UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES - GENERAL

Case No.	CV 06-7821AHM (AJWx)	Date	March 26, 2010
Title	ROSEMARY DORSETT v. SANDOZ, INC.		

Present: The Honorable	A. HOWARD MATZ, U.S. DISTRICT JUDGE	
Stephen Montes	Not Reported	
Deputy Clerk	Court Reporter / Recorder	Tape No.

Attorneys **NOT** Present for Plaintiffs: Attorneys **NOT** Present for Defendants:

Proceedings: IN CHAMBERS (No Proceedings Held)

I. INTRODUCTION

This is a products liability case arising from the suicide death of Noe Carrasco, the son of Plaintiff Rosemary Dorsett. Defendant Sandoz, Inc. ("Sandoz") originally filed this motion on March 27, 2007, as a motion to dismiss on the ground that federal law preempted Plaintiff's claims. On April 2, 2007, the Court granted Plaintiff's ex parte application to convert the motion into a motion for summary judgment and gave Plaintiff additional time to respond. On February 14, 2008, the Court granted Sandoz's unopposed motion to stay this case pending the Supreme Court's decision in *Wyeth v. Levine*, — U.S. —, 129 S. Ct. 1187 (2009). While the case was stayed, the Court granted Plaintiff's motion to temporarily lift the stay to substitute Eli Lilly and Company ("Lilly") in place of one of the Doe defendants. Plaintiff then filed her operative pleading, the Second Amended Complaint ("SAC"), on January 6, 2009. *Wyeth* was decided on March 4, 2009 and the Court reopened the case on March 24, 2009. Thereafter, Lilly filed a motion for judgment on the pleadings on statute of limitations grounds, which the Court denied on October 28, 2009. Lilly has also filed a motion for summary judgment on the ground of federal preemption, presenting similar, though not identical, arguments to those of Sandoz. The Court will refer to Lilly and Sandoz collectively as "Defendants" when appropriate. For the following reasons, the Court DENIES Defendants' motions for summary judgment and finds that Plaintiff's claims are not preempted.[1]

[1]Docket Nos. 31 & 79.

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II. BACKGROUND[2]

A. Crux of This Case

[2]All the facts recited in this order are undisputed unless otherwise noted.

On August 20, 2004, Carrasco committed suicide by shooting himself in the garage of his friend's home. Second Amended Complaint ("SAC") ¶ 5. Carrasco was 26 years old. He had been taking fluoxetine, the generic version of the drug Prozac, for approximately 36 days before his death. SAC ¶ 55.

Carrasco began taking fluoxetine on or about July 15, 2004. SAC ¶ 55; Mem. at 3. Fluoxetine, like Prozac, is a selective seratonin reuptake inhibitor ("SSRI"). Mem. at 3. SSRIs are a class of antidepressants used to treat depression, anxiety disorders, and some personality disorders.

Defendant Sandoz manufactures and markets generic fluoxetine. Its warning label for fluoxetine was identical to the label on its brand name equivalent, Prozac, manufactured by Lilly. At the time of Carrasco's death, the Sandoz label contained the following language, which was standard for all SSRIs:

> Suicide: The possibility of a suicide attempt is inherent in major depressive disorder and may persist until significant remission occurs. Close supervision of high-risk patients should accompany initial drug therapy. Prescriptions for Drug Z should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose.

As for Lilly, it asserts that its label was changed at some point in July 2004 (shortly before Carrasco's death) to include an enhanced warning, which stated, in part:

> **Clinical worsening and suicide risk** – Patients with major depressive disorder, both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality), whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Although there has been a longstanding concern that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients, a causal role for antidepressants in inducing such behaviors has not been established. **Nevertheless, patients being treated with antidepressants should be observed closely for clinical worsening and suicidality, especially at the**

> **beginning of a course of drug therapy, or at the time of dose changes, either increases or decreases.**

Lilly's Exs. X & Z; SUF ¶¶ 24, 27 (emphasis in original). The warning went on to state that "[a]lthough there has been a long-standing concern that antidepressants may have a role in inducing or worsening of depressions and emergence of suicidality in certain patients, a causal role for antidepressants in inducing such behaviors has not been established." *Id.* Sometime afterward—at the hearing, the parties represented that it was in December 2004—Sandoz placed this language in its label.

Plaintiff Rosemary Dorsett ("Dorsett") is Carrasco's mother. She alleges that Defendants failed to provide any warning through any medium about the association between fluoxetine and suicidality;[3] and that based upon the state of knowledge as it existed at the time, Defendants knew or should have known that fluoxetine was a substance associated with producing preoccupation about and acts of self-harm and could be dangerous and unsafe. SAC ¶¶ 55-57. According to Dorsett, Defendants should have provided "a stronger warning regarding the association between fluoxetine and suicidality through a variety of mediums, including but not limited to labeling, continuing education, symposiums, posters, advertisements. . . ." SAC ¶ 53. *See also* SAC ¶¶ 56-57. Dorsett has not provided a specific warning about a causal relationship between SSRIs and suicidality in adults that she says should have been placed on the label. *See infra*, p. 23-24.

Dorsett is suing for common law negligence, strict liability, breach of express warranty, and for survival. SAC ¶¶ 54-85. Defendants have moved for partial summary judgment of Plaintiff's failure-to-warn claims on the grounds that Plaintiff's state product-liability claims are preempted by the Federal Food, Drug and Cosmetic Act ("FDCA") and by regulations promulgated by the Food and Drug Administration ("FDA"). Defendants seek an order that as a matter of law they may not be held liable for their failure, as of July 2004, to include in the labeling for fluoxetine *any* warning regarding the risk of suicide beyond that which was approved by the FDA.

B. Statutory and Regulatory Background

The "essential purpose" of the FDCA is "to ensure that any product regulated by the

[3] "Suicidality" is suicidal thinking and behavior.

FDA is 'safe' and 'effective' for its intended use." *Food and Drug Admin. v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 133 (2000). The FDA's mission is to "promote the public health by promptly and efficiently reviewing clinical research and taking appropriate action on the marketing of regulated products in a timely manner" and to "protect the public health by ensuring that . . . human and veterinary drugs are safe and effective." 21 U.S.C. § 393(b)(1), (2). The FDA fulfills its mission, in part, by overseeing the approval process for new drug products, regulating drug labeling content, and issuing public health advisories if the safety of a drug product comes into question.

In 1962, Congress amended the FDCA to require all drug manufacturers to submit a new drug application ("NDA") to the FDA for permission to market a new drug product. *See generally* 21 U.S.C. § 355; Public Law 87-781 (1962). Applications for new drugs must include scientific data showing the drug's safety as well as its effectiveness for its intended use. 21 U.S.C. § 355(b); 21 C.F.R. pt. 314.

In 1984, pursuant to the Hatch-Waxman Act, the FDA implemented an abbreviated new drug application procedure ("ANDA") for manufacturers of generic drug products. 21 U.S.C. § 355(j). By using the "innovator" drug as the basis for the generic drug's approval, ANDA applicants are not required to include clinical data to demonstrate the drug's safety and effectiveness. *Id*. Instead, ANDA applicants must demonstrate that their product is bioequivalent to (that is, performs in the same manner as) the innovator drug. *See generally* 21 C.F.R. § 320.

The statutory provision governing the ANDA procedure provides:

> An abbreviated application for a new drug shall contain. . .information to show that the labeling proposed for the new drug is the same as the labeling approved for the listed drug referred to in clause (i) except for changes required because of differences approved under a petition filed under subparagraph (C) or because the new drug and the listed drug are produced or distributed by different manufacturers.

