No. 16-4050

UNITED STATES COURT OF APPEALS FOR THE TENTH CIRCUIT

ALEXANDER CERVENY, VICTORIA CERVENY, AND CHARLES CERVENY
Plaintiffs/Appellants,

v.

AVENTIS, INC.
Defendant/Appellee

Appeal from the United States District Court for the District of Utah

The Honorable Dee Benson, United States District Judge
District Court Case No. 2:14-CV-00545

REPLY BRIEF OF APPELLANTS

Oral Argument is Requested

Christopher L. Schnieders KS#22434
Adam S. Davis KS#24263
WAGSTAFF & CARTMELL, LLP
4740 Grand Ave., Suite 300
Kansas City, MO 64112
Tele: (816) 701-1100
Fax: (816) 531-2372
cschnieders@wcllp.com
adavis@wcllp.com

Counsel for Plaintiffs/Appellants

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Cases

Statutes

Testimony

ARGUMENT

I. Introduction

In evaluating this appeal, the Court should ask itself this question: Had Defendant Aventis, Inc. ("Aventis") warned before the fall of 1992 about a risk of birth defects for women taking Clomid, is it clear that the FDA would have required Aventis to remove that information from its label? The Court's answer should be "no," because the answer cannot be clear when Aventis never tried to add such information to the label. The only evidence that arguably supports such a conclusion is the denial of a citizen petition many years later. Meanwhile, in 1987 the FDA requested that Aventis add a warning about the risk of harm to the fetus if Clomid is ingested while pregnant—information that the FDA felt was important for women, such as Ms. Cerveny, who were using Clomid to conceive.

Presumably recognizing the difficulty of their argument, Aventis and its supporting amici have tried to change the inquiry espoused in the seminal case of *Wyeth v. Levine*, 555 U.S. 555 (2009). The *Wyeth* Court held that FDA approval of a drug label does not preempt a state-law tort claim, unless the manufacturer presents "clear evidence that the FDA would not have approved a change to" the label. *Id.* at 571. This dictum[1] established a question of fact as to whether there is

[1] One of the amicus briefs argues that the statement was not dictum. (PRMA/Biotechnology Br. at 9 n.7). But courts have referred to it as such. *See In*

clear evidence regarding the action that the FDA would have taken. *See, e.g.*, *Dolin v. SmithKline Beecham Corp.*, No. 12 C 6403, 2016 WL 537949, at *1 (N.D. Ill. Feb. 11, 2016) (stating that "GSK has failed to meet its **demanding burden** of demonstrating by clear evidence that the FDA would have rejected a Paxil-specific adult suicide warning …") (emphasis added).

Over four briefs, Aventis and six amici[2] have tried to move the target, suggesting that Aventis can only change its label in limited circumstances, and that the inquiry should be whether a label change would have been **proper** under FDA regulations. There are several problems with that approach, beginning with the fact that the United States Supreme Court posed a different question.

The Defense Advocates prefer their question because the Supreme Court's question cannot be answered with anything resembling certainty. There is no "clear evidence" as to what would have happened had Aventis changed its label before Mrs. Cerveny used Clomid. The limited evidence cuts both ways. The FDA proposed a warning similar to the one advocated by Plaintiffs, approximately five years before Mrs. Cerveny used the drug; and, the FDA later rejected a citizen petition, which asked the FDA to **force** a label change.

---

re Tylenol (Acetaminophen) Mktg., Sales Practices & Prod. Liab. Litig., 144 F. Supp. 3d 699, 727 (E.D. Pa. 2015).

[2] At times, this brief will refer to Aventis and the six amici collectively as "The Defense Advocates."

As stated in *Dolin*, the "clear evidence" burden is "demanding." This Court should conclude that the "clear evidence" showing cannot be made when the only evidence supporting preemption is the denial of a citizen petition—and when the manufacturer has never sought the label change at issue. The Court should also conclude that the FDA's 1987 request for a warning about birth defects demonstrates that the FDA would have permitted a warning about birth defects. For these reasons, this Court should reverse the grant of summary judgment.

Alternatively, the Court should allow for further discovery, or it should remand the case for litigation of the Cervenys' remaining claims.

II. This Court should reject efforts by The Defense Advocates to change the standard enunciated in *Wyeth*, and should conclude that the rejection of a citizen petition, alone, does not constitute clear evidence as to how the FDA would have responded had Aventis strengthened the Clomid label.

There is no preemption in this case because Aventis never sought a label change to warn about the risk of birth defects when taking Clomid, and the only evidence supporting Aventis's "clear evidence" argument is the denial of a citizen petition. The Court should reject The Defense Advocates' efforts to change the inquiry that the *Wyeth* Court laid out.

A. The Supreme Court in *Wyeth* made clear that the **only** exception to its ruling against preemption requires "clear evidence" that the FDA actually would have forced a manufacturer to rescind a label change.

