Demahy v. Wyeth Inc et al Doc. 36

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF LOUISIANA

JULIE DEMAHY	CIVIL ACTION
VERSUS	NO: 08-3616
WYETH INC., ET AL	SECTION: J

ORDER & REASONS

Before the Court is Defendant Actavis Inc.'s ("Actavis") **Motion to Dismiss (Rec. Doc. 19)** under Rule 12(b)(6) based on federal conflict preemption. The motion came before the Court for oral argument on September 17, 2008, and was taken under advisement. Having reviewed the motion, the memoranda of counsel, the parties' statements at oral argument, and the applicable law, the Court finds as follows.

FACTS & PROCEDURAL HISTORY

Plaintiff Julie Demahy ("Demahy"), a fifty-eight year old female, began taking metoclopramide, the generic version of the name brand drug Reglan, in 2002 and continued treatment until April 2006. Metoclopramide is prescribed for treatment of gastroesophagal reflux disease, commonly known as acid reflux. In October of 2007, Demahy was diagnosed by physicians at the University of Texas, Southwestern Medical Center with tardive dyskenesia, which the doctors believed had been caused by long-term use of metoclopramide. Tardive dyskenesia is a neurological disorder that causes involuntary movements of the face, torso,

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and extremities.

As a result of her injuries allegedly caused by her treatment with metoclopramide, Demahy filed suit against Wyeth Inc., Schwarz Pharma, Inc., and Actavis in the 22nd Judicial District Court for the Parish of St. Tammany. In her state court complaint, Demahy asserted personal injury claims under the Louisiana Products Liability Act ("LPLA"), specifically for failure to warn of the risks of neurological disorder after long-term use of metoclopramide. In addition, Demahy claims that Actavis breached its duty to provide updated information regarding the hazards of metoclopramide to the Food and Drug Administration ("FDA"), which would have resulted in more adequate warnings on the labels for the drug. Further, Demahy claims that Actavis intentionally concealed scientific research regarding the risks of metoclopramide with respect to neurological disorders in order to mislead the medical community and prevent FDA action.

The case was removed to this Court on June 6, 2008 (Rec. Doc. 1). Defendants Wyeth, Inc. and Schwarz Pharma, Inc. have been dismissed from the suit without prejudice (Rec. Doc. 15). Thus, only defendant Actavis remains. Actavis, formerly Purepak Pharmaceutical Company, is a generic manufacturer of metoclopramide, and according to Demahy's pharmacy records was the manufacturer of the metoclopramide she consumed. The parties

do not dispute that Actavis's label and package insert for its generic metoclopramide was at all relevant times identical to the label and package insert for the name brand drug.

THE PARTIES' ARGUMENTS

Actavis argues that Demahy's products liability claims under the LPLA should be dismissed as a matter of federal conflict preemption. Specifically, Actavis asserts that under the relevant provisions of the Food, Drug, and Cosmetics Act ("FDCA"), the label and package insert for its generic product need not and in fact could not have been altered from the label and package insert that was approved by the FDA for name brand metoclopramide. As such, Actavis argues that Demahy's LPLA failure-to-warn claims are preempted both as a matter of direct conflict preemption, since Actavis's failure-to-warn duties under the LPLA directly conflict with its duties to maintain identical labels under the FDCA, and as a matter of so-called "obstacle preemption," since compliance with failure-to-warn tort principles under the LPLA would frustrate the goals of the FDCA and the 1984 Hatch-Waxman Amendments to the FDCA.

The Hatch-Waxman Amendments provided differing approval standards for generic drug manufacturers from those applicable to name brand drug manufacturers. See 21 U.S.C. § 355(j) (2008). According to Actavis, the Hatch-Waxman Amendment codified FDA regulations in order to streamline generic drug approval and

eliminate the need for generic manufacturers to replicate the time-consuming and costly drug safety research already performed by the name brand manufacturer. The truncated process by which a generic drug is approved is referred to in §355(j) as an Abbreviated New Drug Application ("ANDA") as opposed to the more extensive New Drug Application ("NDA") required for name brand drugs. Under the ANDA process, Actavis asserts that generic drugs are not subject to the same initial and continuing testing and reporting requirements as name brand drugs. Additionally, according to Actavis, the FDA mandates that generic drug labels must *always* remain identical to the FDA-approved labels of the pioneer name brand drug. See §355(j)(2)(A)(v). As such, Actavis argues that the FDA has specifically rejected the availability to generic drug manufacturers of the Changes Being Effected ("CBE") mechanism provided in 21 C.F.R. §314.70, which allows name-brand drug manufacturers to make unilateral post-approval labeling changes, subject to FDA notice and approval. Accordingly, Actavis asserts that Demahy's LPLA claims are preempted because any state law duty to alter or increase generic drug label warnings over and above the labeling approved by the FDA conflicts with the requirements and goals of the FDCA and applicable regulations.

In opposition, Demahy claims that the §355(j) ANDA labeling requirements apply only during the *initial approval* process for a

generic drug. After a generic drug has been approved by the FDA via the ANDA process, however, Demahy asserts that the generic manufacturer has a continuing duty under the LPLA and the FDCA to include warnings regarding newly discovered risks "as soon as there is reasonable evidence of a causal association with a drug." 21 C.F.R. §§201.57(c)(6)(I) & 201.80(e).

Demahy argues further that while it is "questionable" whether generic manufacturers can utilize the CBE procedures under 21 C.F.R. §314.70 to unilaterally add new safety information to their labels, Actavis still had some duty to at least notify the FDA of possible adverse side effects. Thus, because Actavis essentially did nothing, it should be liable under the LPLA for failure to warn of the adverse neurological side effects of metoclopramide that allegedly caused Demahy's tardive dyskinesia.

In response, Actavis reiterates that generic drug labels must always remain identical to those of the name brand drug. Also, Actavis argues that the regulations relied on by Demahy regarding the duty to update labels are inapplicable to generic drug manufacturers.

LAW & DISCUSSION

As set forth by the Supreme Court in Bell Atlantic Corp. v. Twombly, 127 S. Ct. 1955 (2007), the standard to be applied when deciding a Rule 12(b)(6) motion is not whether it is conceivable

that some set of facts could be developed to support the allegations in the complaint, but rather whether the plaintiffs have stated enough facts in the complaint to allow a court to conclude that it is "plausible" that the plaintiffs are entitled to relief. The Court must accept as true all well-plead allegations and resolve all doubts in favor of the plaintiff. Tanglewood East Homeowners v. Charles-Thomas, Inc., 849 F.2d 1568, 1572 (5th Cir. 1988).

As a preliminary matter, it should be noted that Demahy's claims are preempted to the extent they allege fraud-on-the-FDA under state law with regard to Actavis's alleged intentional concealment of medical research concerning the neurological effects of metoclopramide. See Buckman Co. v. Pl.'s Legal Comm., 531 U.S. 341, 348 (2001) (holding that "state law fraud-on-the-FDA claims conflict with, and are therefore impliedly pre-empted by, federal law"). Therefore, any fraud-on-the-FDA claim by Demahy under Louisiana law is preempted and must be dismissed under Rule 12(b)(6) for failure to state a cause of action.

