

**IN THE UNITED STATES DISTRICT COURT  
FOR THE EASTERN DISTRICT OF PENNSYLVANIA**

ANDREA PERRY and GEORGE PERRY,	)	
Both individually and as next friends of	)	
ANDREAS PERRY, a minor,	)	
	)	
Plaintiffs,	)	
	)	
vs.	)	Civil Action No. 05-CV-5350
	)	
NOVARTIS PHARMACEUTICALS	)	<b>(Oral Argument Requested)</b>
CORPORATION,	)	
	)	
Defendant.	)	

**PLAINTIFFS' MEMORANDUM OF LAW IN OPPOSITION TO  
DEFENDANT NOVARTIS' MOTION TO DISMISS PLAINTIFFS'  
FAILURE-TO-WARN CLAIMS ON FEDERAL PREEMPTION GROUNDS**

Andreas Perry, the son of Plaintiffs Andrea and George Perry, developed lymphoma as a result of using Elidel, a topical immunosuppressant prescribed for the treatment of his eczema. Plaintiffs brought suit against Defendant Novartis, the manufacturer of Elidel, alleging, *inter alia*, that Novartis had failed to provide adequate warnings of Elidel's risks. (Second Amended Compl. ¶ 99.)

Novartis has moved to dismiss the failure-to-warn claims asserted in Counts II and III of Plaintiffs' First Amended Complaint on federal preemption grounds. (Doc. 28, June 7, 2006 ("Novartis Mem.")).<sup>1</sup> In its motion and supporting memorandum, Novartis

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<sup>1</sup> Since Defendant filed this motion, Plaintiffs' counsel moved for leave to amend the complaint and filed their proposed Second Amended Complaint with the court. (See Doc. 39 & attachment 1, July 7, 2006; Doc. 40, July 10, 2006.) The proposed complaint continues to assert failure-to-warn claims against Novartis (Second Amended Compl., Counts IV and XV), and Plaintiffs, therefore, treat Novartis' motion as one to dismiss those claims on preemption grounds. The Second Amended Complaint also contains numerous other counts—including claims for defective design (Count I), negligence (Count II), fraud (Counts III and VII), infliction of emotional distress (Count VI), breach of warranties (Counts IX and XI), and violation of Pennsylvania's consumer protection law (Count XIII), as well as claims against Novartis' sales representatives (Counts V, VIII, X, XII, XIV, XVI)—that would not appear to be covered by Novartis' preemption motion. Plaintiffs do not address those claims in this memorandum.

does not challenge the facts alleged by Plaintiffs (nor could it on a motion to dismiss). Rather, Novartis relies entirely on two recent developments: (1) the federal Food and Drug Administration's assertion, in the Preamble to the Final Rule entitled "Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products," 71 Fed. Reg. 3922, 3936 (Jan. 24, 2006) ("Preamble"), that "FDA approval of labeling under the [federal Food, Drug and Cosmetic] act . . . preempts conflicting or contrary State law,"" (*see* Novartis' Mem. at 5 (*quoting* 71 Fed. Reg. at 3934)); and (2) a recent decision, by another judge in this district, that deferred to the views of the FDA on preemption (as expressed both in the preamble and also in an *amicus curiae* brief submitted in the case) and therefore dismissed a products liability suit involving a generic version of a very different drug, Paxil (paroxetine hydrochloride). *Colacicco v. Apotex, Inc.*, \_\_\_ F. Supp. 2d \_\_\_, 2006 WL 1443357 (E.D. Pa. May 25, 2006).

The Court should deny Novartis' preemption motion. The FDA's sweeping preemption claim in the recent Preamble is not supported by legal precedent. It contradicts statutory authority, the FDA's regulations, and its regulatory purpose. Indeed, the FDA's claim is contrary to the agency's own longstanding views on preemption. For these reasons, the vast majority of courts that have considered this issue, both before and after the issuance of the FDA Preamble, have held that FDA labeling does not preempt state failure-to-warn claims.

Nor does the *Colacicco* decision justify dismissing the Perry family's claims, as Novartis contends. *Colacicco* is an outlier among recent cases addressing FDA preemption. The *Colacicco* court never evaluated the legal arguments and precedent

against the FDA’s preemption claim;<sup>2</sup> the court simply concluded that it was obliged to defer to the FDA’s judgment on this issue. *Id.* at \*16. That conclusion was in error. The FDA’s views on preemption are not entitled to deference under the standards articulated by the United States Supreme Court in *Skidmore v. Swift & Co.*, 323 U.S. 134 (1994), and *United States v. Mead*, 533 U.S. 218 (2001). In any event, the facts in *Colacicco* are readily distinguishable from those alleged here. Indeed, there is a strong argument that the Preamble does not even apply to this case.

## STATEMENT OF FACTS

### FDA Regulation of Prescription Drugs

All prescription drugs marketed in this country must first be approved by the FDA. To obtain permission to market a new product, a drug company must first submit a “new drug application” (“NDA”) for the FDA’s review and approval. 21 U.S.C. § 355(a), (b). An NDA must include information about the clinical trials that demonstrate the safety and effectiveness of the product, proposed labeling, and other information. *Id.* § 355(b), (d).