21 U.S.C. § 355(j)(2)(A)(v). Thus, the ANDA procedure is only available for those generic drug products that are "the same as" an already-approved FDA drug. *See* 21 C.F.R. § 314.92(a)(1). "[T]he term 'same as' means identical in active ingredient(s), dosage form, strength, route of administration, and conditions of use . . . ." *See* 21 C.F.R. § 314.92(a)(1). This means that the packaging and labeling of the innovator drug and generic drug

must—with limited exceptions—be identical at the time the ANDA application is submitted.

In January 2006 the FDA issued a new final rule on the content and format of labeling, which went into effect in June 2006. Under both the new and old rule, the labeling "must contain a summary of the essential scientific information needed for the safe and effective use of the drug." 21 C.F.R. § 201.56(a)(1). Also, it "must be informative and accurate and neither promotional in tone nor false or misleading in any particular." 21 C.F.R. § 201.56(a)(2).

The FDA must withdraw approval if, after notice and hearing, subsequent evidence shows that the drug is unsafe, if the application contains any untrue statement of material fact, or for a number of other statutorily prescribed reasons. 21 U.S.C. § 355(e); 21 C.F.R. § 314.150(a). In addition, the FDA "may" seek to withdraw approval for a new or generic drug for a number of other reasons. 21 C.F.R. § 314.150(b). One of those reasons is if the labeling for the drug is "false or misleading in any particular" and the manufacturer did not correct the labeling after receiving notice from the FDA. 21 C.F.R. § 314.150(b)(3). The FDA may also seek to withdraw approval if the labeling for a generic drug "is no longer consistent with that for the listed drug," with two exceptions that are not relevant here. 21 C.F.R. § 314.150(b)(10).

FDA regulations also provide for changes to approved drug labels initiated by the manufacturer.[4] *See* 21 C.F.R. § 314.70 (concerning supplements and other changes to an approved application); 21 C.F.R. § 314.97 (applying §§ 314.70 and 314.71 to approved abbreviated applications). Under the so-called Changes Being Effected ("CBE") regulation, after the FDA receives a supplemental application from a manufacturer, the manufacturer may distribute products with changes in the labeling that "add or strengthen a contraindication, warning, precaution, or adverse reaction" or "add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the

[4] Prior to 1965, "the FDA regulations applicable to drugs prohibited companies from adding warnings or other information without prior approval." *Caraker v. Sandoz Pharma. Corp.*, 172 F. Supp. 2d 1018, 1034 (S.D. Ill. 2001) (citing 25 Fed. Reg. 12,592, at 12,595 (1960)).

drug product." 21 C.F.R. §§ 314.70(c)(6)(iii) (effective to June 29, 2006).[5] *See Wyeth*, 129 S. Ct. at 1196 (discussing the CBE process). If the FDA disapproves the supplemental application, it may order the manufacturer to cease any distribution that may have begun. 21 C.F.R. § 314.70(c)(7).

Finally, the regulations require manufacturers to revise their labeling to "include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved." 21 C.F.R. § 201.57(e) (effective to Jun. 29, 2006), *cited in Cartwright v. Pfizer, Inc.*, 369 F. Supp. 2d 876, 883 (E.D. Tex. 2005).[6]

C. SSRIs, Suicidality, and SSRI Litigation

In the past two decades there has been significant debate and inquiry in the medical, pharmaceutical and regulatory communities about the link between SSRIs and suicide. *See* Def. Ex. 7, Memorandum from Thomas P. Laughren, M.D., Director of Division of Psychiatry Products, FDA Center for Drug Evaluation and Research, to Members of the Psychopharmacologic Drugs Advisory Committee ("PDAC") (November 16, 2006). This section of this Order summarizes scientific and regulatory developments, this Court's opinion in *Motus v. Pfizer,* 127 F. Supp. 2d 1085 (C.D. Cal. 2000), and the changes that have occurred since *Motus*.

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[5]The regulation was amended in 2008 to specify that a manufacturer may only change its label "to reflect newly acquired information." Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices, 73 Fed. Reg. 49,603, at 49,609 (Aug. 22, 2008) (to be codified at 21 C.F.R. pts. 314, 601, and 814). The Court will base its decision on the regulations as they existed at the time of Carrasco's death in 2004, but, as the Supreme Court has noted, the addition to the regulation does not change the preemption analysis. *Wyeth v. Levine*, — U.S. —, 129 S. Ct. 1187, 1196-97 (2009).

[6]This section of the C.F.R. was amended in a new rule affecting prescription drugs, issued on January 24, 2006 and effective on June 30, 2006. *See* section C.1 *infra*. The new language reads " reasonable evidence of *a causal association* with a drug; a causal relationship need not have been definitely established." 21 C.F.R. § 201.57(e) (effective to Jun. 30, 2006) (emphasis added).

1. Pre-2000 SSRI suicidality knowledge and labeling.

As noted above, for many decades antidepressant drug labels, presumably including Sandoz's fluoxetine label at the time Noe Carrasco was given his prescription,[7] carried the following standard language:

> Suicide: The possibility of a suicide attempt is inherent in major depressive disorder and may persist until significant remission occurs. Close supervision of high-risk patients should accompany initial drug therapy. Prescriptions for Drug Z should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose.

Pl.'s Ex. 11, Memo from Thomas Laughren, M.D., FDA Center for Drug Evaluation and Research, to Members of the PDAC at 1 (January 5, 2004). As Dr. Laughren noted, this warning "does not explicitly warn of the possibility that antidepressant drugs may have a causal role in the emergence of suicidality early in treatment." *Id.* Concern about the connection between suicide and SSRIs intensified in 1990, when a Harvard Medical School psychiatrist published a paper suggesting that some patients became suicidal as a result of their treatment with Fluoxetine (Prozac). Def. Ex. 7 at 2. As Dr. Laughren of the FDA noted, however, demonstrating a causal link between increased risk of suicide and SSRIs may be elusive because "depression is a serious disorder that itself is associated with suicidality." Def. Ex. 7 at 3.

In the 1990s, the FDA considered and rejected citizen petitions requesting that the FDA revise the labeling of SSRIs – including Prozac – to include warnings about an increased risk of suicide or suicidal thoughts. *Motus*, 127 F. Supp. 2d at 1089-90. In its July 1991 denial of a citizen petition, the FDA stated that "[t]he data and information available at this time do not indicate that Prozac causes suicidality or violent behavior . . . ." *Motus*, 127 F. Supp. 2d at 1089. In its June 1992 decision, the FDA stated that evidence was "not sufficient to reasonably conclude that the use of Prozac is possibly associated with suicidal ideation and behavior." *Id*. at 1090. In a February 17, 1995 letter, the FDA drew Lilly's attention to an article in the British Journal of Medicine by Susan S. Jick, et al., which found that fluoxetine treatment was associated with a higher relative risk of suicide than the other

[7] The Court cannot find in the record any evidence of precisely what was said in the label on the product he was given.

antidepressants in that study. Pl. Ex. 44. The letter stated, "Although the study was less than ideal for addressing this question and included no other selective serotonin reuptake inhibitors, it may be desirable to inform prescribers of this finding." *Id.* Lilly declined to include a suicidality warning in its label at that time, and the FDA took no regulatory action against it. SGI & Lilly's Response to SGI ¶¶ 114-115. In its June 1997 response to a citizen petition, the FDA stated that "no credible scientific evidence has caused the agency to depart from its conclusion that the current Prozac labeling appropriately reflects the level of concern about Prozac and suicidality." *Id.*

2. The Court's opinion in *Motus v. Pfizer*, 127 F. Supp. 2d 1085 (C.D. Cal. 2000).

In 2000, this Court denied a motion for summary judgment based on a claim of preemption in a failure-to-warn case involving another antidepressant, Zoloft. Because Defendants have relied heavily on what they perceive as the differences between this case and *Motus*, the Court will summarize *Motus* and review the scientific and regulatory developments since 2000.