A. Federal Conflict Preemption

Actavis asserts that Demahy's LPLA failure-to-warn claims are barred as a matter of implied federal conflict preemption[1]

[1] The parties do not dispute the fact that the FDCA itself does not expressly preempt state law failure-to-warn claims against generic drug manufacturers. Therefore only implied conflict preemption is at issue.

under the FDCA and applicable interpretive regulations and other position documents of the FDA.

The principles of implied conflict preemption proceed from the Supremacy Clause of the United States Constitution, and provide that federal law must prevail over state law when "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." Freightliner Corp. v. Myrick, 514 U.S. 280, 287 (1995) (internal quotations and citations omitted) (emphasis added). Conflict preemption is "fundamentally a question of congressional intent," as opposed to instances of express preemption in which Congress enacts a statute that expressly provides for preemption of state law. Geier v. Am. Honda Motor Co., 529 U.S. 861, 884 (2000). As such, analysis of implied federal conflict preemption should proceed from a "presumption against pre-emption [sic]" when a case concerns whether state authority conflicts with the existence of federal authority. New York v. F.E.R.C., 535 U.S. 1, 17-18 (2002). Thus when federal authority is at odds with state law, a court must "start with the assumption that the historic police powers of the States," such as health and safety regulation, "were not to be superseded . . . unless that was the clear and manifest purpose of Congress. " Hillsborough County, Fl. v. Automative Med.

Labs., Inc., 471 U.S. 707, 715 (1985).

B. Agency Interpretations and Judicial Deference

When a court reviews an agency's construction of a statute that it administers, the court must determine "whether Congress has directly spoken to the precise question at issue," for if Congressional intent is clear, both "the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress." Chevron U.S.A., Inc. v. Natural Res. Def. Council, Inc., 467 U.S. 837, 842-43 (1984). However, "if the statute is silent or ambiguous with respect to the specific issue," the court must determine "whether the agency's construction is based on a permissible construction of the statute." Id. at 843. On these terms, agency regulations are controlling "unless they are arbitrary, capricious, or manifestly contrary to the statute." Id. at 844. Under these broad principles, the Supreme Court has developed three different deference analyses for specific types of agency actions.

1) Chevron Deference

Besides the process of enacting administrative regulations, however, administrative agencies "necessarily make all sorts of interpretive choices, and while not all of those choices bind judges to follow them, they certainly may influence courts facing questions the agencies have already answered." United States v. Mead Corp., 533 U.S. 218, 227 (2001). Nonetheless, "[t]he fair

measure of deference to an agency administering its own statute has been understood to vary with the circumstances, and courts have looked to the degree of the agency's care, its consistency, formality, and relative expertness, and to the persuasiveness of the agency's position." Id. at 228 (citations omitted). In this analysis, "the fact that the agency has from time to time changed its interpretation . . . does not . . . lead [to the conclusion] that no deference should be accorded the agency's interpretation of the statute." Chevron, 467 U.S. at 863-64. Additionally, under the Court's holding in Chevron, when Congress has generally conferred authority on an agency, Congress expects the agency to speak with the binding authority of law "when it addresses ambiguity in the statute or fills a space in the enacted law," even if there was no congressional intent for a particular result. Mead Corp., 533 U.S. at 229. In this regard, "[i]t is fair to assume that Congress contemplates administrative action with the effect of law when it provides for a relatively formal administrative procedure tending to foster the fairness and deliberation that should underlie a pronouncement of such force." Id. Accordingly, most cases in which courts have afforded the high level of Chevron deference to agency statements have involved only the results of notice-and-comment rulemaking, namely regulations, or formal adjudications. Id. at 230. Nonetheless, the Court has occasionally afforded Chevron

deference to unofficial agency interpretations depending on the circumstances, but only when the agency's interpretation is "reasonable" and when the authorization and procedure for promulgating the interpretation evidences congressional intent that it be binding. Meade, 533 U.S. at 229-31.

2) Auer Deference

In addition to this high Chevron standard of deference, the Supreme Court has developed a second standard of deference when the language of the regulation is ambiguous. An agency's interpretation of its own ambiguous regulation is entitled to deference unless it is "plainly erroneous or inconsistent with the regulation" being interpreted. Auer v. Robbins, 519 U.S. 452, 461 (1997) (internal quotation marks omitted). As such, the Fifth Circuit employs a two-step test when interpreting an agency regulation: 1) whether the regulation is "ambigu[ous] **with respect to the specific question considered**;" and 2) whether the agency's interpretation of its ambiguous regulation is "plainly erroneous or inconsistent with the regulation." Belt v. EmCare, Inc., 444 F.3d 403, 408 (5th Cir. 2006) (citing Christensen v. Harris County, 529 U.S. 576, 588,(2000) & Auer, 519 U.S. at 461) (emphasis added).

3) Skidmore Deference

Finally, in addition to Chevron and Auer deference, the Court has developed the third and least deferential Skidmore

standard for situations in which an agency lacks the congressional authority required for Chevron deference and the regulation at issue is not ambiguous, thus precluding Auer deference. This Skidmore standard provides that an agency's "rulings, interpretations, and opinions" are not controlling on courts, but merely "constitute a body of experience and informed judgment to which courts and litigants may properly resort for guidance." Skidmore v. Swift & Co., 323 U.S. 134, 140 (1944). As such, an agency's informal position statements are subject to "some weight" and should "make a difference" in a court's preemption analysis. See Geier, 529 U.S. at 883. Nonetheless, the weight of deference under Skidmore is affected by "the thoroughness evident in its consideration, the validity in its reasoning, its consistency with earlier and later pronouncements, and all those factors which give it power to persuade, if lacking power to control." Skidmore, 323 U.S. at 140. Essentially, under Skidmore a court merely considers whether the agency statement at issue has the "power to persuade." Id.

Along with the development of these three differing standards of deference, the Supreme Court has held that an agency's preemption interpretations of the statutes it is authorized to implement may be entitled to some level of deference. Geier, 529 U.S. at 883 (noting that Department of Transportation's comments supporting the preemptive affect of its

Federal Motor Vehicle Safety Standard promulgated under the National Traffic and Motor Vehicle Safety Act should "make a difference" in the Court's conflict preemption analysis). In fact, the Court has held that federal regulations, as well as federal statutes, can themselves preempt state law. Hillsborough, 471 U.S. at 713.

C. The FDA's Position on Preemption of State Law Failure-to-Warn Claims under the FDCA.

Actavis has pointed the Court to five specific pieces of evidence that support its position that the FDCA, applicable regulations, and informal FDA position statements have consistently over the past twenty years supported the proposition that state law failure-to-warn claims based on the inadequacy of generic drug labels are preempted as matter of conflict preemption. Each of these pieces of evidence will be treated in succession.