If the FDA finds that the application would be approvable if certain changes were made or conditions were met, it will send the applicant an “approvable letter” describing the information the FDA requires or the conditions the applicant must meet to obtain approval. 21 C.F.R. § 314.110(a). Before reaching a final decision on an NDA, the FDA will convene an advisory committee to consider the NDA and the FDA’s analysis of it. 21 C.F.R. § 14.160. If, after reviewing the application, the FDA finds that the drug is

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<sup>2</sup> Indeed, the *Colacicco* court acknowledged that “these decisions, authored by eminent jurists, are forceful, analytical, and—if the Court believed it was authorized to make the analysis—it might very well agree with them.” *Id.* at \*16.

safe and effective for its intended use and that the labeling is not false or misleading, the FDA will send an approval letter to the applicant. 21 U.S.C. § 355(c)(1)(A).

FDA approval includes approval of the labeling, which must, among other things, identify contraindications, warnings, precautions, and adverse reactions. *Id.* §§ 201.56, 201.57. Subsequently, FDA approval is required before the manufacturer can make certain labeling changes, but it may make other labeling changes without prior approval. 21 C.F.R. §§ 314.70(b), (c). Among the changes in the latter category are changes “[t]o add or strengthen a contra-indication, warning, precaution, or adverse reaction.” *Id.* § 314.70(c)(2)(i). Thus, the label is not fixed as of the date of FDA approval. Rather, a company’s obligation to provide physicians and patients with up-to-date warnings and precautions continues as long as the product is marketed.

Even after approval of an NDA, the FDA may convene an advisory committee meeting to consider action with respect to the drug, such as appropriate action in light of a newly-discovered hazard. 21 C.F.R. § 14.171.

### **Regulatory History of Elidel**

Elidel (pimecrolimus) belongs to a class of immunosuppressant drugs known as calcineurin inhibitors (“CIs”). It is applied topically – to the skin – to treat eczema (atopic dermatitis). (Second Amended Compl. ¶¶ 36-39.)

The FDA granted Novartis marketing approval for Elidel in December 2001. (*Id.* ¶ 38.) Even at that time, concerns were raised about a relationship between CIs and cancer. Prograf, an injectable CI previously approved for use as an immunosuppressant in organ transplants, was known to increase the risk of cancer and carried an appropriate

black box warning. Similarly, pre-clinical studies of Elidel suggested that it might increase the risk of malignancies in children. (*Id.* ¶¶ 40-41, 44.)

The labeling language Novartis proposed to the FDA obscured these concerns. The proposed label for Elidel provided some highly technical information about the pre-clinical carcinogenicity findings in the “Precautions” section. However, the “Information for Patients” section of the proposed label contained absolutely no information about cancer risks and no “Warnings” were included. (*Id.* ¶¶ 59, 61.)

Because of its concerns about carcinogenicity, the FDA placed significant restrictions on Elidel. The agency approved the drug only for short-term and intermittent treatment of atopic dermatitis (eczema), and only as second-line therapy where traditional topical corticosteroids could not be used or had proven ineffective. (*Id.* ¶ 38.) Moreover, the FDA required Novartis to engage in further post-approval clinical studies of Elidel’s cancer risk, especially in children. (*Id.* ¶ 42.)

Following FDA approval, Novartis aggressively promoted Elidel, and, due to these efforts, millions of prescriptions for it have been written. (*Id.* ¶¶ 57, 58.) Plaintiffs allege that, despite Defendant’s knowledge of the association between Elidel use and cancer, Novartis promoted Elidel as safe for use, with fewer side effects and adverse reactions than other treatments for eczema. (*Id.* ¶ 63.)

As evidence increased of individuals developing lymphomas and other serious health effects following use of Elidel, the FDA took steps to increase warnings concerning these risks. In 2003, an FDA advisory committee recommended that Novartis add a black box warning against use of Elidel by children under two. (*Id.* ¶ 45). In March 2005, the FDA ordered Novartis to add a black box warning about Elidel’s cancer

risks and Novartis finally added such a warning in January of this year. (*Id.* ¶¶ 48-49.)

But this came far too late for Andreas Perry.

### **Andreas Perry's Medical History**

Andreas Perry was born in April 2001. Like many young children, he suffered from eczema, an uncomfortable but non-life-threatening condition. Within weeks of his second birthday, Andreas was prescribed Elidel as first-line treatment for his eczema. Plaintiffs were assured that Elidel was safe, effective, and appropriate treatment for Andreas' condition; they were not warned that by using Elidel Andreas's risk of developing cancer would increase. Six months later, in October 2003, Andreas was diagnosed with lymphoblastic lymphoma. (*Id.* ¶¶ 76-81.)

## **LEGAL STANDARD**

When considering a motion to dismiss, this Court must accept the allegations in the complaint as true and construe all reasonable inferences in the light most favorable to the Plaintiffs. *U.S. Express Lines Ltd. v. Higgins*, 281 F.3d 383, 388 (3d Cir. 2002). The Court may not dismiss a complaint for failure to state a claim unless it is clear that no relief could be granted under any set of facts that could be proved consistent with the allegations. *Doe v. Delie*, 257 F.3d 309, 313 (3d Cir. 2001).