Victor Motus took Zoloft sometime in November 1998, and on November 12, 1998, he committed suicide. *Motus*, 127 F. Supp. 2d at 1086. His widow sued Pfizer, the manufacturer. Pfizer argued that under conflict preemption principles, Motus's state law-based failure to warn claims were preempted, because the FDA had considered and rejected the inclusion of suicide warnings in Zoloft's labeling. *Id.* at 1087. This Court disagreed.

The FDA had instructed Pfizer to use specific text in its labeling. That text is the "standard language" quoted above and used in the Sandoz label at the time Carrasco was given his prescription. In reaching the conclusion that Pfizer had not established impossibility of compliance with state law requirements, the Court agreed with prevailing court opinions that FDA standards for labeling were minimum standards. *Id.* at 1092. Construing the regulations, the Court found that they permitted Pfizer to strengthen Zoloft's warnings without prior FDA approval. *Id.* at 1093-94. In light of FDA decisions rejecting stronger warnings for Prozac, this Court wrote:

> Moreover, and perhaps most importantly, although FDA did not require Pfizer to include suicide-related warnings in Zoloft's label, FDA has not prohibited Pfizer from doing so. On the occasions cited by Pfizer that FDA considered

> links between suicide and SSRIs, FDA did find that the evidence did not support requiring manufacturers to include additional suicide-related warnings. But FDA never stated that it would be impermissible to include additional warnings. This is consistent with the regulatory provision governing warning labels, 21 C.F.R. § 201.57(e), which indicates only those warnings that must be included in drug labeling, but does not prohibit any warnings.

Id. at 1096.

Pfizer had produced evidence that in 1991, 1992, and 1997 the FDA refused to require suicide warnings for Prozac (fluoxetine), the SSRI in question in this case. *See Motus*, 127 F. Supp. 2d at 1089-90. The Court also reviewed Pfizer's "independent" expert-prepared evidence in support of the proposition that stronger warnings would over-deter the use of Zoloft, and concluded that there was "an absence of persuasive evidence establishing a threat of overdeterrence." *Id*. at 1097-98. Pfizer had also proffered a comment by a doctor on the PDAC committee to the effect that there was concern in the scientific community that modifications to the labeling "might" result in a reduction in use, thereby ultimately causing overall injury to the public health, but that he was making no statement as to the correctness of the different positions on the debate on this question. *Id*. at 1098. The Court found that this statement by the PDAC member did not demonstrate "that FDA has found or has relied on a finding that strengthened suicide warnings would overdeter SSRI use." *Id*.

3. SSRI-suicidality knowledge and labeling to August 2004.

Over the years, as new drug applicants submitted information to the FDA, additional scientific data about the risks of suicide was developed. *See* Memorandum from Thomas P. Laughren, M.D., to Members of PDAC and Peds AC (Jan. 5, 2004), Lilly's Ex. U. Between 1995 and 2003, the FDA found no increased risk of suicidality from Prozac in adults, but the parties dispute the thoroughness of the FDA's analysis. *See* SGI ¶¶ 19, 128-132. Although the FDA and its advisors had been studying the relationship between SSRIs and suicidality for some time, its consideration of this issue reached an "important milestone" in September 2003, when it received a report from GlaxoSmithKline ("Glaxo") that pediatric patients taking Paxil were at an increased risk for suicide. *Id.* at 11. After PDAC assessed Glaxo's data, the FDA issued a public health advisory, warning that "preliminary data suggested an

excess of reports for suicidality in pediatric patients." *Id*. at 12.[8] However, on January 5, 2004, the FDA's Dr. Thomas Laughren issued a memorandum stating that "there does not appear to be an increased risk of completed suicide associated with assignment to either active drug or placebo in *adults* with [major depressive disorder]." Lilly's Ex. U, SUF ¶ 22 (emphasis added).

In August 2003, Wyeth (the manufacturer of Effexor) voluntarily enhanced its suicide precaution with respect to pediatric patients without any repercussions by the FDA. SGI ¶ 135. Later on, in May 2006, Glaxo *sua sponte* issued its own adult suicide warning using the CBE process, and the FDA did not object to Glaxo's label change. SGI ¶¶ 163-64. As noted above, the CBE regulation allowed Glaxo to "add or strengthen a contraindication, warning, precaution, or adverse reaction" or to "add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product . . . ." 21 C.F.R. §§ 314.70(c)(6)(iii)(A) & (C).

Since late 2003, the FDA has been strengthening and refining its warning labels for SSRIs. In March 2004, the FDA sent a letter to Lilly instructing it to revise its Prozac warning label regarding suicidality. Lilly's Ex. X. That month, the FDA also issued a Public Health Advisory entitled "Worsening Depression and Suicidality in Patients Being Treated by Anti-Depressant." Lilly's Ex. Y; SUF ¶¶ 26-27. In that advisory the FDA noted that it "asked manufacturers of the following antidepressant drugs [which included fluoxetine] to include in their labeling a Warning statement that recommends close supervision of adult and pediatric patients treated with those agents for worsening depression or the emergence of suicidality." *Id.* The FDA's recommended "Warning Information" stated, in part:

> Health care providers should carefully monitor patients receiving antidepressants for possible worsening of depression or suicidality...Although FDA has not concluded that these drugs cause worsening depression or suicidality, health care providers should be aware that worsening of symptoms could be due to the underlying disease or might be the result of drug therapy.

[8] The Health Advisory was addressed to Health Care Professionals. It discussed increased reports of suicide and suicidality among pediatric patients who were being treated with some antidepressant drugs (including Fluoxetine) and emphasized that the drugs should be used with caution. Plaintiff's Ex. 57.

Id. Lilly incorporated the recommended changes in July 2004. SUF ¶¶ 27.

At no point prior to Carrasco's suicide in August 2004 did Lilly request to add suicide or suicidality language to the Prozac warning label. SUF ¶¶ 206-07. Consequently, of course, the FDA never rejected any such request.

4. SSRI-suicidality knowledge and labeling after Carrasco's August 2004 death.

On September 3, 2004, two weeks after Carrasco's suicide, the FDA issued a letter to all generic fluoxetine manufacturers, including Sandoz, instructing them to revise their labels to include the stronger suicide warning that Lilly had already incorporated in July 2004. Pl.'s Ex. 3. The FDA mandatory warning label stated, in relevant part:

> **Clinical worsening and suicide risk** – Patients with major depressive disorder, both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality), whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Although there has been a longstanding concern that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients, a causal role for antidepressants in inducing such behaviors has not been established. **Nevertheless, patients being treated with antidepressants should be observed closely for clinical worsening and suicidality, especially at the beginning of a course of drug therapy, or at the time of dose changes, either increases or decreases.**

Pl.'s Ex. 3 at 6 (emphasis in original).