1) **Abbreviated New Drug Application Regulations, 54 Fed Reg 28872, 28884 (proposed July 10, 1989) (hereinafter "1989 Proposed Rule")**

The first piece of evidence Actavis cites stems from the proposed rule and comments created during the FDA's initial rulemaking process to implement the provisions of the 1984 Hatch-Waxman amendments. See 1989 Proposed Rule at 28872 ("[FDA] is proposing regulations to implement [the Hatch-Waxman amendments]"). The proposed rules were intended to "benefit

consumers by making generic drug products available more quickly." Id. The relevant portion of the 1989 Proposed Rule cited by Actavis provides the following:

> In addition, the act requires that an applicant include in the ANDA information adequate to show that the proposed labellng [sic] for its drug product is the same as that of the reference listed drug except for changes required because of differences approved under a petition or because the drug product and the reference listed drug are produced or distributed by different manufacturers. . . .
>
> FDA emphasizes that the exceptions to the requirement that a generic drug's labeling be the same as that of the listed drug are limited. The agency will not accept ANDA's for products with significant changes in labeling (such as new warnings or precautions) intended to address newly introduced safety or effectiveness problems not presented by the listed drug. Such labeling changes do not fall within the limited exceptions in sections 505(j)(2)(A)(v) and 505(j)(3)(G) of the act. Moreover, FDA does not believe that it would be consistent with the purpose of section 505(j) of the act, which is to assure the marketing of generic drugs that are as safe and effective as their brand-name counterparts, to interpret section 505(j)(2)(A)(v) of the act as permitting the marketing of generic drugs with diminished safety or effectiveness and concomitantly heightened labeled warnings. Thus, where a proposed change in a generic drug, e.g., in packaging or inactive ingredients or, for a petition-approved drug, in the approved change, would jeopardize the safe or effective use of the product so as to necessitate the addition of significant new labeled warnings, the proposed product would not satisfy the labeling requirements of sections 505(j)(2)(A)(v) and 505(j)(3)(G) of the act.
>
> To assist the agency in determining if the applicant's proposed labeling is the "same as" that of the reference listed drug, except for the types of differences described above, FDA proposes in § 314.94(a)(8)(iv) to require the applicant to include in the ANDA a side-by-side comparison of the applicant's proposed labeling with the currently approved labeling for the listed drug referred to in the ANDA with all differences annotated and explained.

Id. at 28884.

Actavis cites the above quoted portion of the 1989 Proposed Rule for the proposition that "[f]or almost twenty years, the FDA has consistently stated that generic labeling must, **at all times be identical** to name brand labeling and that only it, alone, may determine whether generic labeling should be revised." Def.'s Reply Mem. Supp. Sum. J., 1 (emphasis added). However, the 1989 Proposed Rule does not address the question of whether generic labels must **always** be identical to that of the name brand pioneer drug; rather, the 1989 Proposed Rule concerns **only the initial ANDA application and approval process**, and thus only concerns whether the generic label must be the same as the name brand at the time of the initial ANDA application. See generally 1989 Proposed Rule at 2875-76. Neither party disputes the fact that a generic drug must have the "same" label as the name brand pioneer drug at the time of an initial ANDA application. The crucial question, which the 1989 Proposed Rule does not address, is whether a generic drug *that has already been approved* via the ANDA process can change its label to include new or different warnings without FDA approval. Thus Actavis's reference to the 1989 Proposed Rule merely begs the question at issue in this case of whether a generic drug manufacturer can update its labels to comply with state law tort duties after initial FDA approval without violating the FDCA.

Furthermore, it is interesting to note that from the very beginning, the FDA has required that ANDA applicants include labels that are the "same" as those approved for the name brand pioneer drug. The 1989 Proposed Rule makes numerous references to this "same as" requirement. On the other hand, the FDA's regulation that specifically applies to *withdrawal* of generic drug approvals after the initial ANDA approval provides that an such approval can be withdrawn if the label for the generic is "no longer **consistent with** that for the listed drug." 21 C.F.R. §314.150(b)(1)(2008). If the FDA truly intended generic drug labels to be the "same as" the name brand drug labels throughout the life of the generic drug, the discrepancy between the manifold use of the phrase "same as" in the FDA's initial rulemaking on the *pre-approval* ANDA process is curious in comparison to the use of the phrase "consistent with" in the regulation governing *post-approval* processes. Further implications of 21 C.F.R. §314.150 with respect to Actavis's preemption arguments are discussed in section C(3) below.

Finally, the 1989 Proposed Rule itself contemplates approval of post-ANDA unilateral labeling changes by generic drug manufacturers. In discussing the different procedural protections that must be afforded to NDA and ANDA approved manufacturers during the approval withdrawal process, the FDA commented:

> The agency recognizes, however, that ANDA holders may be entitled to more extensive procedural protections when the agency proposes to withdraw approval of their applications under sections 505(e) of the act rather than under 505(j)(5) of the act. This result is procedurally fair because of the different types of issues to be resolved under the two sections of the act. When the agency proposes to withdraw an ANDA under section 505(e) of the act, rather than section 505(j)(5) of the act, **the basis for withdrawal will directly concern aspects of safety and effectiveness, labeling, or manufacturing** that are specific to the ANDA holder's product; the basis for such a withdrawal will not be the safety and effectiveness of the underlying drug substance. **In a 505(e) proceeding that concerns only a specific ANDA and not the underlying drug substance, therefore, the ANDA holder will be in the best position to present relevant evidence and to represent its interests**. In many instances, an ANDA holder alone will possess the information essential to resolving factual issues necessary for the agency to make an informed judgment about whether or not approval of the application should be withdrawn or suspended for grounds specified under section 505(e) of the act.

1989 Proposed Rule at 28904, § N (emphasis added). This portion of the 1989 Proposed Rule references 21 U.S.C. §505(e), which provides various grounds under which the Secretary of the FDA can withdraw an approval of "any drug under [§505]," which would include ANDA approved drugs under §505(j). 21 U.S.C. §505(e)-(j) (2008). One of these grounds specifically applicable to withdrawal of §505(j) generic ANDA approvals is if "on the basis of new information before him . . . the labeling of such drug . . . is false or misleading." Id. at §505(e). All this taken together suggests that a generic drug manufacturer could in fact unilaterally change its label warnings after initial ANDA

approval, subject to the FDA's approval of the change and after due process proceedings on the issue of withdrawal. Therefore, not only does the 1989 Proposed Rule initially beg the question of whether generic manufacturers can make unilateral changes after ANDA approval, it actually *answers* the question by indicating that generic manufacturers can do so, subject to due process approval or withdrawal by the FDA. As a result, the 1989 Proposed Rule actually undermines Actavis's argument on preemption by indicating that generic manufacturers can make unilateral post-ANDA approval labeling changes.

Finally, this excerpt from §N of the 1989 Proposed Rule sheds light on the meaning of 21 C.F.R. §314.97 (discussed in further detail below in section C(3)). Section 314.97 provides that a generic manufacturer "shall comply with the requirements of [21 C.F.R.] §314.70," which outlines the CBE procedures that include the requirements and process for making unilateral post-approval label changes. See 21 C.F.R. §§314.70(c)(6).[2] Section

[2] 21 C.F.R. §314.70(c)(6) provides in pertinent part that the holder of an NDA approval may make labeling changes "[t]o add or strengthen a contraindication, warning, precaution, or adverse reaction" when there is evidence of a causal association sufficient to meet the standard for label inclusion under 21 C.F.R. §201.57(c). 21 C.F.R. §314.70(c)(6)(iii)(A)(2008). The current language of this provision went into effect on September 22, 2008. The reference to the §201.57(c) evidentiary standard requires that warnings be based on "clinical data" or possibly "serious animal toxicity." 21 C.F.R. §201.57(c). Thus, the reference to §201.57(c)in §314.70(c)(6)(iii)(A) ensures that any added warnings will be sufficiently substantiated to merit inclusion on the label.