In *Wyeth*, the Court soundly rejected the idea that the FDA's labeling decisions preempted state-law tort claims, noting that "the manufacturer bears responsibility for the content of its label at all times." *Wyeth*, 555 U.S. at 570. The Court also recognized that the manufacturer could unilaterally change its label through the Changes Being Effected ("CBE") process. *Id.* at 568-69. Aventis suggests that the CBE process can only be invoked in narrow circumstances, but in *Wyeth* the Supreme Court rejected this "cramped" reading of the CBE regulation. *Id.* at 570. The Court further recognized that the "new information" needed to invoke the CBE process could be a reanalysis of old data. *Id.* at 569-70.

Wyeth also argued that had it used the CBE process to change the label, the FDA could have forced it to rescind that change. The Court agreed conceptually, but stated that "absent clear evidence that the FDA would not have approved a change to Phenergan's label, we will not conclude that it was impossible for Wyeth to comply with both federal and state requirements." *Id.* at 571.

The Defense Advocates assert that this presents a legal question as to whether the proposed label change would have complied with the FDA's standard of adding warning when there is "reasonable evidence of an association" between the drug and the adverse event. (*See, e.g.*, Aventis Br. at 25). There are several

problems with this argument—most notably that it contravenes Supreme Court precedent. The issue in *Wyeth* was, what would have happened had the manufacturer used the CBE process to add the proposed warning? *Wyeth*, 555 U.S. at 571. Thus, the issue is factual. *See In re Incretin-Based Therapies Products Liab. Litig.*, 142 F. Supp. 3d 1108, 1105 (S.D. Cal. 2015) (stating that application of the "clear evidence" standard is "necessarily fact-specific"); *Dobbs v. Wyeth Pharms.*, 797 F. Supp. 2d 1264, 1270 (W.D. Okla. 2011) (same).

While the conflict with Supreme Court precedent is sufficient to rebut the argument, several additional points explain why the inquiry should focus on what the FDA **would have** done, not what it allegedly **should have** done:

- The standard advocated by The Defense Advocates turns the preemption inquiry into a merits inquiry. Plaintiffs will develop their proof of the association between Clomid and birth defects through their experts.
- The doctrine of "impossibility" preemption applies when it is, literally speaking, impossible to comply with federal and state law. *Mount Olivet Cemetery Ass'n v. Salt Lake City*, 164 F.3d 480, 486 (10th Cir. 1998). Thus, the issue is whether it was **possible** for Aventis to change the label—not whether a particular standard was met.
- The "reasonable evidence of an association" standard applies only to warnings. It does not apply other sections of the label, such as adverse

events. *See Schedin v. Ortho-McNeil-Janssen Pharm., Inc.*, 808 F. Supp. 2d 1125, 1143 (D. Minn. 2011), *aff'd in part, rev'd in part sub nom. on other grounds by In re Levaquin Products Liab. Litig.*, 700 F.3d 1161 (8th Cir. 2012) (discussing differences between "warnings and precautions" and "indications and usage" sections). Other sections could contain important risk information. *See Reckis v. Johnson & Johnson*, 28 N.E.3d 445, 458-59 (2015) (discussing potential changes to the "Stop use and ask a doctor if" and the "Allergy alert" sections of the label). The "clear evidence" standard applies to the entire label. *Wyeth*, 555 U.S. at 571. Thus, the Defense Advocates' argument would improperly apply the "reasonable evidence of an association" standard to aspects of the label where that standard is inapplicable.

This Court, therefore, should reverse the district court unless it is convinced that the FDA would have **rescinded** a label change, had Aventis warned of the risk of birth defects before Mrs. Cerveny used the drug.

B. The weight of authority supports a rule that there can be no "clear evidence" preemption unless the manufacturer has actually attempted to change its label.

Applying that standard, the Court should first conclude that there can be no "clear evidence" of preemption where, as here, the manufacturer never sought the label change at issue.

The Defense Advocates claim that *Wyeth* does not support this conclusion because *Wyeth* does not expressly require such a submission. (Product Liab. Advisory Council Br. at 22-23). *Wyeth* does not define "clear evidence," as that issue was not central to the holding. But there are aspects of *Wyeth* that support Plaintiffs' interpretation, and additional case law supports this position.

Wyeth strongly rejected federal preemption of state-law tort claims, holding that the manufacturer has the power to change the label and the primary responsibility for its content. *Wyeth*, 555 U.S. at 568-70. The Court made its "clear evidence" statement while rejecting the argument that the FDA could have rescinded a unilateral change to the Phenergan label. *Id.* at 571. Thus, it is logical to conclude that "clear evidence" of such a rejection would require an actual attempt to change the label by the manufacturer.[3]

Aventis claims that the weight of authority counsels against requiring a manufacturer's submission, but there is little authority on its side. *Incretin-Based Therapies*, which is on appeal, is the only real support for the argument that a

[3] Plaintiffs are not arguing that the FDA must have rejected the **exact** language proposed by a plaintiff. Plaintiffs agree that preemption applies where the manufacturer submits, and the FDA rejects, a label change that is substantively the same as a change proposed by a plaintiff—assuming that there is no other basis for a distinction, such as new evidence or the manufacturer withholding important risk information from the FDA. This Court need not decide whether a formal rejection is needed or whether rejection of a detailed but informal proposal would suffice, because in this case there is no evidence that Aventis has ever sought to add the risk information proposed by the Plaintiffs.