## **ARGUMENT**

### **PLAINTIFFS' CLAIMS ARE NOT PREEMPTED**

#### **I. Plaintiffs' Failure-to-Warn Claims Do Not Conflict with the FDCA, FDA Regulations, or the FDA's Approval of Elidel.**

Novartis does not contend that the Federal Food, Drug and Cosmetic Act ("FDCA"), 21 U.S.C. § 355, expressly preempts state failure-to-warn suits (express preemption). Neither does it contend that federal regulation of prescription

pharmaceuticals occupies the field to the exclusion of state law (field preemption), nor that it would be impossible for Novartis to comply with both FDA regulations and a tort judgment against it (direct conflict preemption based on “impossibility”). Novartis contends only that the Perrys’ claims are impliedly preempted, because state tort liability would “stand[] as an obstacle to or frustrat[e] federal objectives” (implied conflict preemption). (Novartis Mem. at 3.)<sup>3</sup>

This Court should reject Defendant’s contention. The Perrys’ claims against Novartis do not conflict with either the FDCA or FDA regulations. In fact, state tort liability for inadequate warnings complements and furthers the objectives of the federal regulatory scheme.

**A. There is a Strong Presumption Against Preemption.**

To begin with, it is important to recall that, because preemption upsets the balance of power between the federal government and the states as independent sovereigns, there is a “basic presumption against pre-emption.” *Bates v. Dow Agrosciences LLC*, 544 U.S. 431, 449 (2005); *see Maryland v. Louisiana*, 451 U.S. 725, 746 (1981) (“Consideration under the Supremacy Clause starts with the basic assumption that Congress did not intend to displace state law.”). Any claim of preemption, especially a claim of implied conflict preemption, must overcome this presumption. *Rice v. Santa Fe Elevator Corp.*, 331 U.S. 218 (1947).

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<sup>3</sup> Several justices of the Supreme Court have noted that implied conflict preemption is increasingly disfavored. *See Bates v. Dow Agrosciences LLC*, 544 U.S. 431, 455 (2005) (Thomas, J., joined by Scalia, J., concurring in judgment in part and dissenting in part) (stating that the Supreme Court is becoming “increasing[ly] reluctan[t] to expand federal statutes beyond their terms through doctrines of implied pre-emption. This reluctance reflects that pre-emption analysis is not ‘[a] freewheeling judicial inquiry into whether a state statute is in tension with federal objectives,’ but an inquiry into whether the ordinary meanings of state and federal law conflict”) (*quoting Gade v. Nat’l Solid Wastes Mgmt. Ass’n.*, 505 U.S. 88, 111 (Kennedy, J., concurring in part and concurring in judgment)) (other citations omitted).

Moreover, a number of factors heighten the presumption against preemption of state tort claims. First, a court must assume that Congress did not intend to preempt state law addressing traditional areas of state concern, such as public health and safety. *Rice*, 331 U.S. at 230 (“[W]e start with the assumption that the historic police powers of the States were not to be superseded by the Federal Act unless that was the clear and manifest purpose of Congress”). Second, a court must not readily presume that Congress intended to deprive an injured person of his traditional remedies, especially if the federal act does not provide an alternative form of relief. *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 487 (1996) (“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.”). Finally “[t]he case for federal pre-emption is particularly weak where Congress has indicated its awareness of the operation of state law in a field of federal interest, and has nonetheless decided to ‘stand by both concepts and to tolerate whatever tension there [is] between them.’” *Bonito Boats, Inc. v. Thunder Craft Boats, Inc.*, 489 U.S. 141, 166-67 (1989) (quoting *Silkwood*, 464 U.S. at 256).<sup>4</sup>

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<sup>4</sup> State tort actions against pharmaceutical manufacturers have existed for more than a century. *See, e.g., Thomas v. Winchester*, 1852 WL 4748, \*1 (N.Y. 1852) (“A dealer in drugs and medicines, who carelessly labels a deadly poison as a harmless medicine, and sends it so labeled into market, is liable to all persons, who, without fault on their part, are injured by using it as such medicine in consequence of the false label.”). Congress was well aware of these suits when it enacted the federal Food, Drug and Cosmetic Act in 1934. In fact, Congress decided not to include a private right of action for damages in the FDCA on the grounds that it was “unnecessary,” because a “common-law right of action exists.” Adler & Mann, *Preemption and Medical Devices: The Courts Run Amok*, 59 Mo. L. Rev. 895, 924 & n.130 (1995) (quoting Hearings on S. 1944 Before a Subcomm. Of the Comm. On Commerce, U.S. Senate, 73<sup>rd</sup> Cong., 2d Sess. 400, 403 (1934)).

Novartis cannot and does not overcome this strong presumption against preemption.

**B. The FDCA Expressly Prohibits Preemption Except in Cases of “Direct and Positive Conflict.”**

Congress has expressly limited the extent of implied conflict preemption under the FDCA. In response to the rash of birth defects caused by thalidomide, Congress significantly strengthened the regulation of pharmaceuticals in the Drug Amendments of 1962, Pub. L. 87-781.<sup>5</sup> In so doing, Congress adopted language that severely restricted the potential preemptive effect of federal law. Section 202 of the 1962 act provides:

Nothing in the Amendments made by this Act to the Federal Food, Drug, and Cosmetic Act shall be construed as invalidating any provision of State law which would be valid in the absence of such amendments unless there is a *direct and positive conflict* between such amendments and such provision of State law.<sup>6</sup>

The FDA, in its 2006 Preamble, acknowledges the relevance of this statutory provision, but attempts to minimize its significance by arguing that “[t]he existence of a legislative provision addressing preemption does not bar the operation of ordinary principles of implied preemption.” 71 Fed. Reg. at 3935, n.8 (citing *Geier*, 529 U.S. at 869). We respectfully disagree. By its terms, the quoted statutory language plainly limits implied conflict preemption to cases of “direct and positive conflict” between state and federal law. No such conflict exists here.