314.97 was first proposed in the 1989 Proposed Rule; additionally, in the FDA report regarding the final rulemaking process for 21 C.F.R. §314, the FDA notes that they "received no comments on [§314.97] and . . . finalized it without change." Abbreviated New Drug Application Regulations, 57 Fed. Reg. 17950, 17965 (Apr. 28, 1992). Thus throughout the entire life of the regulations governing generic drug labeling changes, §314.97 has mandated, without any opposition or comment, that generic manufacturers "shall comply" with the CBE labeling change provisions of §314.70(c)(6). As a result, generic manufacturers should be able to unilaterally change their labels after initial ANDA approval, albeit subject to FDA oversight and approval under §314.70(c)(6).

Under the above analysis, the appropriate level of deference that this Court should give the 1989 Proposed Rule is essentially irrelevant, because the 1989 Proposed Rule does not shed any pertinent light on the issue of whether the FDCA preempts Demahy's failure-to-warn claims under the LPLA. Furthermore, to the extent that the 1989 Proposed Rule is relevant at all to the issue of preemption, it actually contemplates unilateral labeling

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The prior version of §314.70(c)(6)(iii)(A), which would have been in effect during the period relevant to this case, provided essentially the same CBE procedure for labeling changes, but without reference to "evidence of a causal association" under §201.57(c). Regardless, the differences between the current and former versions of §314.70(c)(6)(iii)(A) are irrelevant to this analysis. See 21 C.F.R. §314.70(c)(6)(iii)(A) (2007).

changes by generic manufacturers, and thus goes against a finding of preemption as argued by Actavis.

2) Abbreviated New Drug Application Regulations, 57 Fed. Reg. 17950 (Apr. 28, 1992) (hereinafter "1992 Final Rule")

The next pieces of evidence cited by Actavis in support of its preemption argument are FDA comments on the final rule that enacted the federal regulations promulgated under the Hatch-Waxman amendments and which govern the ANDA application process. See 1992 Final Rule, at 17950 ("These regulations implement title I of the [Hatch-Waxman Amendments]. This final rule covers subjects such as ANDA content and format, approval and nonapproval of an application, and suitability petitions.").

Again, as with Actavis's reference to the 1989 Proposed Rule, the 1992 Final Rule specifically deals only with labeling requirements for generic manufacturers who are in the *initial ANDA application process*, and does not address post-approval labeling changes. See, e.g., 1992 Final Rule, at 17951-52. Nonetheless, Actavis cites the 1992 Final Rule for the proposition that generic labels must always be the same as name brand labels throughout the life of the generic drug. However, the section of the 1992 Final Rule that Actavis cites is the FDA's response to a public comment on 21 C.F.R. §314.1, which lays out the scope of §314, suggesting that the "FDA accept ANDA's with warnings or precautions in addition to those" on the name brand pioneer drug's label. Id. at 17953. The FDA

disagreed with the comment and stated that "the applicant's proposed labeling" for a generic ANDA must be the "same as" that of the listed name brand drug. Id. Thus, as with the 1989 Proposed Rule, the comment relates only to "applicants," not manufacturers who have already received ANDA approval, and uses the "same as" language, which is crucially different from the "consistent with" language of §314.150(b)(1). In fact, the 1992 Final Rule expressly distinguishes between ANDA "**applicants**," the manufacturers seeking ANDA approval, and ANDA "**holders**," those who have received approval. See, e.g., 1992 Final Rule at 17951 ("The final rule is substantially similar to the proposal, although FDA has made some minor changes, such as requiring **applicants** to include a table of contents in the review copies of an ANDA . . . and other minor changes regarding periodic reports from ANDA **holders.**") (emphasis added).

Further, Actavis specifically cites Comment 20 of the 1992 Final Rule, which includes the FDA's response to a public comment suggesting that generic manufacturers be allowed to submit a suitability petition[3] for an ANDA "for a product whose labeling differs from the [name brand] drug by being 'more clear or offer[ing] better directions regarding how the drug should be

[3] A suitability petition is the mechanism by which a manufacturer may seek approval for "drugs that have a different active ingredient, route of administration, dosage form, or strength." 1992 Final Rule, at 17957.

taken." Id. at 17957, Cmt. 20. The FDA first noted that "[l]abeling differences . . . are not proper subjects for a suitability petition," then went on to "remind[] applicants that the labeling for an ANDA product must be the same as the labeling for the [name brand] product." Id. The comment also notes that an ANDA applicant who believes that the labeling for a proposed drug product should differ from that of the name brand drug should contact the FDA for a determination of whether both the generic and name brand labels should be changed. Id. Again, this section refers only to ANDA "applicants," and not to generic manufacturers who have already obtained ANDA approval.

The 1992 Final Rule does include the FDA's first suggestion that a generic manufacturer cannot make post-approval label changes without prior FDA approval. In response to a public comment suggesting that the FDA allow ANDA applicants to deviate from the name brand label to add safety-related information, the FDA suggested that "[a]fter 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." Id. at 17961, cmt. 40 (emphasis added). While this suggestion supports Actavis's position that generic manufacturers cannot change their labels without prior FDA approval, the comment cannot be taken at face value. First,

it should be noted that the comment is in response to a suggestion that *applicants* be allowed to deviate from the name brand label. Thus, to the extent that the FDA's response suggests that ANDA *holders* must receive FDA approval before making label changes, the response is outside the public comment's scope. Second, this non-responsive comment by the FDA flies in the face of 21 C.F.R. §314.97, which as noted above mandates that generic manufacturers shall comply with the provisions of 21 C.F.R. §314.70, the regulation that establishes the CBE procedures. Finally, Comment 40 does not expressly preclude generic manufacturers from making unilateral label changes; it merely suggests that they "should provide" relevant information to the FDA. This permissive language in a non-responsive comment does not constitute a definitive statement by the FDA that generic manufacturers cannot unilaterally update their labels. Thus not only is this non-responsive, and merely permissive, comment extraneous, it is also inconsistent with §§314.97 and 314.70. As a result, Comment 40 is either irrelevant or merely entitled to Skidmore deference, and does not have the power to persuade in support of Actavis's preemption position.

Finally, as it did in the 1989 Proposed Rule, the FDA suggests in the 1992 Final Rule that generic manufacturers *can unilaterally change their labels* without prior FDA approval. In

response to a comment suggesting that NDA and ANDA holders should submit the same post-marketing reports on their products, the FDA stated:

> After careful consideration, FDA has revised § 314.98 [the post-marketing reporting provision] to require ANDA applicants to submit a periodic report of adverse drug experiences even if the ANDA applicant has not received any adverse drug experience reports **or initiated any labeling changes**. As revised, the requirement is identical to that imposed on NDA holders. **Periodic reports by ANDA holders will help FDA determine whether ANDA products have appropriate labeling** and ensure that no adverse drug experiences go unreported.

1992 Final Rule, 17965, cmt. 53. This comment, in the context of post-marketing reporting requirements, *clearly* contemplates that a generic manufacturer with ANDA approval may initiate labeling changes. Furthermore, the comment anticipates such unilateral labeling changes by ANDA holders because it notes that post-marketing reporting requirements "will help FDA determine whether ANDA products have appropriate labeling," which suggests that labels may have been changed by ANDA holders after initial approval. Therefore, as in the 1989 Proposed Rule, the FDA expressly contemplates unilateral label changes by generic manufacturers with ANDA approvals. As such, the 1992 Final Rule does not support Actavis's preemption position.