manufacturer's attempt to change the label is not a prerequisite for preemption. *See Incretin-Based Therapies*, 142 F. Supp. 3d at 1124.[4] Aventis also cites *Reckis* as contrary to Plaintiffs' argument, but *Reckis* almost entirely rejected the defendants' preemption argument. *Reckis* found preemption only where the FDA rejected a specific reference to a disease as being overly confusing. *Reckis*, 28 N.E.3d at 458. *Reckis* declined to find preemption substantively and wrote that "even assuming for sake of argument that we could predict the FDA would have rejected a citizen petition proposal to add only this warning, that would not answer whether the FDA would have rejected the warning had it been sought by the defendants themselves." *Id.* at 459.

Aventis also relies on language from Justice Sotomayor's **dissent** in *PLIVA, Inc. v. Mensing*, 564 U.S. 604 (2011). Theorizing as to what might constitute "clear evidence" under *Wyeth*, she wrote that a party could show that "the FDA had itself considered whether to request enhanced warnings," and that the FDA had taken no action. *Id.* at 637 (Sotomayor, J., dissenting).

Of course, this dissenting opinion does not reflect the view of the Court. As Aventis acknowledged, only two justices (Sotomayor and Ginsburg) signed both the *Wyeth* majority and the *Mensing* dissent. Plus, Judge Sotomayor was merely

[4] Notably for the Section III argument, in *Incretin-Based Therapies*, there was far more evidence to support preemption than there is here. (*See* Opening Br. at 34-26).

hypothesizing as to how generic manufacturers "might" show impossibility preemption. *Id.* Nothing in the language suggests that she was announcing a rule of law—particularly one that would **limit** suits against brand-name manufacturers. Justice Sotomayor went on to state that the "presumption against pre-emption has particular force when the Federal Government has afforded defendants a mechanism for complying with state law, even when that mechanism requires federal agency action." *Id.* at 638.[5]

Meanwhile, the majority opinion in *Mensing* used important language in discussing *Wyeth*. The majority described the Court as holding 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." *Mensing*, 564 U.S. at 624 n.8. The FDA could only "rescind" a label change if one had already been made—meaning that the manufacturer had used the CBE process to change the label. To take action on a citizen petition, the FDA would have to **mandate** a label change, not rescind one. (Aplt. App. at 470, 509).

One federal court recognized this distinction, concluding that "*Wyeth* and *Mensing* stand for the proposition that to trigger pre-emption, a brand-name

[5] Justice Sotomayor also stated that the issues regarding the clear evidence standard are "questions of fact to be established through discovery." *Id.* at 637. If this Court gives any weight to Justice Sotomayor's dissent, that statement supports Plaintiffs' argument for further discovery, addressed in Section IV *infra*.

manufacturer must show that the FDA would not have approved a proposed label change that is the basis for a state law failure to warn claim; indeed, the brand name manufacturer likely must proffer evidence of the FDA's **rejection of an actual label change."** *Schedin*, 808 F. Supp. 2d at 1132-33. Other courts have taken a similar view. *See In re Tylenol*, 144 F. Supp. 3d at 727 ("The Supreme Court opined in dicta that a failure-to-warn claim may be preempted if a drug manufacturer submitted a CBE change and the FDA rejected it."); *Reckis*, 28 N.E.3d at 459 (stating that the FDA's response to a citizen petition "would not answer whether the FDA would have rejected the warning had it been sought by the defendants themselves").

These courts are correct, as the context of the Court's statement in *Wyeth* reveals. To produce "clear evidence" that a label change was impossible, a manufacturer must produce evidence that it attempted a label change.

C. All of the evidence that supposedly supports preemption derives from the denial of a citizen petition, and that single denial leaves substantial doubt as to whether the FDA would have taken action had Aventis strengthened its label before 1992.

Another reason that this Court should reject Aventis's preemption argument is that it is supported only by the denial of a citizen petition. This Court should conclude that a citizen petition denial, alone, fails to establish "clear evidence" as to how the FDA would have reacted had the manufacturer used the CBE process to change the label.

One amicus brief accuses Plaintiffs of promoting a standard not endorsed by any court. (PRMA/Biotechnology Br. at 24). But it is the district court's ruling in this case that was unprecedented. The Defense Advocates have cited to no other case in which preemption was found based solely on the denial of a citizen petition. It was an anomalous result, given that most courts recognize the high bar set by *Wyeth* for establishing impossibility preemption. *See Shipley v. Forest Labs., Inc.*, No. 1:06-CV-00048-TC, 2015 WL 4199739, at *10 (D. Utah July 13, 2015) (stating that "courts applying the clear evidence standard have almost universally found the manufacturers evidence inadequate to support conflict preemption.") (quotations omitted).