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<sup>5</sup> The 1962 act, for the first time, required the FDA to evaluate new drugs for efficacy as well as safety. At least as important, the 1962 act prohibited drug manufacturers for marketing a product without affirmative FDA approval; prior to the act, a new drug application would be deemed automatically approved if the FDA failed to act on the application within 60-180 days. Thus, our modern system of pharmaceutical regulation derives from the 1962 act.

<sup>6</sup> Pub. L. 87-781, Title II, section 202, 76 Stat. 793 (Oct. 10, 1962) (emphasis added). This provision was not codified in the U.S. Code, but rather set out as a note under 21 U.S.C. §321, the definitional provision of the FDCA.

**C. There is No “Direct and Positive Conflict” Between Plaintiffs’ Claims and the FDA’s Labeling Regulations.**

**1. The FDA’s Regulations Permit Manufacturers to Strengthen Label Warnings Without Prior Approval.**

State failure-to-warn tort lawsuits, such as the Perrys’ suit against Novartis, do not interfere—let alone pose a “direct and positive conflict”—with the federal regulatory scheme for prescription drugs. Rather, such suits provide a complementary system of protections for consumers of drugs that furthers federal objectives.

Most importantly, the FDCA does not prevent pharmaceutical manufacturers from strengthening warnings on their products. FDA regulations expressly permit manufacturers to make certain labeling changes to increase safety without prior approval, simply by notifying the agency of the changes. 21 C.F.R. § 314.70(c). Specifically, manufacturers may use this Changes Being Effected (“CBE”) supplement process

- (A) To add or strengthen a contraindication, warning, precaution, or adverse reaction;
- (B) To add or strengthen a statement about drug abuse, dependence, psychological effect, or overdose;
- (C) To add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product; [and]
- (D) To delete false, misleading, or unsupported indications for use or claims of effectiveness . . . .

21 C.F.R. § 314.70(c)(6)(iii)(A)-(D).<sup>7</sup> Numerous courts have cited this CBE procedure for strengthening warnings as a basis for concluding that failure-to-warn claims are not preempted. *See, e.g., Witczak v. Pfizer, Inc.*, 377 F. Supp. 2d 726, 732 (D. Minn. 2005) (“This particular regulation was promulgated precisely to allow drug-makers to quickly

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<sup>7</sup> This CBE supplement process remains in full effect following the effective date (June 30, 2006) of the new final labeling regulations issued in January. The only change to this provision effected by the new rule is to exclude the new “Highlights” section of drug labels from amendment through the CBE process. 71 Fed. Reg. at 3932, 3997.

strengthen label warnings when evidence of new side effects are discovered.”) (citing 30 Fed. Reg. 993 (Jan. 30, 1965)); *see also Osburn v. Anchor Labs.*, 825 F.2d 908 (5th Cir. 1987) (“FDA regulations [] did not prevent [the manufacturer] from adding to its warning labels”); *Eve v. Sandoz Pharm. Corp.*, No. IP 98-1429-C-YS, 2002 WL 181972 (S.D. Ind. Jan. 28, 2002); *Ohler v. Purdue Pharma, L.P.*, No. Civ. A. 01-3061, 2002 WL 88945 (E.D. La. Jan. 22, 2002); *Motus v. Pfizer, Inc.*, 127 F. Supp. 2d 1085 (C.D. Cal. 2000); *Bansemer v. Smith Labs., Inc.*, No. 86-C-1313, 1990 WL 132579 (E.D. Wis. Sept. 12, 1988); *McEwen v. Ortho Pharm. Corp.*, 528 P.2d 522 (Or. 1974). Indeed, as one court has observed:

[t]o argue that, once the FDA approves a package insert, the defendant has no further duty to give an adequate warning creates an incentive for pharmaceutical companies to oppose all efforts by the FDA to secure clearer package inserts. If that were the case, drug manufacturers could avoid liability simply by resting on the formerly approved package insert (regardless of how long ago the approval occurred and how much information about the drug had changed) and resist all efforts to change it.

*Globetti v. Sandoz Pharms. Corp.*, No. CV 98-TMP-2649-S, 2001 WL 419160 at 2 n.1 (N.D. Ala. March 5, 2001).

The FDA itself has recognized repeatedly that “drug labeling does not always contain the most current information and opinion available to physicians about a drug because advances in medical knowledge and practice inevitably precede formal submission of proposed new labeling by the manufacturer and approval by the FDA.” 44 Fed. Reg. 37434, 37435 (June 26, 1979). Therefore, FDA regulations place the onus on drug manufacturers to strengthen label warnings as soon as possible: “[T]he labeling shall be revised 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).<sup>8</sup> Moreover, even before a label can be revised, manufacturers are free to use other means to warn of potential health risks:

These labeling requirements do not prohibit a manufacturer, packer, relabeler, or distributor from warning health care professionals whenever possibly harmful adverse effects associated with the use of the drug are discovered. The addition to labeling and advertising of additional warnings, as well as contraindications, adverse reactions, and precautions regarding the drugs, or the issuance of letters directed to health care professionals (*e.g.*, “Dear Doctor” letters containing such information) is not prohibited by these regulations.