In January, February and March of 2005, the FDA issued letters to manufacturers mandating, for the first time, a black box warning concerning the increased risk of suicidality for children and adolescents. In March 2005, Sandoz submitted revised warning labels to the FDA. The new Sandoz label included a black-box warning stating, in relevant part:

> **Antidepressants increased the risk of suicidal thinking and behavior (suicidality) in short-term studies in children and adolescents with major Major Depressive Disorder (MDD) and other psychiatric disorders. Anyone considering the use of fluoxetine or any other antidepressant in a child or adolescent must balance this risk with the clinical need. Patients who are started on therapy should be observed closely for clinical worsening, suicidality, or unusual changes in behavior.**

Pl.'s Ex. 4 (emphasis in original). On Sandoz's label, the warning following the black box stated:

> **Clinical worsening and suicide risk**: Patients with major depressive disorder, both adult and pediatric, may experience worsening of their depression and/or the emergence of suidical ideation and behavior (suicidality), whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. There has been a long standing concern that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients. Antidepressants increased the risk of suicidal thinking and behavior (suicidality) in short-term studies in children and adolescents with Major Depressive Disorder (MDD) and other psychiatric disorders.

Pl.'s Ex. 4 at 8 (emphasis in original).

As is apparent in the evolution of warnings from 2003 to 2005, the initial focus of PDAC's inquiry and of FDA and manufacturer revisions to warning labels was on pediatric patients. However, in 2005, the FDA began a "comprehensive review of 295 individual antidepressant trials that included over 77,000 adult patients with major depressive disorder (MDD) and other psychiatric disorders, to examine the risk of suicidality in adults who are prescribed antidepressants." Third Supp. Authority Ex 1 at 8.[9] On December 13, 2006, the

[9]Press Release, U.S. FDA, "FDA Proposes New Warnings About Suicidal Thinking, Behavior in Young Adults Who Take Antidepressant Medications." (May 2, 2007).

PDAC met to consider the FDA's meta-analysis of the data. Def. Ex. 8.[10] According to the minutes of the PDAC meeting, the PDAC found that the FDA's analysis demonstrated that "the finding of increased short-term risk for suicidality with antidepressant treatment in pediatric patients does appear to extend into the younger adults." Def. Ex. 8 at 247. The PDAC also found that "beyond age 30, antidepressants begin to show an expected protective effect for suicidality, which is most pronounced beyond age 65." Def. Ex. 8 at 247. Finally, the PDAC "was clear to note that age is a possible proxy to a different causation which the FDA needs to further investigate." Def. Ex. 8 at 247. The PDAC meeting concluded with a vote recommending the revision of labeling to include extension to young adults and further recommending that the label change be extended into the black box. Def. Ex. 8 at t 248. The PDAC decided to leave it to the FDA to determine the precise age limit for a required warning. Mem. Ex. 9 at 249.

Based on the PDAC's recommendation, the FDA on August 2, 2007 approved revisions to labels to incorporate the PDAC's recommendations. Lilly's SUF ¶ 37. These remain the suicidality warnings as they exist today. The FDA's new black box warning states, in relevant part:

> **Suicidality & Antidepressant Drugs—Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of [Insert established name] or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. . . .**

SUF ¶ 37 (emphasis in original). The warning following the black box is similar to that

[10]According to the briefing material for the PDAC's meeting on December 13, 1006, the meta-analysis involved 372 placebo-controlled antidepressant trials and almost 100,000 patients. Def. Ex. 7, Thomas P Laughren, M.D., FDA Center for Drug Evaluation and Research, to Members of the PDAC (Nov. 16, 2006).

inside the black box, with the addition of the age-bracket information:

> **WARNINGS – Clinical worsening and suicide risk**
> Patients with major depressive disorder, both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality), whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Suicide is a known risk of depression and certain other psychiatric disorders, and these disorders themselves are the strongest predictors of suicide. There has been a long standing concern, however, that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients during the early phases of treatment. Pooled analyses of short-term placebo-controlled trials of antidepressant drugs. . . showed that these drugs increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults (ages 18-24) with major depressive disorder and other psychiatric disorders. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older.

Pl.'s Ex. 6 (emphasis in original).

5. The FDA's evolving position on preemption

Starting in 2001, the FDA began to take a position in favor of preemption in SSRI litigation. After this Court's decision in *Motus*, the FDA submitted an *amicus* brief in support of preemption in Pfizer's appeal.[11] Prior to its *Motus* brief, the FDA had not

[11]Def. Ex. 1, FDA *Amicus* Brief, *Motus v. Pfizer, Inc.*, Nos. 02-55372, 02-55498 (9th Cir. Sep. 19, 2002). The Ninth Circuit affirmed this Court's decision to dismiss for lack of proximate cause and did not reach the preemption issue. *Motus v. Pfizer, Inc.*, 358 F.3d 659 (9th Cir. 2004).

intervened on its own initiative in private tort litigation on behalf of manufacturers.[12] Following *Motus*, the FDA submitted four more *amicus* briefs: in *Dowhal v. SmithKline Beecham Consumer Healthcare*, No. S109306 (Cal. July 18, 2003), *Kallas v. Pfizer*, No. 2:04CV0998 PGC (D. Utah Sept. 15, 2005), *Colacicco v. Apotex, Inc.*, No. 05-5500-MMB (E.D. Pa. May 10, 2006), and the appeal in *Colacicco v. Apotex, Inc.*, No. 06-3107 (3d Cir. Dec. 4, 2006).[13] Not long after its submission in the *Colacicco* appeal, the FDA issued a detailed position paper on preemption in a 2006 regulatory preamble. Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922 (Jan. 24, 2006) (to be codified at 21 C.F.R. pts. 201, 314, & 601).

In *Wyeth*, the Supreme Court found that the FDA's position in its 2006 preamble "does not merit deference" for several reasons: the FDA did not provide notice to States and interested parties of its "sweeping position" on the FDA's pre-empting effect; the preamble was "at odds with what evidence we have of Congress' purposes; and it reverses the FDA's own longstanding position without providing a reasoned explanation . . . ." *Wyeth v. Levine*, — U.S. —, 129 S. Ct. 1187, 1201 (2009). After the *Wyeth* decision, the FDA withdrew its *amicus* briefs in the *Colacicco* case, which was the only one of the above-listed cases still pending. Thus, this Court will give no weight whatsoever to the position the FDA articulated in these *amicus* briefs and in the 2006 preamble.

III. LEGAL STANDARDS FOR SUMMARY JUDGMENT

Federal Rule of Civil Procedure 56(c) provides for summary judgment when "the pleadings, depositions, answers to interrogatories, and admissions on file, together with the affidavits, if any, show that there is no genuine issue as to any material fact and that the moving party is entitled to judgment as a matter of law." The moving party bears the initial burden of demonstrating the absence of a "genuine issue of material fact for trial." *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 256 (1986). A fact is material if it could affect the

[12]In 1996 the Supreme Court invited the FDA to intervene as amicus in a case involving a medical device. In that case, the FDA took the position that preemption should not apply to the tort claims at issue. *See* Brief for the United States as Amicus Curiae Supporting Respondents/Cross-Petitioners, *Medtronic v. Lohr*, 518 U.S. 470 (Nos. 95-754, 95-886) (March 13, 1996).

[13]Def. Exs. 2-5.

outcome of the suit under the governing substantive law. *Id.* at 248. The burden then shifts to the nonmoving party to establish, beyond the pleadings, that there is a genuine issue for trial. *Celotex Corp. v. Catrett*, 477 U.S. 317, 324 (1986).