Again, as with the 1989 Proposed Rule, the level of deference this Court should give the 1992 Final Rule is irrelevant since the 1992 Final Rule does not speak directly to the issue of preemption. The only suggestion of preemption in

the 1992 Final Rule is couched in permissive terms, and is then undermined by the FDA's later recognition of the possibility of unilateral label changes by generic manufacturers.

Nonetheless, the 1989 Proposed Rule and the 1992 Final Rule, to the extent that they are relevant, are entitled to the high level of Chevron deference afforded agency decisions made pursuant to notice-and-comment rulemaking. However, in contrast to Actavis's arguments, the relevant portions of the 1989 Proposed Rule and 1992 Final Rule reveal that the *FDA took no direct position* on this issue of preemption in those notice-and-comment produced statements, and even suggested the possibility of unilateral labeling changes by generic manufacturers. In fact, only very recently (see section C(4) below) has the FDA directly addressed whether generic manufacturers can unilaterally alter their labels with respect to preemption of state law failure-to-warn claims. As such, the FDA's position on preemption of state law failure-to-warn claims against generic manufacturers has *not been consistent* over the last twenty years. Moreover, the only relevant portions of the 1989 Proposed Rule and the 1992 Final Rule that are subject to Chevron deference actually suggest that the FDA *historically confirmed* the right of generic manufacturers to unilaterally alter their labels. This conclusion is bolstered by the fact that the FDCA does not expressly preempt state law products liability claims, and the

fact that such claims come under the traditional and presumptively non-preempted power of the states to protect the health and safety of their citizens.

Furthermore, to the extent the 1989 Proposed Rule and the 1992 Final Rule can be construed as FDA interpretations of their ambiguous regulations on the exact issue of preemption, they would be subject to Auer deference. However, because the rules are inconsistent with other FDA statements and regulations, they are not entitled to Auer deference. As such, they are entitled to Skidmore deference only, and they do not have the power to persuade under that standard.

3) **21 C.F.R. §314.150**

The third piece of evidence allegedly supporting Actavis's arguments regarding conflict preemption is 21 C.F.R. §314.150, which has already been discussed to some extent above. Section 314.150 establishes the grounds under which the FDA can withdraw approval of an NDA or ANDA. 21 C.F.R. §314.150 (2008). Actavis cites §314.150 for the proposition that generic drugs must always follow the labeling of the name brand drug "verbatim" even after initial approval of the generic product via the ANDA process.

However, as discussed above, §314.150 does not use the word "verbatim" or the phrase "same as" in its provisions applicable to withdrawal of an ANDA based on labeling changes. The text of §314.150 provides in pertinent part that the FDA may withdraw an

ANDA if "the labeling for the drug product that is the subject of the abbreviated new drug application is **no longer consistent with** that for the listed drug referred to in the abbreviated new drug application, except for differences approved in the [ANDA]." Id. Again, as noted above, the term "no longer consistent with" does not mean "verbatim," "identical," or "same as." A generic label may be "consistent with" a name brand label even if it is not exactly the "same as" that label. Further, even if the generic label includes additional warnings that do not appear on the name brand label, these additional warnings may still be "consistent with" the general purpose of the name brand label to inform the consumer of the relevant risks of the drug. Regardless, the conspicuous use of the phrase "consistent with" as opposed to the phrase "same as" which appears in the FDA's regulatory comments, and the term "verbatim" which appears in Actavis's pleadings, suggests that generic labels may not necessarily have to be exactly the same as name brand labels throughout the life of the generic product. Thus, §314.150 does not expressly prohibit generic manufacturers from making unilateral labeling changes under the CBE process, and therefore does not support Actavis's preemption argument.

4) **Supplemental Applications Proposing Labeling Changes for Approved Drugs,Biologics, and Medical Devices, 73 Fed Reg 2848, 2849-2850 (proposed January 16,2008) (hereinafter "2008 Proposed Rule").**

The next evidence Actavis relies on are the FDA's comments in a recent proposed rule concerning amendments to the regulations governing supplemental applications for proposed labeling changes for approved drugs. 2008 Proposed Rule, at 2848. The 2008 Proposed Rule is intended to update and codify the FDA's allegedly "longstanding view" on when labeling changes can be made without prior FDA approval via the CBE process. The 2008 Proposed Rule includes the first and only explicit notice-and-comment produced statement by the FDA that generic drug manufacturers cannot utilize the CBE label change procedure under 21 C.F.R. §314.70(c)(6)(iii)(A):

> **FN1 CBE changes are not available for generic drugs approved under an [ANDA] 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. See 21 CFR 314.150(b)(10); see also 57 FR 17950, 17953, and 17961.

2008 Proposed Rule, at 2849, n.1 (emphasis added).

It should first be noted that the 2008 Proposed Rule's main purpose is to propose changes to the mechanics of the §314.70 CBE procedures. As a result, the 2008 Proposed Rule has *nothing whatsoever to do with* the existence or availability of those procedures to ANDA holders. Furthermore, while the FDA does expressly indicate that the CBE procedure is not available to generic drug manufacturers with ANDA approval, this comment is relegated to a mere *footnote* in the *Supplementary Section* of a *proposed rule* that *does not mention ANDA or generic manufacturers*

anywhere else in the entirety of the proposed rule. The FDA essentially took the opportunity to make a significant statement on preemption of generic drug labeling claims in the relative obscurity of a footnote in the introductory statement of a document that has nothing at all to do with rules pertaining to generic drugs or to the ANDA process. The Fifth Circuit has suggested that a footnote to a finalized regulation, even though it may have been the product of notice-and-comment rulemaking, may not be entitled to Chevron or Auer deference. See Langbecker v. Elec. Data Systems Corp., 476 F.3d 299, 311 n.22 (5th Cir. 2007). As such, a footnote in a *proposed* rule should not be afforded any significant level of deference.

Additionally, this statement in a footnote in the 2008 Proposed Rule *contradicts the FDA's own regulations*. As noted above, 21 C.F.R. §314.97 provides in full: "[an ANDA 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." 21 C.F.R. §314.97 (2008). Thus because §314.70(c)(6)(iii)(A) explicitly allows for unilateral labeling changes, and since §314.97 explicitly mandates that ANDA applicants and holders "shall comply" with §314.70, the FDA's statement that generic manufacturers with ANDA approval cannot utilize CBE labeling changes *directly contradicts the FDA's own regulations*.