44 Fed. Reg. at 37447.<sup>9</sup>

Because knowledge about the risk posed by particular drugs will change over time, and because drug manufacturers are free to add warnings concerning newly discovered hazards without prior FDA approval, the vast majority of courts to consider the issue have concluded that most FDA labeling requirements establish only minimum safety standards that lack the power to preempt state tort claims.<sup>10</sup>

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<sup>8</sup> The January rulemaking redesignated this section as 21 C.F.R. § 201.80(e), effective June 30, 2006, and preserves it for drugs labeled under the old labeling regulation, such as Elidel. 71 Fed. Reg. at 3988, 3996. New section 201.57(c)(6) applies a virtually identical requirement to drugs labeled under the new regulations: “In accordance with §§ 314.70 and 601.12 of this chapter, the labeling must be revised to include a warning about a clinically significant hazard as soon as there is reasonable evidence of a causal association with a drug; a causal relationship need not have been definitely established.” 71 Fed. Reg. at 3990.

<sup>9</sup> In this same regulatory preamble, the FDA disclaimed any intent to preempt state tort law: “It is not the intent of the FDA to influence the civil tort liability of the manufacturer.” 44 Fed. Reg. at 37437.

<sup>10</sup> *See, e.g., Tobin v. Astra Pharm.*, 993 F.2d 528 (6th Cir. 1993); *Hill v. Searle Labs.*, 884 F.2d 1064, 1068 (8th Cir. 1989) (“FDA regulations are generally minimum standards”); *Wells v. Ortho Pharm. Corp.*, 788 F.2d 741, 746 (11th Cir. 1986) (“An FDA determination that a warning is not necessary may be sufficient for federal regulatory purposes but still not be sufficient for state tort law purposes.”); *Brochu v. Ortho Pharm. Corp.*, 642 F.2d 652 (1st Cir. 1981); *Salmon v. Parke Davis & Co.*, 520 F.2d 1359 (4th Cir. 1975); *McNellis v. Pfizer, Inc.*, No. 05-1286, 2005 WL 3752269, at \*7 (D.N.J. Dec. 29, 2005) (“[T]he FDCA and the FDA’s regulations do not conflict with New Jersey’s failure to warn law because those federal regulations merely set minimum standards with which manufacturer’s must comply”); *Cartwright v. Pfizer, Inc.*, 369 F. Supp. 2d 876, 882 (E.D. Tex. 2005) (“Numerous courts over the years have recognized that the FDCA and its associated regulations set out minimum requirements that drug manufacturers must follow which may be supplemented by state tort laws which are stronger”); *Witczak v. Pfizer, Inc.*, 377 F. Supp. 2d at 732 (“Federal labeling laws are minimum standards; they do not necessarily shield manufacturers from state law liability”); *Ohler*, 2002 WL 88945 at \*10 (“FDA regulations appear to be minimum standards except in cases of express preemption”); *Kociemba v. Searle & Co.*, 680 F. Supp. 1293, 1299 (D. Minn. 1988) (“FDA regulation of prescription drugs establishes minimum standards, both as to design and warning”) (citing *Graham v. Wyeth Labs.*, 666 F. Supp. 1483 (D. Kan. 1987); *Caraker v. Sandoz Pharm.*

The FDA argues in the Preamble that it interprets the FDCA “to establish both a ‘floor’ and a ‘ceiling,’” and thereby preempts state laws imposing greater safety requirements. 71 Fed. Reg. at 3935. The agency reaches this conclusion on the grounds that “additional disclosures of risk information can expose a manufacturer to liability under the act.” *Id.* But, as the agency is forced to concede, such liability will only attach “if the additional statement is unsubstantiated or otherwise false or misleading.” *Id.* In other words, the Act does not impose a “ceiling” on truthful, substantiated risk information, precisely the type of warnings sought by the Perrys.

In fact, the FDA itself has acknowledged previously that its regulations establish only minimum standards that lack the power to preempt state tort claims. Most recently, in 1998, the FDA issued regulations concerning medication guides for prescription drugs to be given to consumers at the point of sale. 63 Fed. Reg. 66378 (1998). The FDA rejected a suggestion by drug manufacturers that it preempt “State regulation with respect to civil tort liability claims and other labeling requirements,” and instead expressly acknowledged that state law, including state tort law, is not in conflict with the FDCA:

FDA does not believe that the evolution of state tort law will cause the development of standards that would be at odds with the agency’s regulations. FDA’s regulations establish the minimal standards necessary, but were not intended to preclude the states from imposing additional labeling requirements. States may authorize additional labeling but they cannot reduce, alter, or eliminate FDA-required labeling. *Id.* at 66384.

There is an additional reason why the Perrys’ claims do not conflict with FDA regulations, articulated by the U.S. Supreme Court in its most recent pronouncement on federal preemption in the product liability context: *Bates v. Dow Agrosciences*, 544 U.S. 431 (2005). *Bates* held that common-law design defect, manufacturing defect, negligent

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*Corp.*, 172 F. Supp. 2d 1018 (S.D. Ill. 2001); *Mazur v. Merck & Co., Inc.*, 742 F. Supp. 239 (E.D. Pa. 1990); *In re Tetracycline Cases*, 747 F. Supp. 543 (W.D. Mo. 1989).