"When the party moving for summary judgment would bear the burden of proof at trial, it must come forward with evidence which would entitle it to a directed verdict if the evidence went uncontroverted at trial. In such a case, the moving party has the initial burden of establishing the absence of a genuine issue of fact on each issue material to its case." *C.A.R. Transp. Brokerage Co., Inc. v. Darden Rests., Inc.*, 213 F.3d 474, 480 (9th Cir. 2000) (citations omitted). In contrast, when the non-moving party bears the burden of proving the claim or defense, the moving party can meet its burden by pointing out the absence of evidence from the non-moving party. The moving party need not disprove the other party's case. *See Celotex*, 477 U.S. at 325. Thus, "[s]ummary judgment for a defendant is appropriate when the plaintiff 'fails to make a showing sufficient to establish the existence of an element essential to [his] case, and on which [he] will bear the burden of proof at trial.'" *Cleveland v. Policy Mgmt Sys. Corp.*, 526 U.S. 795, 805-06 (1999) (citing *Celotex*, 477 U.S. at 322).

When the moving party meets its burden, the "adverse party may not rest upon the mere allegations or denials of the adverse party's pleadings, but the adverse party's response, by affidavits or as otherwise provided in this rule, must set forth specific facts showing that there is a genuine issue for trial." Fed. R. Civ.P. 56(e). Summary judgment will be entered against the non-moving party if that party does not present such specific facts. *Id.* Only admissible evidence may be considered in deciding a motion for summary judgment. *Id.*; *Beyene v. Coleman Sec. Serv., Inc.*, 854 F.2d 1179, 1181 (9th Cir.1988).

"[I]n ruling on a motion for summary judgment, the nonmoving party's evidence 'is to be believed, and all justifiable inferences are to be drawn in [that party's] favor.'" *Hunt v. Cromartie*, 526 U.S. 541, 552 (1999) (quoting *Anderson*, 477 U.S. at 255). But the non-moving party must come forward with more than "the mere existence of a scintilla of evidence." *Anderson*, 477 U.S. at 252. Thus, "[w]here the record taken as a whole could not lead a rational trier of fact to find for the nonmoving party, there is no genuine issue for trial." *Matsushita Elec. Indus. Co., Ltd. v. Zenith Radio Corp.*, 475 U.S. 574, 587 (1986) (citation omitted).

IV. DISCUSSION

A. Standards for Federal Preemption

In this section the Court will merely reiterate what it said in *Motus*. This analysis does not necessarily take into account other courts' *post-Motus* characterizations of the scope or nature of pre-emption.

The Supreme Court has explained that there are three ways in which federal law will preempt a state law:

> First, Congress can define explicitly the extent to which its enactments pre-empt state law. . . .
> Second, in the absence of explicit statutory language, state law is pre-empted where it regulates conduct in a field that Congress intended the Federal Government to occupy exclusively. Such an intent may be inferred from a "scheme of federal regulation . . . so pervasive as to make reasonable the inference that Congress left no room for the States to supplement it," or where an Act of Congress "touch[es] a field in which the federal interest is so dominant that the federal system will be assumed to preclude enforcement of state laws on the same subject." . . . Although this Court has not hesitated to draw an inference of field pre-emption where it is supported by the federal statutory and regulatory schemes, it has emphasized: "Where . . . the field which Congress is said to have pre-empted" includes areas that have "been traditionally occupied by the States," congressional intent to supersede state laws must be "clear and manifest." . . .
> Finally, state law is pre-empted to the extent that it actually conflicts with federal law. Thus, the Court has found pre-emption where it is impossible for a private party to comply with both state and federal requirements, . . . or where state law "stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress."

English v. General Elec. Co., 496 U.S. 72, 78-79 (1990) (citations omitted) (holding that nuclear fuel production employee's state law claim for intentional infliction of emotional distress was not preempted by the Energy Reorganization Act). These categories are not "rigidly distinct;" in particular, "conflict" and "field" preemption often overlap. *Id.* at 79 n.5.

The party contending that a claim is preempted bears the burden of establishing preemption. *Jimeno v. Mobil Oil Corp.*, 66 F.3d 1514, 1526 n.6 (9th Cir. 1995). The Supreme Court has established a presumption against finding preemption, especially where state or local regulation of matters related to health and safety are concerned. *See Medtronic, Inc. v. Lohr*, 518 U.S. 470, 485 (1996)("[T]he historic police powers of the States were not to be superceded by the Federal Act unless that was the clear and manifest purpose of Congress."); *N.Y. State Conference of Blue Cross & Blue Shield Plans v. Travelers Inc. Co.*, 514 U.S. 645, 654-55 (1995); *Hillsborough County v. Automated Medical Labs.*, 471 U.S. 707, 715 (1985).

B. The Supreme Court's Decision in *Wyeth*

In *Wyeth*, the Supreme Court addressed the question of whether the FDA's regulation of drug labeling under federal law preempts a plaintiff's state law tort claim for failure to provide an adequate warning. *Wyeth v. Levine*, — U.S. —, 129 S. Ct. 1187, 1194 (2009). Levine sued Wyeth, a major drug manufacturer in Vermont state court, alleging common law negligence and strict liability for failure to adequately warn of the risks of intravenous administration of an anti-nausea drug. Levine alleged that as a result of that failure her arm had to be amputated. *Id.* at 1191. The jury verdict for plaintiff was upheld by the Vermont Supreme Court. *Wyeth* appealed to the United States Supreme Court, asserting that it could not be found liable under state tort law because Levine's claims were subject to both conflict preemption—*i.e.*, Wyeth claimed it could not comply with both the state-law duties on which Levine based her claims and its federal labeling duties—and to "obstruction preemption"— *i.e.*, requiring Wyeth to comply with a state-law duty to provide a stronger warning "would obstruct the purposes and objectives of federal drug-labeling regulation," *Id.*, at 1199.

On the issue of conflict preemption, the *Wyeth* Court held that the tort claims were not preempted, because "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 [the manufacturer] to comply with both federal and state requirements." *Id.* at 1198. The Court found it very unlikely that the FDA would bring an enforcement action against a manufacturer for strengthening a warning pursuant to its authority to do so under the CBE regulation. It stated, "And the very idea that the FDA would bring an enforcement action against a manufacturer for strengthening a warning pursuant to the CBE regulation is difficult to accept—neither Wyeth nor the United States has identified a case in which the FDA has

done so." *Id.* at 1197. The Court explained that the "manufacturer bears responsibility for the content of its label at all times. It 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 . . . . Thus, when the risk of gangrene from [the method of drug administration] became apparent, Wyeth had a duty to provide a warning that adequately described that risk and the CBE regulation permitted it to provide such a warning before receiving the FDA's approval." *Id.* at 1198. The Court also relied on the findings that the FDA had not intended to prohibit a more stringent warning and that the manufacturer had not presented data to the FDA specifying dangers of such a warning, or proposing a warning that the FDA rejected. *Id.* *Compare* SGI ¶¶ 206-207 (stating that prior to Carrasco's suicide, Lilly never proposed and the FDA never rejected a request by Lilly to add suicide or suicidality language to its warning labels).

The Supreme Court also rejected Wyeth's "obstruction pre-emption" argument that "requiring it to comply with a state-law duty to provide a stronger warning about IV-push administration would obstruct the purposes and objective of federal drug labeling regulation." The Court found "no merit in this argument, which relies on an untenable interpretation of congressional intent and an overbroad view of an agency's power to preempt state law." *Id.* at 1199. (*See* section II C(5), *supra*.) Although the Court noted "that an agency regulation with the force of law can pre-empt conflicting state requirements," it went on to reject the FDA's reliance on its 2006 "Preamble": "We are faced with no such regulation in this case, but rather with an agency's mere assertion that state law is an obstacle to achieving its statutory objectives." *Id.* at 1200-01.