1. *Aventis's efforts to characterize the evidence supporting preemption as something more than the denial of the citizen petition are unavailing.*

This Court should reject Aventis's claim that there is any evidence supporting its argument beyond the citizen petition denial. Aventis contests the assertion that the sole evidence supporting preemption is the citizen petition denial, citing the FDA's inaction during Clomid's life as an FDA-approved drug and the time lapse between Mrs. Cerveny's ingestion of Clomid and the citizen petition denial. (Aventis Br. at 29-33).

First, Aventis cites the FDA's failure to demand the label change sought by Plaintiffs as evidence of preemption. (Aventis Br. at 29-30).[6] The district court also made this assertion. (*See* Opening Br. at 31 n.10, citing Aplt. App. at 727-28). But the *Wyeth* Court made clear that FDA inaction, alone, is not evidence to support preemption. *See Wyeth*, 555 U.S. at 558-59 (concluding that prior FDA approval was not a defense to the plaintiffs' tort claims). Such an argument also contradicts *Wyeth's* statement that the manufacturer "bears responsibility for the content of its label at all times." *Id.* at 570-71. Because Aventis was responsible for its label, the FDA's failure to act unilaterally is meaningless.

Aventis claims that Plaintiffs seek to ignore the regulatory record, (Aventis Br. at 32), but Plaintiffs are making no such assertion. As discussed *infra*, Plaintiffs rely in part on communications between the FDA and Aventis in 1987. If there were communications in which the FDA tried to **prevent** Aventis from adding a particular warning, those communications might also be relevant. But no such communications exist. The point is, the FDA's failure to insist on a label change, by itself, is legally insignificant, based on the holding in *Wyeth*.

Finally, Aventis argues that the lapse in time between Mrs. Cerveny's use of Clomid and the denial of the citizen petition is somehow "clear evidence" of preemption. This argument is tied to the citizen petition denial, so it fails to offer

[6] Notably, the FDA did not have the authority to require a label change in 1992. (See Opening Br. at 7 n.3).

additional evidence to support preemption. The argument also is directed to the wrong inquiry. The accumulation of additional evidence might support a merits argument. But again, the issue is what the FDA **would have** done, not what it **should have** done, had Aventis changed its label. *See Wyeth*, 555 U.S. at 571; *Dolin*, 2016 WL 537949, at *1; *see also Mason v. SmithKline Beecham Corp.*, 596 F.3d 387, 396 (7th Cir. 2010) (holding that "GSK did not meet its burden of demonstrating by clear evidence that the FDA **would have** rejected a label change") (emphasis added).

In assessing what the FDA **would have** done, a time lapse between the plaintiff's use of the drug and the FDA's action counsels against preemption. *See, e.g.*, *Hunt v. McNeil Consumer Healthcare*, 6 F. Supp. 3d 694, 701 (E.D. La. 2014) (rejection of citizen petition in 2006 does not reveal how the FDA would have responded in 2010).

Thus, the only evidence that arguably supports preemption remains the FDA's denial of the citizen petition. This Court should reject the district court's decision to become the first court to find preemption on such a limited record.

2. The Supreme Court in Wyeth *made clear that these issues should be evaluated in the context of reality, and the denial of a citizen petition says little about how the FDA would respond to a manufacturer's voluntary label change.*

In addressing the impact of the citizen petition denial, The Defense Advocates largely ignore the realities of the situation. Instead, they insist that

merely because the legal standard is the same when the FDA evaluates a citizen petition, the denial of a citizen petition should have the same legal force as the FDA rejecting a manufacturer's label change.

First, several courts have recognized the important distinction between the denial of a citizen petition—through which the FDA declines to act—and the rejection of an attempted label change—through which the FDA takes affirmative action. *See Reckis*, 28 N.E.3d at 459 (quoted *supra*, p. 8); *see also Schedin*, 808 F. Supp. 2d at 1133 ("That the FDA did not require a label change … in the face of a Citizen's Petition, not supported by the manufacturer[,] does not constitute clear evidence that the FDA would have **rejected** a label change proposed by Ortho–McNeil before Schedin was prescribed Levaquin.") (emphasis in original); *Dorsett v. Sandoz, Inc.*, 699 F. Supp. 2d 1142, 1157 (C.D. Cal. 2010) (stating that rejections of citizens petitions "constituted determinations that the warnings should not be *mandated*; they were not determinations that manufacturers could not choose to add warnings that they believed were scientifically substantiated") (emphasis in original); *cf. In re: Zofran (Ondansetron) Prod. Liab. Litig.*, No. 1:15-MD-2657-FDS, 2016 WL 287056, at *3 (D. Mass. Jan. 22, 2016) ("The identity and process by which a labeling change is requested may be material because the procedural method used could affect the FDA's response to the proposed change.").

Another key point, advanced by the Supreme Court in *Wyeth*, is that the law should take practical realities into account. In *Wyeth*, the Court explained that the "FDA has limited resources to monitor the 11,000 drugs on the market, and manufacturers have superior access to information about their drugs, especially in the postmarketing phase as new risks emerge." *Wyeth*, 555 U.S. at 578-79. Thus, the Court concluded, state-law tort claims were an important aide to the FDA's purposes. *See id.* at 579 (stating that "the FDA long maintained that state law offers an additional, and important, layer of consumer protection that complements FDA regulation").