Finally, and perhaps most importantly, even if the FDA's footnoted statement in the 2008 Proposed Rule were not extraneous and contradictory, it is entitled to no deference whatsoever under Fifth Circuit precedent. In no uncertain terms, the Fifth Circuit has held that "proposed regulations are entitled to no deference until final." In Re Appletree Markets, Inc., 19 F.3d 969, 973 (5th Cir. 1994). Therefore, not only is the statement that generic manufacturers cannot make CBE labeling changes irrelevant in its own context and contradictory to the FDA's own regulations, it is not entitled to any deference at all under Fifth Circuit law. Therefore, the 2008 Proposed Rule does nothing to support Actavis's position.

a) Cases Applying the Non-Preemption Analysis

Further, and consistent with the above analysis, the District Court for the Western District of Washington has held that generic drug manufacturers have the same ability as name brand manufacturers to unilaterally update their labels via the CBE provisions of §314.70. Laisure-Radke v. Par Pharm., Inc, 2006 WL 901657 (W.D. Wash. 2006). The Laisure-Radke court was faced with the same issue currently before this Court, namely whether there was a conflict between Washington state law failure-to-warn claims based on generic drug labels and the FDCA. Id. at *3. The defendant generic drug manufacturer in Laisure-Radke argued that under the Hatch-Waxman Amendments to the FDCA

and 21 C.F.R. §314.94, which requires ANDA applicants to submit side-by-side comparisons of the approved name brand and proposed generic labels, "a generic manufacturer simply cannot deviate its labeling from that of the [name brand] drug." Id. The court noted that generic and name brand labels must indeed be identical during the initial ANDA approval process, but found that "*once the ANDA is approved*, generic manufacturers have the same power and duty to add or strengthen their warnings, as do the manufacturers of pioneer drugs, and therefore the same liability." Id. (emphasis in original). The Laisure-Radke court relied on the Fourth Circuit's 1994 decision in Foster v. American Home Products Corp., which reviewed the issue of whether a name brand manufacturer can be held liable for negligent misrepresentation caused by another company's generic product. Id. (citing Foster, 29 F.3d 165 (4th Cir. 1994). The Foster court held that under 21 C.F.R. §§314.70 and 314.97, generic manufacturers have the same ability to alter a generic drug's labeling to strengthen or add warnings as name brand manufacturers. Id. at *4 (citing Foster, 29 F.3d at 169). Although the Foster court addressed a different legal issue, the Laisure-Radke court found its reasoning persuasive. As such, the Laisure-Radke court held that under §314.70, which expressly applies to generic drug manufacturers under §314.97, "once a generic drug 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." Id. at *5.

It should be noted that the Laisure-Radke decision was handed down in 2006, before the FDA's footnoted statement in the 2008 Proposed Rule that generic manufacturers cannot utilize the CBE process to make unilateral label changes. However, as discussed above, the statement in the 2008 Proposed Rule is contradictory and extraneous, and also commands no deference from a Fifth Circuit court.

Further, several cases have agreed with the Foster/Laisure-Radke analysis even after the advent of the 2008 Proposed Rule. Like the Foster case, these cases arose in the context of claims against name brand manufacturers for failure to update their own labels, which in turn rendered the labels of generic drugs inadequate. Thus, these cases essentially involved claims against name brand manufacturers for faulty labeling on generic drugs that the name brand manufacturers did not even produce. See, e.g., Swicegood v. Pliva, Inc., 543 F. Supp. 2d 1351, 1358 (N.D. Ga. 2008); Morris v. Wyeth, 2008 WL 2677048, *3 (W.D. Ky. 2008); Smith v. Wyeth, Inc., 2008 WL 2677051, *3 (W.D. Ky. 2008); Wilson v. Wyeth, Inc., 2008 WL 2677049, *3 (W.D. Ky. 2008).[4] Due

[4] The cases from the Western District of Kentucky were apparently all related as the decisions employ virtually identical language and all deal with issues of liability for

to the posture of these cases, the issue of preemption was not raised by the parties, and as such the courts either expressly avoided the preemption issue, or spoke on the issue in dicta only. See, e.g. Swicegood, 543 F. Supp. 2d at 1358 n.1 (noting that defendants did not argue for dismissal based on federal statutory preemption, but also noting that Georgia courts have held that state common law claims are not preempted by the FDCA). Nonetheless, all these cases rely to some degree or another on the policy arguments presented in Foster:

> We do not accept the assertion that a generic manufacturer is not responsible for negligent misrepresentations on its product labels if it did not initially formulate the warnings and representations itself. When a generic manufacturer adopts a name brand manufacturer's warnings and representations without independent investigation, it does so at the risk that such warnings and representations may be flawed. In cases involving products alleged to be defective due to inadequate warnings, the manufacturer is held to the knowledge and skill of an expert . . . . The manufacturer's status as expert means that at a minimum he must keep abreast of scientific knowledge, discoveries, and advances and is presumed to know what is imparted thereby. The same principle applies in the instant case; as an expert, a manufacturer of generic products is responsible for the accuracy of labels placed on its products. 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. 21 C.F.R.§ 314.70 (1993). 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

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generic labeling of metoclopramide.

> 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 169-70 (internal quotations and citations omitted) (emphasis added). In the context of the above language from Foster, the Swicegood court held that "Defendant [generic manufacturer] had the ability - albeit with approval from the FDA - to add to or strengthen a contraindication, warning, precaution, or adverse reaction." 543 F. Supp. 2d at 1358 (citing 21 C.F.R. §314.70 and Colacicco v. Apotex, Inc., 432 F. Supp. 2d 514, 523 (E.D. Pa. 2006)). Also, the Morris/Smith/ Wilson cases held that "FDA regulations allow the manufacturer of a generic drug "[t]o add or strengthen a contraindication, warning, precaution or adverse reaction . . . without prior FDA approval." Morris, 2008 WL 2677048 at *4; Smith, 2008 WL 2677051 at *4; Wilson, 2008 WL 2677049 at *4. While these courts did not squarely address the issue of preemption, they relied on the Foster/Laisure-Radke policy analysis, which is itself supported by the interplay between §§314.70 and 314.97. Thus these cases support the proposition that state law failure-to-warn claims are not preempted by the Hatch-Waxman Amendments or the relevant FDA statements on preemption.

Finally, the California Court of Appeal has recently held that the FDCA does not preempt state-law failure-to-warn claims. McKenney v. Purepac Pharm. Co., 83 Cal. Rptr. 3d, 810 (Cal. App.

5th Dist. Sept. 25, 2008). The McKenney case involved the same defendant[5] as in this case and the same failure-to-warn claims under California law based on the absence of a tardive dyskenesia warning on the label for generic metoclopramide. Id. at 813. Citing the 1992 Final Rule for support, the McKenney court found "no reason to distinguish between original or [name brand] drugs and their generic equivalents for federal preemption purposes." Id. at 818. Thus, the McKenney court correctly noted that the 1992 Final Rule actually takes a *non-preemption* position, and properly concluded that the FDA's conflicting statements do not support preemption.

Actavis has cited several other post-2008 Proposed Rule decisions that have found preemption of state law failure-to-warn claims for inadequate generic drug labeling based on the FDA's statement in the proposed rule. See Mensing v. Wyeth, ---- F. Supp. 2d ----, 2008 WL 2444689, * 8 (W.D. Minn. 2008); Gaeta v. Perrigo Pharmaceuticals Co., 2008 WL 2548813, *4 (N.D. Cal. 2008); Bolin v. Smithkline Beecham Corp., 2008 WL 3286973, *8 (S.D. Fla. 2008); Masterson v. Apotex Corp., 2008 WL 3262690, *4 (S.D. Fla. 2008); Valerio v. Smithkline Beecham Corp., 2008 WL 3286976, *8 (S.D. Fla. 2008). However, none of these cases address the apparent contradiction between the FDA's statement in

[5] As noted above, Actavis was formerly Purepac Pharmaceutical Company.

the 2008 Proposed Rule and the clear mandate of §314.97 that generic manufacturers "shall comply" with the requirements of §314.70. As such, the analysis of the Foster/Laisure-Radke cases is more persuasive, since that analysis takes into account the contradiction between the footnoted language of the 2008 Proposed Rule and the binding mandate of §§314.97 and 314.70.

