given patent as a reason to allocate issues of construction to the judge. *Id.* at 390. Thus, it held that the responsibility for resolving the issue should rest with the judge, not with the jury. *Id.* at 391.

¶ 63 The argument made here by Merck was rejected by the Third Circuit in *Fosamax*, 852 F.3d

at 291-92. It noted that the "clear evidence" test was not one asking a jury to supply a plenary construction of the CBE regulation or of some other written instrument. *Id.* at 292. Rather, the clear evidence test asks the jury to apply the requirements of that regulation to the evidence in the case, to predict how the FDA probably would have responded if the defendant had attempted to change its label. *Id.* The Third Circuit stated that the operative language of the CBE regulation—" 'reasonable evidence of a causal association' "—is "neither uncommon nor abstruse," and it "requires law-to-fact applications of the sort that courts routinely give to juries in tort cases." *Id.* "It combines two classic jury questions: (1) whether a causal link between two events is too attenuated, and (2) whether the evidence meets a certain proof threshold." *Id.* "These determinations are well within the province of a properly instructed jury, and we do not think that their inclusion in the larger *Wyeth* inquiry merits reallocation of the factfinding function." *Id.* As discussed above, we agree with the Third Circuit's analysis on this point.

¶ 64 Finally, Merck argues that it is not unusual for courts addressing a primarily legal issue to make "preliminary" or "subsidiary" factual determinations to do so. It gives the example that judges will determine facts to assess whether personal jurisdiction exists (see *Madison Miracle Productions, LLC v. MGM Distribution Co.*, 2012 IL App (1st) 112334, ¶ 35) or as part of a choice-of-law analysis (see *Townsend v. Sears, Roebuck & Co.*, 227 Ill. 2d 147, 154 (2007)). For the reasons discussed above, we believe the nature of the fact-finding called for under the *Wyeth* inquiry as the parties presented it to the trial court goes far beyond the kind of preliminary fact-finding that a judge performs in resolving personal jurisdiction and choice-of-law disputes. It requires much more extensive and substantive fact-finding appropriately decided after a full trial, and thus the jury should be the appropriate fact-finder. We thus reject Merck's arguments that reasons of judicial competence or the need for uniformity provide a basis for holding that the

judge should make the factual determinations involved in the *Wyeth* inquiry.

¶ 65 CONCLUSION

¶ 66 For the foregoing reasons, our answer to the certified question is that a jury should resolve the issue of whether a defendant drug manufacturer has presented "clear evidence" that the FDA would not have permitted the manufacturer to include in a drug's labeling the warning alleged to be necessary by the plaintiffs.

¶ 67 Certified question answered.