The parties have cited various lower courts' decisions on FDA preemption since *Wyeth*. The overwhelming weight of the authority has rejected pre-emption claims by both brand-name and generic drugs. The most recent decision to find no pre-emption for generic manufacturers is *Demahy v. Actavis, Inc.*, 593 F.3d 428 (5th Cir. 2010). The most recent decision to find no preemption for a brand name manufacturer in connection with an SSRI suicide case (involving Paxil) is *Mason v. SmithKline Beecham Corp.*, — F.3d —, 2010 WL 605922 (7th Cir. Feb. 23, 2010).

C. Both Defendants' Claims on Conflict Preemption

The Defendants argue that *Wyeth* does not foreclose preemption here because there is stronger evidence in this case than in *Wyeth* that the FDA would have refused to permit a

more stringent label.

Preemption may be implied where compliance with both federal and state requirements is impossible. *Florida Lime & Avocado Growers, Inc. v. Paul,* 373 U.S. 132, 142-43 (1963). The Defendants argue that federal law precluded them from including any additional warnings of a risk of suicide or suicidality in their labeling. They assert that additional warnings of a risk of suicide/suicidality in SSRI drug labeling would have rendered the label misbranded under the FDCA and the FDA regulations. *See* 21 U.S.C. §§ 352(a),(f). Sandoz additionally argues that regulations prohibit generic manufacturers from changing a label without prior FDA approval.

The risk of FDA enforcement action against Sandoz would have rendered compliance impossible as of July 15, 2004, when Carrasco began taking fluoxetine, only if there was "clear evidence that the FDA would not have approved a change" to Prozac's label. *Wyeth*, 129 S. Ct. at 1198. Like the defendant in *Motus*, the Defendants here rely on the fact that prior to Carrasco's prescription, the FDA had rejected citizen petitions to add a warning to the Prozac label about the risk of suicide. Defendants also point to a 2002 FDA decision to the effect that, based on a review of all SSRI drugs, the scientific evidence did not show an association between SSRIs and suicide, as well as a January 2004 FDA memorandum stating that there did not appear to be an increased risk of suicide in adults from use of SSRIs.

The FDA's rejections of citizen petitions in the 1990s do not constitute clear evidence that warnings of such an association in July 2004 would have been false and misleading, and hence not permitted. As this Court concluded in *Motus*, the FDA's rejection of those 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. *Motus* at 1096.

In the period between 2002 and Carrasco's prescription, the FDA's position was changing and had changed, at least in part because of GlaxoSmithKline's report to the FDA in September 2003 that company studies showed an increased risk for pediatric patients. As a result of the Glaxo report, the FDA replaced its prior opposition to any possible warning with the position that there was no evidence to support a finding of increased risk of suicidality in adults, as evidenced in the January 5, 2004 Dr. Laughren memorandum. Lilly's SUF ¶ 22. However, in March 2004, the FDA issued a Public Health Advisory asking manufacturers to include in their labeling a warning recommending close supervision

of adult and pediatric patients treated with those agents for worsening depression or the emergence of suicidality." Def. Ex. 6 at 231. Therefore, unlike in 2002 and earlier, by March 2004 the FDA accepted that scientific evidence did show an association between SSRIs and suicide in pediatric patients and it was in the process of determining whether such an association existed for adult patients as well.

Given these developments in the state of scientific knowledge in the SSRI industry leading up to July 2004, it cannot be said that there is clear evidence that in July 2004 the FDA would have prohibited additional suicidality warning language.[14]

Defendants do not offer evidence of any instances where additional safety warnings for an approved drug, whether through a labeling change or some other medium, rendered a drug "misbranded." On the contrary, there have been several notable instances in which SSRI drug manufacturers' strengthened warnings were *not* rejected as "misbranding" by the FDA. For example, in 2003, amid concerns that the SSRI Effexor caused increased risk of suicide among pediatric patients, the drug's manufacturer, Wyeth, unilaterally added additional warnings to its labels and issued a "Dear Health Care Professional" letter noting the warnings to practitioners. Pl.'s Ex. 10. In 2006, GlaxoSmithKline, manufacturer of Paxil, unilaterally strengthened the suicide and suicidality warnings in Paxil's label to warn of an increased risk for young adults and issued a "Dear Health Care Professional" letter notifying practitioners of the new warning. Pl.'s Ex. 12. These manufacturers' actions were consistent with their obligation under the regulations to revise their labeling to "include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug." 21 C.F.R. § 201.57(e) (effective to Jun. 29, 2006)." Defendant has provided the Court with no evidence that the FDA took any action against either Wyeth or GlaxoSmithKline for "misbranding" their products. On the contrary, after these manufacturers voluntarily strengthened the warnings on their labels, the FDA issued new *mandatory* labeling requirements to reflect the same conclusions about the risk of suicidality in pediatric patients and, later, in young adult patients. Pl.'s Exs. 10 & 12. At the hearing,

[14]At the hearing, Lilly relied on the FDA's August 2007 warning label change, which stated, "Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24." SUF ¶ 37. However, this language, from 2007, does not provide "clear evidence" that the FDA would not have approved a broader suicidality warning that pertained to young adults in 2004. *See Wyeth*, 129 S. Ct. at 1198.

counsel for Lilly attempted to distinguish Wyeth's and GlaxoSmithKline's actions, saying that their enhanced warning labels were based on data for Effexor and Paxil, not Prozac, and that the studies focused primarily on pediatric patients. *See* Pl.'s Supp. Exs. 56 & 75. Lilly's counsel is incorrect. Though the Wyeth studies and warning pertained to pediatric patients, Ex. 56, the GlaxoSmithKline warning also addressed adult patients, Ex. 75 at 12. Moreover, and more fundamentally, Lilly's argument fails because Lilly ignores its burden here. To establish a preemption defense, a drug manufacturer must produce "clear evidence that the FDA would not have approved a change to [the drug's] label." *Wyeth*, 129 S.Ct. at 1198. A mere possibility that the FDA might not have allowed an enhanced suicidality warning for Prozac, despite allowing it for Effexor and Paxil, is not enough to warrant preemption.

As stated in *Cartwright v. Pfizer, Inc.*, 369 F. Supp. 2d 876, 885-86 (E.D. Tex. 2005), "Given the hearings by both Congress and the FDA regarding suicidality, the FDA's PDAC's recent decision to recommend black box warnings regarding suicidality in children and adolescents, and the numerous experts who have concluded that there is a link between SSRIs, like Zoloft, and suicidality, it would be inconceivable to this Court to argue that an additional warning regarding suicidality would be false or misleading." Defendants offer nothing but theoretical assumptions of what the FDA would have done , and that is not enough to warrant a finding of preemption. *See Witczak v. Pfizer, Inc.*, 377 F. Supp. 2d 726, 731 (D. Minn. 2005) (finding no direct conflict where Pfizer's claim of direct conflict rests on "speculative hypotheticals") (citing *Gade v. Nat'l Solid Wastes Mgmt. Ass'n*, 505 U.S. 88, 110 (1992) (Kennedy, J., concurring)).