Additionally, none of the cases cited by Actavis distinguish between the "consistent with" language of §314.150, which is the regulation that Actavis and most other generic manufacturers have relied on for the proposition that generic labels must always be the "same as" name brand labels, and the "same as" language used in the FDA's comments on the regulation during the proposal and final rulemaking processes (in the 1989 Proposed Rule and the 1992 Final Rule).

Finally, none of these cases address the fact that the 1989 Proposed Rule and the 1992 Final Rule actually suggest a non-preemption position, as noted by the McKenney court. Accordingly, these cases are not persuasive.

b) The Mensing Decision

The case cited by Actavis that most directly supports the FDA and Actavis's preemption position is Mensing v. Wyeth, which was expressly adopted by the other 2008 cases from the Southern District of Florida that Actavis has cited. ---- F. Supp. 2d ----, 2008 WL 2444689 (W.D. Minn.); see also Bolin v. Smithkline

Beecham Corp., 2008 WL 3286973, 8 (S.D. Fla. 2008). As such, a close reading and criticism of the Mensing decision will bolster the non-preemption analysis.

Mensing involved the exact same claims that Demahy has brought before this Court, namely that generic metoclopramide manufacturer Actavis negligently failed to include warnings of the risk of tardive dyskinesia on its labels in violation of state law failure-to-warn duties. 2008 WL 3286973 at *1. Specifically, the Mensing plaintiff argued that "Actavis . . . ignored scientific and medical literature establishing a higher risk of developing tardive dyskinesia, failed to request a labeling revision to the FDA, and failed to report safety information directly to the medical community." Id. In opposition, Actavis argued that plaintiff's claims were conflict preempted. Id. In response to the preemption argument, plaintiff asserted that while generic manufacturers may be required to submit identical labels to that of the name brand drug during the *initial* ANDA approval process, they nonetheless have a duty to update their labels *post-ANDA* approval to include newly discovered warnings. Id.

The Mensing court initially considered the pertinent provisions of the FDCA, the legislative history of the act, the governing regulations, and the FDA's comments on the regulations to conclude that a generic manufacturer cannot unilaterally alter

its labels. Id. at *5. In support of its finding of preemption, the Mensing court initially cited the 1989 Proposed Rule in holding that "the FDA's own comments in implementing the Hatch-Waxman Act support the conclusion that a generic manufacturer is not free to unilaterally alter the labeling from that of the name brand drug." Id. However, as noted in the above discussion, the 1989 Proposed Rule was concerned only with pre-ANDA approval requirements, not post-ANDA approval duties. Also, the 1989 Proposed Rule itself goes on to suggest that generic manufacturers *can* unilaterally change their labels post-ANDA approval, subject to FDA approval. See 1989 Proposed Rule at 28904, § N (discussed above at section C(1)).

Next, the Mensing court cited §314.150 and the portions of the 1992 Final Rule discussed in section C(2) above to support its finding of preemption. Mensing, 2008 WL 2444689 at * 5-6. Specifically, the Mensing court noted that §314.150 allows for withdrawal of an ANDA if a generic label is no longer "consistent with" the name brand label, and quoted the 1992 Final Rule comment that "[a]fter approval of an ANDA, if an ANDA holder believes that new safety information should be added, it should provide adequate supporting information to FDA" for the FDA to determine whether a label change is appropriate. Id. However, the Mensing court did not discuss the significant difference between the "consistent with" language of §314.150 and the "same

as" language used throughout the FDA's 1989 Proposed Rule and 1992 Final Rule. Also, the Mensing court did not point out that the "should provide" language of the 1992 Rule is simply permissive and not mandatory, whereas the language of §314.97 is mandatory. Finally, the Mensing court ignored other statements by the FDA in the 1992 Final Rule that suggest that generic manufacturers can unilaterally alter their labels.

The Mensing court also disagreed with plaintiff's argument that the CBE mechanism provided in §314.70 allows generic drug manufacturers to make unilateral label changes. Relying on an FDA amicus brief, the Mensing court pointed out the FDA's argument that:

> Although [21 C.F.R. §314.97] contains a provision requiring [ANDA] applicants to 'comply with the requirements of §314.70 . . .' *that provision does not modify the requirement that the drug label for a generic drug must be the* ***same as*** *the label for the approved innovator drug . . . Any ambiguity in the regulatory text has been clarified by FDA, which explained at the time of the promulgation that the regulations do not authorize drug manufacturers to add new warnings to the approved labeling for the innovator drug.* ***See*** 57 Fed. Reg. at 17961, 17953, 17955.

Mensing, 2008 WL 2444689 at *7 (emphasis in original).

Although the Mensing court may have been entitled to rely on the FDA's amicus position regarding the ambiguity between §314.97 and §314.70, this Court is not required to give full deference to the FDA's statements in an amicus brief. See Belt v. EmCare, Inc., 444 F.3d 403, 416 n.35 (5th Cir. 2006) (noting that Auer

deference, not Chevron deference, is appropriate for informal agency interpretations "such as . . . *amicus curiae* briefs"). Furthermore, Auer deference is only appropriate if the regulation being interpreted is actually ambiguous; otherwise, only Skidmore deference is necessary. Moore v. Hannon Food Service, Inc., 317 F.3d 489, 494-95 (5th Cir. 2003). Although the FDA claimed in Mensing that it had "clarified" any "ambiguity" in the regulations with respect to the provisions of §314.97, the provisions of that regulation are simple, concise, and patently unambiguous. Therefore, only Skidmore deference is necessary. Accordingly, because the FDA position in Mensing cited only the 1992 Final Rule, with all its internal inconsistencies and irrelevancies, to support its position that it has clarified any ambiguities with regard to §314.97, this Court need not give that position any deference since it does not have the "power to persuade" under Skidmore. Furthermore, the FDA position cited in Mensing makes the assertion that a generic drug label must always be the "same as" the name brand label, without citing to any definitive source for that assertion. This may be due to the fact that there *is no definitive regulation* that dictates that generic drug labels must *always* be the "same as" the corresponding name brand label. As a result, the FDA's position that generic labels must always be the "same as" the name brand label is also not entitled to Auer deference because that

position is inconsistent with the regulations at issue. As such, only Skidmore deference applies, and since the FDA's position cannot persuade, it should receive no deference.

Finally, the Mensing court relied on the FDA's footnote in the supplementary introduction to the 2008 Proposed Rule indicating that generic manufacturers cannot unilaterally change their labels. Mensing, 2008 WL 2444689, *8. As discussed above, Fifth Circuit courts need not give any deference to an agency's statements in proposed rules. Additionally, the FDA's footnote in the 2008 Final Rule is extraneous to the purpose of the proposed rule and is contradictory to the FDA's own regulation in §314.97. As such, the Mensing court's analysis is not persuasive in this matter.