Similarly, this Court should consider the reality that a citizen petition will likely be treated differently than a manufacturer's label change, as the courts cited above recognized. Plaintiff's expert, David B. Ross, M.D., Ph.D., M.B.I., was a medical officer in the FDA for a decade. (Aplt. App. at 467, 504). He testified that citizen petitions to change prescription drug labels were rarely granted, and that he could only recall one instance, from hundreds of CBE applications, where the FDA rejected a manufacturer's proposed label change. (*Id*. at 471, 510).

One amicus brief argues that citizen petitions seeking changes to drug labels are granted with some frequency. (*See* PRMA/Biotechnology Br. at 16). Yet, the referenced testimony tells a different story. Gary Buehler, R.Ph., of the FDA's Office of Generic Drugs ("OGD"), told a Senate committee that of 42 citizen

petitions examined by OGD, "only three petitions led to a change in Agency policy on the basis of data or information submitted in the petition."[7] The hearing testimony indicates that "very few" citizen petitions on generic drug matters "have presented data or analyses that significantly altered FDA's policies."[8] Further, citizen petitions are supposed to be reviewed within six months, but sometimes it takes much longer due to lack of manpower.[9] Thus, the testimony shows that the FDA is overworked—as the *Wyeth* court stated—and that it rarely grants citizen petitions.

Aventis's standards-based argument ignores the reality that the manufacturer would likely present different evidence than a citizen, and that the manufacturer would likely be viewed differently by the FDA.[10] This much is evident from the briefs. Aventis described Terry Mix—the author of the citizen petition at issue here—as having "an agenda." (Aventis Br. at 45). The FDA may have viewed him the same way. Similarly, Aventis posits that the manufacturers are the real

[7] Statement by Gary Buehler, R.Ph., FDA Director of the Office of Generic Drugs, July 20, 2006, available at http://www.hhs.gov/asl/testify/t060720.html (last visited October 13, 2016), at p. 4.

[8] Hearing before the Special Committee on Aging, U.S. Senate, Serial No. 109-28, available at https://www.gpo.gov/fdsys/pkg/CHRG-109shrg30710/html/CHRG-109shrg30710.htm, at p. 7.

[9] *Id.* at p. 12.

[10] As discussed in Plaintiff's Opening Brief, Aventis strengthened its warning language in 2012, the same year that the FDA denied Mr. Mix's motion for reconsideration as to the citizen petition. (*See* Opening Br. at 6, 8-9). Thus, the FDA clearly was open to changes submitted by Aventis.

experts. (*Id.* at 44-45). The FDA would also likely view Aventis as an expert if it made a label change, and thus it would be deferential to that change. *See Wyeth*, 555 U.S. at 578-79 (noting that "manufacturers have superior access to information about their drugs").

The amici challenge Plaintiffs' analogy that finding preemption based solely on a citizen petition is akin to concluding that where a *pro se* plaintiff fails, it follows that a court would deny relief to which the defendant has consented. (Product Liab. Advisory Council Br. at 30). The amici argue that the FDA reviews the citizen petition. Perhaps a more precise analogy is comparing a *pro se* plaintiff's loss with a defendant's request to approve a settlement, which the court then reviews. Regardless, the defendant's consent to the relief is likely to color the court's decision as to whether to accept the proposed relief.

A related point is made by considering this Court's *Daubert* standard. If Plaintiffs proffered Mr. Mix—an attorney—as an expert witness on the adequacy of product labeling, the Court would likely determine that he did not have the expertise necessary to testify. *See United States v. Vann*, 776 F.3d 746, 757 (10th Cir. 2015) (stating that courts must determine whether an expert is qualified "by knowledge, skill, experience, training, or education"). Conversely, if Aventis proffered one of its regulatory experts for such testimony, the Court would likely

rule that expert to be qualified. *See id.* Thus, federal courts are—justifiably—more willing to accept information from one source than from another.

The reality is that the FDA is far less likely to grant a citizen petition, and thereby require a label change, than to allow a change made through the CBE process. Therefore, the denial of a citizen petition, alone, is not "clear evidence" that the FDA would have rejected a label change made through the CBE process.

III. The label change advocated by the FDA in 1987 could only have been directed to women attempting to become pregnant, and the FDA's request is the best available evidence as to what was possible during that time frame.

The most clear evidence as to what the FDA would have done before 1992—had Aventis tried to strengthen the Clomid label—was discussed at length in Plaintiffs' opening brief. In 1987, the FDA proposed to Aventis that it add the following warning to Clomid:

> PREGNANCY CATEGORY X. See Contraindications and Information for Patients
>
> CONTRAINDICATIONS: Clomid is contraindicated in pregnant women. Clomid may cause fetal harm when administered to pregnant women. Since there is a reasonable likelihood of the patient becoming pregnant while receiving Clomid, the patient should be apprised of the potential hazard to the fetus.

(Aplt. App. at 461, 595).