Providing additional warning to a drug label is a far cry from the types of labeling that the FDA has deemed "misbranded." *Cf. United States v. Snoring Relief Labs, Inc.*, 210 F.3d 1081 (9th Cir. 2000) (holding that an over-the-counter anti-snoring mouthpiece was misbranded because of inadequate directions for safe use); *United States v. Johnson*, 471 F.3d 764 (7th Cir. 2006) (affirming criminal sentence of petitioner who sold misbranded repackaged cough suppressant labeled "for research and development only" to Internet customers for recreational use); *United States v. Lane Labs-U.S.A., Inc.*, 427 F.3d 219 (3d Cir. 2005) (affirming district court award of restitution to customers who purchased misbranded topical skin cream and dietary supplement claiming to treat HIV and cancer).

As previously noted, Plaintiff has not proffered the precise language she thinks should have been used. So Defendants have presented a challenge to plaintiff's general allegation of failure to warn. That challenge is, like the one in *Motus*, "overbroad." *Motus*, 127 F.

Supp. 2d at 1095. As the Court previously concluded:

> Although certain suicide warnings could violate federal law because they were false or misleading or were not based on "the essential scientific information needed" for safe use, the Court does not think that any and every suicide-related warning that might be required under state law is necessarily false or misleading, or not based on "the essential scientific information needed" for safe use.

Id. Plaintiff *has* provided examples of warnings that are stronger than the one Defendants provided in July 2004, but still fall short of warning of an actual "association" between SSRIs and suicidality in adults. (Defendants claim such a warning would be preempted.) For example, Dorsett points to the warning that has been on Sandoz's labeling since September 2004: "Patients with major depressive disorder, both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality), whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs." Opp'n at 4; Pl.'s Ex. 3.

The theoretical possibility that the FDA might have found a given warning to be misleading is insufficient to support a finding that Defendants faced a direct conflict between state and federal law. What matters is not whether manufacturers perceive a potential conflict that might subject them to FDA enforcement action, but whether there is clear evidence that the FDA would not have approved any stronger warning—and Defendants have not shown that.

D. Sandoz's Claim Unique to Generics

Sandoz makes another argument, one unique to it: FDA regulations prohibited it from making *any* changes to Fluoxetine labeling that would deviate from that of the "innovator" (or "listed") drug—*i.e.*, , Prozac—because generic drug manufacturers may not make any change in a warning label without prior FDA approval. This contention was not addressed in *Wyeth.* It lacks merit.

Supplements and other changes to an approved generic drug application are governed

by 21 C.F.R. § 314.97. That section states: "The applicant shall comply with the requirements of §§ 314.70 and 314.71 regarding the submission of supplemental applications and other changes to an approved abbreviated application." In turn, the CBE regulation in section 314.70(c) allows manufacturers to distribute products with strengthened warnings upon FDA's receipt of a supplemental application. 21 C.F.R. § 314.70(c)(6)(iii).

Sandoz argues that section 314.70(c) does not apply to generic manufacturers, because generic labels must match those of the innovator drug.[15] It argues that a generic manufacturer may change its warnings only if the FDA approves the changed labels for both the generic and innovator drugs. In support of this contention, Sandoz cites the statutory requirement that generic drug applicants must "show that the labeling proposed for the new drug is the same as the labeling approved for the listed drug," 21 U.S.C. § 355(j)(2)(A)(v). Recently, the Fifth Circuit rejected the argument proffered by Sandoz, noting that "[w]hile Congress plainly intended for a generic drug manufacturer to submit labeling identical to—or the 'same as'—the brand name drug when seeking ANDA approval, the statutory scheme is silent as to the manufacturer's obligations after the ANDA is granted." *Demahy*, 593 F.3d at 436. *See also Laisure-Radke v. Par Pharm., Inc.*, 426 F. Supp. 2d 1163, 1169 (W.D. Wash. 2006) ("[O]nce a generic manufacturer holds an approved ANDA for a particular product, it can add or strengthen a contraindication, warning, precaution, or adverse reaction at any time without prior FDA approval.").

The ANDA process merely frees a manufacturer from the pre-approval clinical trial requirements so long as it can prove that the generic is bioequivalent to the innovator drug. *Schering Corp. v. Food and Drug Admin.*, 866 F. Supp. 821, 823 (D.N.J. 1994), *judgment aff'd*, 51 F.3d 390 (3d Cir. 1995). After the bifurcated application process, generic drug manufacturers and brand name drug manufacturers are treated the same. By the plain text of 21 C.F.R. § 314.97, the CBE process applies to both generic and brand name manufacturers. Both are permitted to distribute drugs containing changes within thirty days of the FDA's

[15]At the hearing, Plaintiff's counsel directed the Court's attention to Sandoz's (then called "Geneva Pharmaceuticals, Inc.") Application to Market a New Drug, where the company representative signed a statement agreeing to "comply with all applicable laws and regulations that apply to approved applications, including . . . [r]egulations on making changes in application in 21 CFR 314.70, 314.71, and . . . 314.97 . . . ." Pl.'s Supp. Ex. 112 at 2. This document is not dispositive of the question of whether section 314.70 applies to Sandoz, but it does lend some support to Plaintiff's position.

receipt of the supplement, and generic and brand name manufacturers alike are required to revise the labeling to "include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved." 21 C.F.R. § 314.70(c)(4); 21 C.F.R. § 201.57(e) (effective to Jun. 29, 2006).[16]

Sandoz nevertheless argues that the Court should find that the FDA has consistently interpreted section 314.70 to be inapplicable to generic manufacturers, and that the Court should defer to this interpretation.[17] In support of this position, Sandoz refers the Court to several guidance documents issued by the FDA. *See* Abbreviated New Drug Applications Regulations, 57 Fed. Reg. 17950, 17961 (Apr. 28, 1992) (to be codified at 21 C.F.R. pts. 2, 5, 10, 310, 314, 320, and 433) ("[T]he ANDA product's labeling must be the same as the listed drug product's labeling . . . . After approval of an ANDA, if an ANDA holder believes that new safety information should be added, it should provide adequate supporting information to FDA, and FDA will determine whether the labeling for the generic and listed drugs should be revised."); the FDA's withdrawn *Amicus Curiae* brief in *Colacicco v. Apotex, Inc*., No. 06-3107 (3rd. Cir. Dec 4, 2006) ("*Colacicco II Amicus* Br.") at 8, n.4; Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices, 73 Fed. Reg. 2848, 2849 n.1 (proposed Jan. 16, 2008) ("CBE changes are not available for generic drugs approved under an abbreviated new drug application under 21 U.S.C. 355(j). To the contrary, a generic drug manufacturer is required to conform to the approved labeling for the listed drug.").

First of all, it is not clear that these pronouncements merit consideration. The *Colacicco amicus* brief has been withdrawn and the 2008 proposed regulation was never adopted. With respect to the comments in the 1992 regulation, the one circuit court to have analyzed these comments—the Fifth Circuit—found that the comments did not speak directly to the ability of a generic manufacturer to use the CBE regulation to revise a

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[16]In a memo dated January 5, 2004 to the members of the FDA's Pharmacological Drugs Advisory Committee ("PDAC"), FDA Psychiatric Drug Products Team Leader Dr. Thomas P. Laughren specifically noted that "sponsors have the authority to make changes of this nature, i.e. that are perceived to strengthen labeling from the standpoint of safety, without prior approval of FDA." (Pl.'s Ex. 11 at 11).