testing, and breach-of-express-warranty claims are entirely exempt from federal preemption under the Federal Insecticide, Fungicide and Rodenticide Act. There, the pesticide manufacturer argued, *inter alia*, that such claims are preempted because they would induce a manufacturer to change its federally-approved labels, thereby running afoul of a statutory prohibition against state law “requirements” that differ from federal law. In rejecting this argument, the Supreme Court held that a common-law claim would not force a manufacturer to make any changes with respect to its product labels; to the contrary, the Court emphasized that “a jury verdict . . . merely motivates an *optional decision . . .*” *Id.* at 1799 (emphasis added). *See also id.* at 1798 (“An occurrence that merely motivates an optional decision does not qualify as a requirement.”). That being so, the Court concluded that the claims were not preempted.<sup>11</sup>

Similarly here, it cannot be said that common-law claims would run afoul of the FDA’s labeling requirements in any respect. At the most, such a claim would merely “motivate[] an optional decision” to change a drug label. And it is impossible to understand how such a decision could possibly run afoul of the FDA’s purposes, given that the agency’s entire regulatory scheme is specifically designed to *permit* manufacturers to add additional warnings to their labels without prior agency approval.

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<sup>11</sup> *Bates* is squarely in keeping with numerous prior decisions holding that common law claims do not conflict with federal law because they merely exert incidental regulatory pressure on manufacturers to change their conduct. *See, e.g., English v. General Electric Co.*, 496 U.S. 72, 85-86 (1990) (upholding employee whistleblower’s state law claim for intentional infliction of emotional distress against nuclear industry employer because effect of damage awards was not direct or substantial enough to warrant preemption); *Goodyear Atomic Corp. v. Miller*, 486 U.S. 174, 186 (1988) (upholding nuclear worker’s state workers compensation claim based on violation of state safety regulation on the ground that compensation award imposes only acceptable incidental regulatory pressure, not unacceptable “direct regulatory authority”); *see also Ferebee v. Chevron Chemical Co.*, 726 F.2d 1529, 1543 (D.C. Cir. 1984) (“Compliance with both federal and state law cannot be said to be impossible. Chevron can continue to use the EPA-approved label and can at the same time pay damages to successful tort plaintiffs such as Mr. Ferebee”).

Thus, there is no “direct and positive conflict” between the Perrys’ failure-to-warn claims and FDA labeling regulations.

## **2. State Failure-to-Warn Claims Complement and Advance the Purposes of the FDCA.**

Indeed, state tort claims, such as those alleged by the Perrys, actually further the purposes of the FDCA. As the Supreme Court has recognized, Congress passed the FDCA to protect consumers from dangerous products. *See United States v. Dotterweich*, 320 U.S. 277, 280, 282 (1943) (House and Senate committee reports indicate that “[t]he purposes of this legislation thus touch phases of the lives and health of people which, in the circumstances of modern industrialism, are largely beyond self-protection”); 62 *Cases, More or Less, Each Containing Six Jars of Jam v. United States*, 340 U.S. 593, 596 (1951) (stating that Congress intended the FDCA to protect consumers who are unable to protect themselves); *United States v. Sullivan*, 332 U.S. 689, 696 (1948).

Congress had a similar purpose—to promote safety and efficacy—when, in the wake of the thalidomide crisis, it enacted the 1962 Drug Amendments, which significantly expanded the FDA’s authority over drug labeling. *See* S. Rep. No. 1744, 87th Cong., 2d Sess., p.1 (1962) (“The purpose of the proposed legislation . . . is to strengthen and broaden existing laws in the drug field so as to bring about better, safer, medicine and to establish a more effective system of enforcement of the drug laws.”).

State tort lawsuits are wholly consistent with this legislative purpose. They protect consumers directly, by providing a remedy to persons injured by unsafe drugs, and also indirectly, by creating financial incentives for pharmaceutical companies to make their products safer and to provide reasonable warnings about the dangers those products pose. As the former Chief Counsel of the FDA, Margaret Jane Porter, has

written, “FDA product approval and state tort liability usually operate independently, each providing a significant, yet distinct, layer of consumer protection.” Margaret J. Porter, *The Lohr Decision: FDA Perspective and Position*, 52 Food & Drug. L.J. 7, 11 (1997).

The FDA Preamble is virtually silent about the legislative purpose behind our nation’s food and drug laws, but subtly seeks to redefine that mission. At several points, the Preamble suggests that the threat posed by state tort litigation may result in “overwarning,” “thereby potentially discouraging safe and effective use of approved products” and “underutilization of beneficial treatments,” which can have a “negative effect on patient safety and public health.” 71 Fed. Reg. at 3934-35. But, apart from ensuring that only safe and effective drugs are approved for use, the FDA has no legitimate statutory role in trying to promote the use of particular drugs. Moreover, additional warnings can have a negative effect only if they inaccurately represent the dangers posed by a drug; accurate warnings will promote proper use.<sup>12</sup>

Instead, it is Novartis’ position in favor of preemption that would undermine the legislative aim of the FDCA. As another federal district court has written, in rejecting a similar preemption argument:

FDA’s and [defendant]’s position [in favor of preemption] vitiates, rather than advances, the FDCA’s purpose of protecting the public. That is, FDA and [defendant] invite the Court to find that in enacting the FDCA for the purposes of protecting public health, Congress not only declined to provide for a private cause of action but also eliminated the availability of common law state claims. This position contravenes common sense . . . .