The district court held that this proposed warning was irrelevant because it was directed at women who were already pregnant. (Aplt App. at 731). However,

the proposed warning clearly recognizes that the target audience for a fertility drug is women who **are not** already pregnant, such as Mrs. Cerveny in 1992.[11]

A treatise cited by Aventis states that, to be compensable, an injury must "be within the class of injury that the warning requirement was meant to avoid." (Aventis Br. at 49). Here, the injury at issue is not merely in the same class; it is the **same injury**. Plaintiffs allege that Aventis failed to warn about the risk of birth defects, and that Alexander Cerveny was born with birth defects. (*See* Aplt. App. at 028-29). The proposed warning states that the drug "may cause fetal harm." It is the same injury, with the only difference being the timing of administration—whether the user was already pregnant.

Aventis claims that case law supports the district court's irrelevance ruling, but none of its cited cases are supportive. The Fifth Circuit case cited by Aventis is inapposite, as the plaintiff attempted to certify a **no-injury** class. *Rivera v. Wyeth-Ayerst Labs.*, 283 F.3d 315, 317 (5th Cir. 2002). The plaintiffs advanced no theories as to what warnings should have been on the drugs, and without damages, they could not prove causation. *Id.* at 321. In *Kapps v. Biosense Webster, Inc.*, 813 F. Supp. 2d 1128, 1157 (D. Minn. 2011), the court dismissed the claim for lack of causation, not based on preemption. In Aventis's final case, it appears that no party asserted that contraindications for patients with mental depression—which

[11] This fact is also evident from the "Indications" section of the label in effect at the time. (*See* Aplt. App. at 579).

the plaintiff did not have—were at issue. *Martin v. Hacker*, 628 N.E.2d 1308, 1313 (N.Y. 1993).

Here, Mrs. Cerveny **was** in the class of patients to which the FDA asked Aventis to direct the proposed warning. The FDA specifically recognized the need to inform patients such as Mrs. Cerveny, who were using Clomid in an attempt to conceive, of the "potential hazard to the fetus." (Aplt. App. at 461, 595). Thus, the Court should reject the argument that the proposed warning is irrelevant. Mrs. Cerveny was within the target audience for the warning; the warning addressed the exact injury at issue; and the warning would have prevented the harm that occurred, based on her affidavit testimony. (Aplt. App. at 603).

In addition, the warning is strong evidence that the FDA would have accepted a warning that specifically apprised patients of the risk of birth defects from using Clomid to conceive. It is undisputed that Clomid causes a risk of birth defects for those who take it while pregnant—that information is now on the label—and that Clomid remains in the body after conception. (*See id.* at 257-61). Thus, the opportunity exists for Clomid to harm the developing fetus.

The FDA did conclude, in response to the citizen petition, that the Clomid remaining in the body after conception was insufficient to cause harm. (Aplt. App. at 387). But for reasons already discussed, the Court should not view that decision as conclusive on how the FDA would have viewed the evidence had Aventis

sought a label change. The 1987 proposed change demonstrates that the FDA was concerned about the drug's effect on the developing fetus. Thus, the FDA likely would have been deferential to Aventis, had it sought to add a warning or other statement of risk.

Even if the Court believes that the FDA would have rejected a **direct** warning about harm to the fetus for women who use Clomid to conceive, it is likely that the FDA would have allowed some type of precaution, in light of its stated concerns. A recent Mississippi case is instructive. In *Cross v. Forest Laboratories*, No. 1:05-CV-00170-MPM-SA, 2015 WL 1534458 (N.D. Miss. Apr. 6, 2015), the defendants argued that the FDA had found no causal link between SSRIs and suicidality in adults. The court held that even if that is true, the plaintiffs were advocating a different label change, "to caution physicians and patients about the need for close observation and certain symptoms that were a precursor to suicidality." *Id.* at *3. Thus, the court did not find preemption. *Id.* at *4.

In this case, the FDA likely would have allowed a precaution stating that there is a hazard to the fetus when the drug is used while pregnant—as was stated in the FDA's proposed label change—and that because the drug remains in the body after conception, there is a potential risk from using the drug to become pregnant. This point ties into Plaintiffs' next argument, that Plaintiffs did not have

the opportunity to develop fully their theories through experts before the district court granted summary judgment. Regardless, the FDA's proposed warning in 1987 is strong evidence that the FDA was concerned enough about birth defects that it would have accepted a warning or precaution about the potential for birth defects after using Clomid to ovulate.

This Court, therefore, should conclude that there is not clear evidence that it was impossible for Aventis to add a relevant warning or precaution to the Clomid label that would have prevented Alexander Cerveny's birth defects.

IV. Plaintiffs' Rule 56 affidavit was not procedurally improper, and the recent *Zofran* decision helps to explain why Plaintiffs should have a full opportunity for discovery before preemption is decided.

At minimum, the Court should remand the case to allow for further discovery. Plaintiffs' Rule 56 affidavit was not procedurally improper, as Aventis claims. The affidavit spelled out the needed discovery and the reasons for it. (Aplt. App. at 618-19). Plaintiffs further explained their reasoning in briefing to the trial court. (Aplt. App. at 494-95).