[17]The Supreme Court in *Wyeth* did not explicitly address the issue of deference to the FDA on the issue of preemption for generics, so the Court will address this issue here.

warning label. *Demahy v. Actavis*, 593 F.3d 428, 442 (5th Cir. 2010). According to the Fifth Circuit, FDA's comment that "if an ANDA holder believes that new safety information should be added, it should provide adequate supporting information to FDA, and FDA will determine whether the labeling for the generic and listed drugs should be revised," 57 Fed. Reg. at 17961, means only that "the FDA is the ultimate arbiter for all changes—whether prompted by a pioneer manufacturer or a generic one." 593 F.3d at 442. "*Every* submitted change requires FDA approval, even one that takes effect immediately through the CBE process." *Id.* Thus, the one presently valid document interpreting the ANDA regulatory scheme does not necessarily prescribe that the CBE process is inapplicable to generic manufacturers.

Moreover, even if the 1992 comments, described on page 26, are read to exclude generic manufacturers from using the CBE process, they would not be entitled to deference in this interpretation. An agency's interpretation of its own regulations is "controlling unless 'plainly erroneous or inconsistent with the regulation.'" *Auer v. Robbins*, 519 U.S. 452, 461 (1997) (quoting *Robertson v. Methow Valley Citizens Council*, 490 U.S. 332, 359 (1989)); *accord Federal Express Corp. v. Holowecki*, 552 U.S. 389, 397 (2008). Here, section 314.97 makes it clear that the CBE regulation in section 314.70 applies to generic drug manufacturers. Section 314.70, in turn, does not contain any language exempting generic drug manufacturers. The position that Sandoz ascribes to the FDA impermissibly stretches the meaning of the provisions at issue, and is inconsistent with sections 314.97 and 201.57(e).

Not only is there no support in the plain text of the regulations for Sandoz's position, there is no support in the Congressional history of the Hatch-Waxman Act of 1984 for shielding generic manufacturers from liability for their warnings. In *Foster v. American Home Products Corp.*, 29 F.3d 165 (4th Cir. 1994), the Fourth Circuit addressed this issue directly:

> Although generic manufacturers must include the same labeling information as the equivalent name brand drug, they are also permitted to add or strengthen warnings and delete misleading statements on labels, even without prior FDA approval. The statutory scheme governing premarketing approval for drugs simply does not evidence Congressional intent to insulate generic drug manufacturers from liability for misrepresentations made regarding their products, or to otherwise alter state products liability law. Manufacturers of generic

> drugs, like all other manufacturers, are responsible for the representations they make regarding their products.

Foster, 29 F.3d at 170. *See also Demahy*, 593 F.3d at 449; *Mensing v. Wyeth, Inc.*, 588 F.3d 603, 607-08 (8th Cir. 2009) (no preemption for a generic manufacturer of a diabetes drug). Like the Fourth, Fifth, and Eighth Circuits, this Court finds the argument distinguishing generic manufacturers from their brand name counterparts unpersuasive.[18]

E. Both Defendants' Claims of Frustration of Congressional Purpose (Obstacle Preemption).

The Defendants also assert what is known as obstacle preemption. Under this doctrine, a court will find preemption where "'under the circumstances of [a] particular case, [the challenged state law] stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress.'" *Crosby v. Nat'l Foreign Trade Council*, 530 U.S. 363, 373 (2000) (quoting *Hines v. Davidowitz*, 312 U.S. 52, 67 (1941)). If the purposes of a Congressional statute cannot be accomplished if state law were allowed to operate, then the state law must yield. *Crosby*, 530 U.S. at 373.

The Defendants argue that allowing state failure-to-warn lawsuits would frustrate the FDA's objectives by interfering with the agency's role in ensuring the accuracy of prescription drug labeling and by over-deterring use of SSRI drugs. This argument was effectively foreclosed by the holding in *Wyeth* that a state failure-to-warn claim did not obstruct the purposes and objectives of federal drug labeling regulation. *Wyeth*, 129 S. Ct. at 1199-1204. The Court held that the manufacturer had not demonstrated that "failure-to-warn claims like Levine's obstruct the federal regulation of drug labeling." *Id.* at 1204. Both *Wyeth* and this case involve failure-to-warn claims, and there is no

[18]Sandoz also cites, and at the hearing relied heavily upon, 21 C.F.R. § 314.150(b)(10). This section merely provides that the FDA "may" initiate a hearing for the withdrawal of a drug's approval if the labeling is "no longer consistent with that for the listed drug;" it does not *require* that the generic drug label be *identical* at all times with the listed drug label. Sandoz cites no evidence to show that the FDA in fact has ever acted under § 314.150(b)(10) to withdraw approval for a strengthened generic drug warning on the grounds that the stronger warning has rendered the generic drug labeling "no longer consistent" with that of the listed drug.

meaningful basis on which to distinguish this case from *Wyeth.*

V. CONCLUSION

FDA labeling regulations and state law adequacy of warning duties have coexisted from the time the FDCA was first enacted. Under California law "a manufacturer discharges its duty to warn if it provides adequate warnings to the physician about any known or reasonably knowable dangerous side effects." *Motus v. Pfizer, Inc.*, 196 F. Supp. 2d 984, 990-91 (C.D. Cal. 2001) (citing *Carlin v. The Superior Court of Sutter County*, 13 Cal. 4th 1104, 1112-13 (1996). Likewise, the FDA requires manufacturers to proactively revise their labels upon learning of "reasonable evidence" of "an association of a serious hazard with a drug" (after June 2006, a "causal association). 21 C.F.R. § 201.57(e). A direct and positive conflict would arise "if a state, by positive law, required a drug manufacturer to include a warning that the FDA had previously rejected as scientifically unsubstantiated, [so] that inclusion could expose the manufacturer to liability for misbranding." *Souther v. Eli Lilly & Co. (In re Zyprexa Products Liability Litigation)*, 489 F. Supp. 2d 230, 275(E.D.N.Y. 2007) (citing 21 U.S.C. § 352). Here, there is no such conflict between the state law duty and the FDA's standard. Even assuming a difference in the state and federal standards, a jury verdict of negligence, which imposes damages but does not compel a manufacturer to change its labels, does not necessarily create a direct and positive conflict. *See id.* at 276-77 (citing *Bates v. Dow Agrisciences LLC*, 544 U.S. 431, 444 (2005) ("None of these common-law rules requires that manufacturers label or package their products in any particular way.")).

Based on the evidence before it, the Court cannot find that it would have been impossible for Defendants to comply with federal and state law or that the application of state law would frustrate Congress's purpose in enacting the FDCA. The Defendants have not provided evidence that state law here "actually conflicts with federal law." *English*, 496 U.S. at 78-79. Absent clear Congressional intent to do so, the Court will not foreclose the traditionally available state law remedy for which the FDCA provides no substitute. *See Medtronic, Inc.*, 518 U.S. at 487 (plurality opinion) ("It is, to say the least, 'difficult to believe that Congress would, without comment, remove all means of judicial recourse for those injured by illegal conduct.' ") (quoting *Silkwood v. Kerr-McGee Corp.*, 464 U.S. 238, 251 (1984)); *Bates*, 544 U.S. at 449 ("If Congress had intended to deprive injured parties of a long available form of compensation, it surely would have expressed that intent more clearly."); *Desiano v. Warner-Lambert & Co.*, 467 F.3d 85, 97 n.9 (2d

Cir. 2006) ("An agency cannot supply, on Congress's behalf, the clear legislative statement of intent required to overcome the presumption against preemption.") (citations omitted). Thus, the Defendants have failed to meet their burden of establishing preemption.

Accordingly, the Court DENIES Defendants' motions for partial summary judgment.[19]

Initials of Preparer : SMO

[19]Docket No. 31 & 79.