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<sup>12</sup> FDA’s argument also ignores the fact that drug labels are not drafted by the FDA, but by the manufacturer, which has an economic incentive to present as little negative information about the product as possible. The FDA can suggest stronger warning language, but the decision ultimately rests with the company, subject only to the FDA’s authority to deny approval for the product or to bring a misbranding action against the manufacturer. See Declaration of Arvin P. Schroff, *Colacicco v. Apotex, Inc.*, ¶¶ 11-16 (attached hereto as ex. 1).

*In Re Paxil Litigation*, No. 01-07937, 2002 WL 31375497 at \*1 (C.D. Cal. Oct. 18, 2002).

For these reasons, most courts, apart from *Colacicco*, that have considered the issue of preemption in light of the FDA Preamble, have concluded that FDA labeling regulations do not have preemptive effect. In *Laisure-Radke v. Par Pharmaceutical, Inc.*, No. C03-3654RSM, slip op. (W.D. Wash. Mar. 29, 2006), for example, the U.S. District Court for the Western District of Washington rejected a motion for summary judgment based on preemption filed by a generic manufacturer of Prozac. The court was

not persuaded that allowing plaintiff's claims to move forward would be a frustration of Congressional purpose. Providing new or additional warnings can hardly be an obstacle to the accomplishment of the full objectives of Congress when federal regulations specifically allow manufacturers to do so, and when Congress has left product liability matters to state law, as long as they do not directly conflict with federal law in that area.

*Laisure-Radke*, No. C03-3654RSM, slip op. at 10 (attached as ex. 2).

Similarly, in *Coutu v. Tracy*, No. C.A. PC/00-3720, 2006 WL 1314261 (R.I. Super. Ct. May 11, 2006), a Rhode Island state court denied a motion for summary judgment by AstraZeneca Pharmaceuticals, the maker of the drug Propofol. The court wrote:

After considering the arguments of both parties, this Court finds that AstraZeneca has failed to meet its heavy burden to establish preemption and, therefore, the defendants' motion for summary judgment is denied. A substantial number of courts have previously declined to find that state law failure to warn claims are preempted by the FDA approval process. Furthermore, there does not appear to be any congressional intent to preempt state law under such circumstances. Finally, the Supreme Court has discouraged federal agencies from changing positions regarding issues that have been previously decided by courts. Ultimately, given these factors, this Court refuses to find that the plaintiffs' claim is preempted. This Court is not convinced that state laws, encouraging more stringent

warning standards, frustrate the purpose of the FDA. Courts have consistently held that FDA regulations regarding labels and warnings for drugs do not preempt state law.

*Id.* at \*4. *See also Jackson v. Pfizer, Inc.*, \_\_\_ F. Supp. 2d \_\_\_, 2006 WL 1506886 (D. Neb. May 31, 2006) (denying preemption motion by manufacturers of Zoloft and Effexor); *In re PremPro Prods. Liab. Litig.*, MDL Nos. 03-CV-1507, 05-CV-00163 (E.D. Ark. June 15, 2006) (denying preemption motion by manufacturer of PremPro and adopting reasoning of *Jackson v. Pfizer*). Finally, there is the recent bench ruling by the Superior Court of New Jersey that prohibited Merck from introducing the FDA Preamble as evidence in a pending Vioxx trial, in which the court stated:

The preamble, as I see it, is a political statement by the FDA. The primary purpose of it is to . . . set forth the FDA's position that they believe there should be federal preemption of all tort actions. That is basically what the preamble is saying. What the preamble is saying is the FDA should be the final word.

It has nothing to do with science. It has nothing to do with what happened back in 2000, 2001, 2002, when these issues were being decided. It is contrary to the U.S. Supreme Court's decisions. It is contrary to all the law on preemption. And I am not going to allow you to use it.

*Doherty v. Merck & Co.*, No. ATL-L-0638-05MT (Tr. 585: 25-25; 586: 1-10) (June 9, 2006) (attached as ex. 3). Thus, there is no conflict whatsoever between the Perrys' failure-to-warn claims and either the FDA's regulations or its statutory purposes.

### **3. There is No Conflict Between Plaintiffs' Claims and the FDA's Actions With Respect to Elidel.**

Nor is there any conflict—let alone a “direct and positive” one—between the Perrys' failure-to-warn claims and the FDA's actions regarding Elidel. From the time Novartis first sought FDA approval of Elidel, the agency expressed concerns about the possibility that use of this drug increases cancer risks. (Second Amended Compl. ¶ 41.)

Because of these concerns, the FDA placed restrictions on Elidel’s approved use for the treatment of eczema and required that Novartis, as a condition of Elidel’s approval, conduct a post-approval study of pediatric patients “to assess the risk of developing systemic malignancies.” (*Id.* ¶¶ 38, 42).

As evidence mounted of an association between Elidel use and cancer, the FDA took steps to alert health care professionals and the public. Eventually, in 2005, the FDA issued a public health advisory about the potential cancer risk posed by Elidel and then required Novartis to add a black box warning—the strongest warning available under FDA labeling regulations—about the cancer risk. (*Id.* ¶ 48.)

At no point in the regulatory process did the FDA ever conclude that a warning about an association between Elidel and cancer was inappropriate; at no point did it ever reject a stronger warning proposed by Novartis or any outside group. Throughout the period from initial FDA approval to the black box warning, Novartis was free to “add or strengthen a . . . warning” without prior FDA approval. 21 C.F.R. § 314.70(c)(6)(iii)(A). Indeed, Novartis may even have been required to do so. 21 C.F.R. § 201.57(e) (requiring a drug label to be revised “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”).