In the case cited by Aventis, the party asking for more discovery failed to file the required affidavit at all, and this Court held that it was not an abuse of discretion to grant summary judgment. *Price ex rel. Price v. W. Res., Inc.*, 232 F.3d 779, 783–84 (10th Cir. 2000).

Here, the affidavit of Christopher Schnieders, Esq., explained in as much detail as possible several categories of information on which Plaintiffs needed additional discovery. (Aplt. App. at 618-19). Mainly, it boils down to three issues. The Plaintiffs should be able to complete expert discovery so that they can more fully develop their theories as to what warnings, precautions, or other risk information should have been included on the label at the relevant time; Plaintiffs should have time to discover whether Aventis had any risk information that was not publicly available—and thus could have been submitted to the FDA; and, Plaintiffs should have time to explore communications between the FDA and Aventis about its label. (*See id.*). For instance, if the FDA ever proposed to Aventis that it add a warning about the risk of birth defects from using Clomid to conceive, that statement would obviously be relevant.

The mere fact that the district court told Plaintiffs to "front-load" discovery does not excuse the court's failure to allow sufficient time for discovery. It was little more than a month from when the Court issued a scheduling order to when Aventis filed its summary judgment motion. (Aplt App. at 008). Plaintiffs essentially had one chance to file a round of discovery to Aventis, no time to seek additional information, insufficient time to develop expert reports, and insufficient time to seek discovery directly from the FDA. (*See* Aplt. App. at 618-19).

The *Zofran* court's recent ruling denying a motion to dismiss is instructive. In discussing the "clear evidence" inquiry, the court wrote that "[w]hatever the contours, in this context, of the word 'evidence,' it surely contemplates some form of fact-based evaluation." *In re: Zofran*, 2016 WL 287056, at *3. Thus, the court held that it was "reluctant to issue a ruling on a motion to dismiss without giving the plaintiffs some opportunity to develop the facts, whatever those facts may be." *Id.* Among other things, the court determined that the plaintiffs had the right to explore whether the defendant possessed risk information that was not publicly available and thus could not have been a part of the citizen petition that was denied. *Id.* The court further held that discovery was needed because "it is not clear at this stage how the warning or warnings plaintiffs allege GSK should have provided compare (or conflict) with the label changes and warnings rejected by the FDA … ." *Id.* at *4.

If this Court does not reject preemption entirely, it should reach the same conclusion. While the motion at issue here was nominally for summary judgment, discovery was so condensed that Plaintiffs had little more of a factual record than they would have had on a motion to dismiss.

V. There is no evidence that it was impossible for Aventis to create a label without certain language, and implied warranties clearly do not involve the label.

Even if this Court determines that Plaintiffs' failure-to-warn claims are preempted, this Court should remand the case for consideration of Plaintiffs' additional claims.

Those remaining claims are for fraud, negligent misrepresentation, and implied warranty. None of these claims are preempted because there is no evidence that it was impossible to create a label without the statement that Plaintiffs allege to be false. In addition, an implied warranty claim is not based on the label, so there is no basis for impossibility preemption.

The claims for fraud and negligent misrepresentation derive from the label, but they are based on false, affirmative statements; they are not based on the failure to provide particular information. *See Schwartz v. Celestial Seasonings, Inc.*, 124 F.3d 1246, 1252 (10th Cir. 1997) (fraud); *Christenson v. Commonwealth Land Title Ins. Co.*, 666 P.2d 302, 305 (Utah 1983) (negligent misrepresentation). In their complaint, Plaintiffs alleged that Aventis's label includes the false information that "no causative evidence of a deleterious effect of Clomid therapy on the human fetus has been seen," despite the existence of ample evidence to the contrary. (Aplt. App. at 022).

There is no evidence that it was impossible for Aventis to create a label without that statement. *Cf. McKay v. Novartis Pharmaceuticals Corp*, 934 F. Supp. 2d 898, 911-12 (W.D. Tex. 2013) (holding that due to plaintiffs' allegations of an "overt misrepresentation," plaintiff's express warranty claim was "distinct" from plaintiff's dismissed failure-to-warn claim). Aventis's suggestion that the FDA's approval of the label insulates it from liability is contrary to *Wyeth*, which states that FDA approval of the label does not insulate the manufacturer even from failure-to-warn claims. *See Wyeth*, 555 U.S. at 558-59.

The argument for reversal is even stronger as to the implied warranty claim. An implied warranty is, by definition, implied. Thus, the claim is not based on the content of the label at all. The key allegations for this claim are:

> 87. At the time that Defendants manufactured, marketed, distributed, supplied and sold Clomid, they knew of the use for which the subject product was intended and impliedly warranted it to be [of] merchantable quality and safe and fit for such use.
>
> ***
>
> 91. Contrary to the implied warranty for the subject product, Clomid was not of merchantable quality, and [was] not safe or fit for its intended uses and purposes, as alleged herein.

(Aplt. App. at 029-30).

These allegations are consistent with Utah law, which holds that a product is not merchantable if it is not "fit for the ordinary purposes for which such goods are used." Utah Code Ann. § 70A-2-316(2)(c). Plaintiffs allege that use of Clomid to

become pregnant causes birth defects. Thus, it is not fit for its ordinary purpose, which is conception.