5) Colacicco v. Apotex, Inc.- 432 F. Supp. 2d 514, 528-29 (E.D. Penn. 2006) (aff'd 521 F.3d 253 (3d Cir. 2008)

The final piece of evidence Actavis presented to this Court in support of its preemption position was the Eastern District of Pennsylvania's decision in Colacicco v. Apotex, Inc., which determined that the FDCA preempts state law failure-to-warn claims against generic drug manufacturers. It should first be noted that the Third Circuit in affirming the Colacicco district court's decision expressly left open the question of "whether actions against generic drug manufacturers are preempted on the basis of their obligations under the Hatch-Waxman Amendments [and limited its holding] to circumstances in which the FDA has

publicly rejected the need for a warning that plaintiffs argue state law requires." Colacicco v. Apotex, Inc.,521 F.3d 253, 271-272 (3d Cir. 2008). There is no allegation or record evidence in the instant case regarding whether the FDA considered and rejected a neurological risk warning for generic metoclopramide. As such, the Third Circuit's decision has no relevance to the specific issue before this Court, namely whether claims against a generic manufacturer are preempted under the Hatch-Waxman Amendments in circumstances in which the FDA has *not publicly rejected* a proposed warning. Therefore, Actavis's assertion that the Third Circuit in Colacicco agreed with the "FDA's longstanding position . . . that a plaintiff's state law failure to warn claims asserted against a generic drug manufacturer are conflict-preempted as a matter of law" is patently erroneous. Def.'s Reply Memo Opp. Summ. J., 1.

Nonetheless, Actavis points this Court to the Colacicco district court's opinion on the issue of preemption of state law failure-to-warn claims against generic manufacturers. Colacicco was fundamentally different from this case in that it involved Pennsylvania state law claims against both name brand and generic manufacturers for failure to warn of the increased risk of suicide caused by certain anti-depressant medications. Colacicco v. Apotex, Inc., 432 F. Supp. 2d 514, 520 (E.D. Pa. 2006). As such, the Colacicco district court's opinion addressed FDA

preemption statements with respect to claims against both name brand and generic manufacturers. After a lengthy discussion of the proper level of deference that should be given to FDA position statements on the issue of preemption, the Colacicco district court determined that it should give deference to the government's amicus briefs filed in the case as well as the FDA's 2006 Preemption Preamble.[6] Id. at 524-25. In response to the plaintiff's specific argument that the §314.70 CBE procedure allows generic drug manufacturers to unilaterally

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[6] The so-called "Preemption Preamble" is the FDA statement that initiated the FDA's broad position regarding preemption of state law failure-to-warn claims under the FDCA. See 71 Fed. Reg. 3922-01, 3933-3936, part D. Comments on Product Liability Implications of the Proposed Rule (Jan. 24, 2006). The Preemption Preamble generally and broadly states the FDA's position that it alone has authority to make the final decision regarding the safety and labeling of prescription drugs, and therefore state law products liability claims against prescription drug manufacturers should be preempted. However, because the Preemption Preamble does not deal specifically with claims against *generic* drug manufacturers, its relevance to the instant case is minimal.

Furthermore, this final preamble section to the rulemaking comments was not subject to the strictures of the rulemaking process, and in fact *"conflict[s]* with statements made in the original notice of proposed rulemaking out of which the 2006 Final Rule grew" See In Re Vioxx, 501 F. Supp.2d 776, 787 (E.D. La. 2007) (emphasis added). In fact, the initial proposed rulemaking notice actually expressly stated that "this proposed rule does not preempt State law . . . [nor] contain policies that have federalism implications or that preempt state law." Requirements on Content and Format of Labeling for Human Prescription Drugs and Biologics; Requirements for Prescription Drug Product Labels, 65 Fed. Reg. 81082, 81103 (Dec. 22, 2002). Accordingly, and despite Actavis's argument to the contrary, only Skidmore deference would be appropriate in the context of the Preemption Preamble. As such, to the extent it is at all relevant to this case, it does not have the power to persuade.

update their labels, the Colacicco district court held that "principles of deference do not allow us to question the FDA's interpretation of its own regulations - e.g. that generic drug manufacturers can not (sic) make changes without prior approval." Id. at 528. The Colacicco district court therefore relied solely on the text of §§314.70 and 314.150, as well as statements by the FDA in the 1992 Final Rule (discussed above in section C(2)) as a basis for its "deference" to the FDA's position on preemption.

Prominently absent from the Colacicco district court's analysis is any discussion of §314.97, the regulation that specifically mandates generic manufacturers to comply with the provisions of §314.70. Furthermore, as noted numerous times in this discussion, the FDA's comments in the 1992 Final Rule regarding whether generic manufacturers can unilaterally update their labels are not entitled to deference because they are inconsistent and ambiguous.

Therefore, because the Colacicco district court decision involved crucially different facts as well as a deference position that is inconsistent with the views of this Court's analysis, this Court does not afford the Colacicco district court's decision persuasive weight in this matter.

6) Summary

In sum, none of the evidence cited by Actavis in this case is dispositive on the issue of whether Demahy's LPLA failure-to-

warn claims are preempted under the FDCA and the applicable regulations and FDA statements. The 1989 Proposed Rule and 1992 Final Rule are generally entitled to Chevron deference, but since those documents do not answer the discrete question before this court, they are irrelevant regardless of the appropriate level of deference. Further, to the extant they are relevant, the 1989 Proposed Rule and the 1992 Final Rule actually contemplate unilateral labeling changes by generic drug manufacturers. Also, to the extent that those statements interpret ambiguous FDA regulations as precluding unilateral label changes by generic manufacturers, they would merit Auer deference. However, because they are inconsistent with the unambiguous language of §314.97 and §314.70 and are thus unreasonable, they are only entitled to Skidmore deference and do not have the power to persuade.

Additionally, the FDA's interpretations of §314.150 are entitled only to Skidmore deference since those interpretations are not consistent with other regulations, namely §314.70 and §314.97, nor are they consistent with other FDA statements on the issue of labeling changes. Thus, these statements should not receive Auer deference, as they are inconsistent with valid regulations, and do not have the power to persuade as a matter of Skidmore deference because they are inconsistent and contradictory.

Furthermore, the 2008 Proposed Rule is not entitled to any

deference in this Court, and the cases relying on that rule are inapposite and unpersuasive.

Finally, the Colacicco case involved crucially different facts in that the proposed warning at issue in that case had been *expressly rejected by the FDA*.

As such, this Court finds that Demahy's failure-to-warn claims under the LPLA are not preempted as a matter of conflict preemption under the FDCA, applicable regulations, and relevant FDA position statements. Accordingly,

IT IS ORDERED that Actavis's Rule 12(b)(6) Motion to Dismiss Demahy's LPLA failure-to-warn claims under a theory of federal conflict preemption is hereby **DENIED**.

However, to the extent that Demahy's claim constitutes a fraud-on-the-FDA claim against Actavis, that claim is preempted under the Supreme Court's ruling in Buckman Co. v. Plaintiff's Legal Committee, 531 U.S. 341, 348 (2001). Accordingly,

IT IS FURTHER ORDERED that Actavis's Rule 12(b)(6) Motion to Dismiss Demahy's claims, to the extant that they allege fraud-on-the-FDA claims under Louisiana law, is hereby **GRANTED.**

New Orleans, Louisiana this 27th day of October, 2008.

CARL J. BARBIER
UNITED STATES DISTRICT JUDGE