That issue is a merits issue that has nothing to do with whether it was possible to change the Clomid warning label. As such, the case should be remanded on at least that issue.

VI. The Court should reject the amici's policy-based arguments, which were largely rebuffed by the Supreme Court in *Wyeth*, and the Court should be concerned about endorsing a road map to preemption.

Despite the assertion that this is "an easy case," (Product Liab. Advisory Council Br. at 6), no fewer than six amicus parties have added their voices, over the course of three briefs. Clearly, this case has substantial importance. The amici surely recognize that a broad interpretation of "clear evidence" preemption would be a financial boon for the pharmaceutical industry—while limiting the ability of injured families such as the Cervenys to recover.

It is unnecessary—and not possible within the Court's page limits—to address all of the amicus arguments. To some extent, they are addressed above. The amici have also raised various policy points, generally suggesting that the public benefits from preemption.

To the extent that policy plays any role in the Court's analysis, there are countervailing considerations, as discussed in *Wyeth*. In *Wyeth*, the defendant argued that state tort-law claims frustrated the purpose of Congress, but the

Supreme Court explained that the exact opposite is true. In 1906, Congress "enacted the FDCA [Food, Drug & Cosmetic Act] to bolster consumer protection against harmful products." *Wyeth*, 555 U.S. at 574. In not providing a federal remedy to redress injuries, Congress evidently "determined that widely available state rights of action provided appropriate relief for injured consumers." *Id.*

Thus, state tort suits complement the purpose of Congress—to ensure that drugs are safe for the general public. The Court explained:

> State tort suits uncover unknown drug hazards and provide incentives for drug manufacturers to disclose safety risks promptly. They also serve a distinct compensatory function that may motivate injured persons to come forward with information. Failure-to-warn actions, in particular, lend force to the FDCA's premise that manufacturers, not the FDA, bear primary responsibility for their drug labeling at all times. Thus, the FDA long maintained that state law offers an additional, and important, layer of consumer protection that complements FDA regulation.

Id. at 579. *Wyeth* applied these principles in rejecting preemption. But if *Wyeth* is viewed as having left a large loophole, through which manufacturers can avoid state tort suits, then those noble objectives will not be achieved.

If the denial of a citizen petition is sufficient to achieve preemption, then manufacturers will have a road map to insulating themselves from liability. While that is clearly not what occurred in this case, the Product Liability Advisory Council brief acknowledges that the industry has used citizen petitions to try to achieve financial gain. (Product Liab. Advisory Council Br. at 29, noting that drug

manufacturers often use citizen petitions "to maintain existing market advantages by delaying the approval of competing drugs—particularly generic drugs"). If this Court affirms the district court, there would be an incentive to file a weak citizen petition on an area of potential concern, in the hope that the petition would be denied.

This Court should instead adhere to the principles of *Wyeth* and conclude that the *Wyeth* exception is not so broad as to include this case, in which the manufacturer never attempted to change the label to reflect the risk information advocated by the Plaintiffs.

CONCLUSION

For these reasons, as well as those stated in their opening brief, the Cervenys respectfully request that this Court reverse the district court's grant of summary judgment and hold that none of their claims are preempted. Alternatively, the Cervenys request that this Court remand the case for further discovery before any preemption issues are decided.

Respectfully Submitted,

/s/ Adam S. Davis

Christopher L. Schnieders KS#22434
Adam S. Davis KS#24263
WAGSTAFF & CARTMELL, LLP
4740 Grand Ave., Suite 300
Kansas City, MO 64112
Tele: (816) 701-1100
Fax: (816) 531-2372
cschnieders@wcllp.com
adavis@wcllp.com

Counsel for Plaintiffs/Appellants

CERTIFICATE OF SERVICE

I hereby certify that I filed the foregoing brief on October 13, 2016, using the Court's CM/ECF electronic filing system, thereby sending notice of the filing to all counsel of record for this appeal.

/s/ Adam S. Davis
Attorney for Plaintiffs/Appellants

CERTIFICATE OF COMPLIANCE WITH RULE 32(a)(7)

I hereby certify that the foregoing brief has 6,976 words, excluding those items that are referenced in Rule 32(a)(7)(B)(iii). Thus, the brief complies with the type volume limitation listed in Rule 32(a)(7)(B)(i).

/s/ Adam S. Davis
Attorney for Plaintiffs/Appellants

CERTIFICATE OF DIGITAL SUBMISSION

I hereby certify that with respect to the foregoing:

(1) All required privacy redactions have been made per 10th Cir. R. 25.5;

(2) If required to file additional hard copies, that the ECF submission is an exact copy of those documents;

(3) The digital submissions have been scanned for viruses with the most recent version of a commercial virus scanning program, Kaspersky Endpoint Security 10 for Windows, Version 10.2.434 (Network Agent), Version 10.2.4.674 (Anti-Virus), last update 10/08/2016, and according to the program are free of viruses.

/s/ Adam S. Davis
Attorney for Plaintiffs/Appellants