The Perrys’ failure-to-warn claims are entirely consistent with and further the FDA regulations and their purpose. Plaintiffs seek to hold Novartis accountable for failing to provide adequate warnings of the cancer risk posed by Elidel, despite “reasonable evidence of an association” of this “serious hazard” with this drug. By so doing, plaintiffs advance the FDCA goal of consumer protection and the regulatory

objective of prompt and effective warnings of serious health risks.<sup>13</sup> As the Supreme Court said in *Bates* about a similar statutory scheme:

Private remedies . . . would seem to aid, rather than hinder, the functioning of FIFRA . . . . FIFRA contemplates that pesticide labels will evolve over time, as manufacturers gain more information about their products' performance in diverse settings. . . . [T]ort suits can serve as a catalyst in this process.

544 U.S. at 451.

Novartis contends that the Perrys' claim that the company should have included a cancer warning in 2003, when Elidel was prescribed for Andreas, would amount to a requirement that the drug be "misbranded." (Novartis' Mem. at 8.) Defendant's argument seriously mischaracterizes and misrepresents the law. Under the FDCA, a drug is misbranded only if its labeling is "false or misleading in any particular" or, ironically, if the labeling "does not provide adequate warnings against any use dangerous to health." 21 U.S.C. § 352(a), (f), (j); 21 U.S.C. § 321(n).<sup>14</sup> As the above regulatory history makes clear, inclusion of a cancer warning in 2003 would not have rendered Elidel's labeling "false or misleading."<sup>15</sup>

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<sup>13</sup> Plaintiffs also have alleged that Novartis advertised, marketed, and promoted Elidel as safer than traditional corticosteroid treatments for atopic dermatitis, in conscious disregard of the limitations that the FDA placed on its approval of the product, and that these actions contributed to the inadequacy of the company's warnings. (Second Amended Compl. ¶¶ 54, 57, 63, 99.) If the Perrys are successful in holding Novartis accountable for such actions, they will advance the FDCA's statutory restriction on pharmaceutical companies promoting their products for unapproved indications. See 21 U.S.C. § 360aaa (providing that a manufacturer may disseminate "written information concerning the safety, effectiveness, or benefit of a use not described in the approved labeling of a drug or device only if the manufacturer meets the enumerated requirements"); 21 U.S.C. § 352 (providing when a drug or device shall be deemed to be misbranded); see also 65 Fed. Reg. 14286 (Mar. 16, 2000) ("An approved new drug that is marketed for a 'new use' is also 'misbranded' under the FDCA, because the labeling of such a drug would not include 'adequate directions for use.'") (citing 21 U.S.C. 352(f)).

<sup>14</sup> Although the FDA can initiate a misbranding action, the ultimate determination whether the product is misbranded, as in plaintiffs' tort suit, must be made by a jury. See *U. S. v. 47 Bottles, More or Less, Jenasol RJ Formula '60'*, 320 F.2d 564, 571 (3rd Cir. 1963) ("Whether or not labeling [of a drug] is false or misleading [within FDCA] is a question of fact for determination by the trial judge in the absence of a jury."); cf. *Bates*, 544 U.S. at 452 (under FIFRA, issues of misbranding are ultimately decided by juries).

<sup>15</sup> Novartis relies on a statement from the FDA's *amicus* brief in *Kallas v. Pfizer, Inc.*, that "state law may not validly require the manufacturer of a drug to warn of a specific danger that FDA, based on the agency's

As a district court in Texas recently observed about a similar contention:

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 and misleading.

*Cartwright v. Pfizer, Inc.*, 369 F. Supp. 2d 876, 885-86 (E.D. Tex. 2005) (emphasis added). It is likewise inconceivable that the FDA would have rejected a proposal by Novartis that a cancer warning be added to the Elidel label, given that the FDA has since required such a warning.

For all of the foregoing reasons, the Perrys' failure-to-warn claims do not pose a direct and positive conflict with the FDCA, the FDA's regulatory structure, or the FDA's specific regulation of Elidel, and are not preempted.

## **II. THE FDA'S ASSERTION OF PREEMPTION IN THE JANUARY 2006 PREAMBLE IS NOT ENTITLED TO DEFERENCE.**

Novartis claims that this Court should disregard the foregoing legal analysis and instead simply defer to the FDA's views on preemption as set forth in the Preamble, which Novartis considers "dispositive." (Novartis' Mem. at 2, 4.) But the FDA preamble is not entitled to deference from this Court. There is a serious question whether the Preamble even applies to this case. Moreover, it is not a formal agency action possessing the force of law, which is entitled to substantial deference under *Chevron v.*

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scientific analysis, did not believe to be sufficiently supported to warrant such a warning." *Amicus Brief for the United States, Kallas v. Pfizer, Inc.*, Case No. 2:04CV0998 PGC, at 23 (D. Utah Sep. 15, 2005) (attached as Exh. E to Novartis' Motion). As discussed in Part III.B., *infra*, the SSRI drug involved in *Kallas* has a very different regulatory history than does Elidel. This is not a case in which the FDA, based on its scientific analysis, came to believe that the risk of cancer was not sufficiently supported to warrant a warning; to the contrary, from the outset the FDA insisted that Novartis conduct further research into this precise danger and ultimately demanded that a black box warning be added to the product label. In any event, the Perrys have not demanded (nor could they) that Novartis include a warning back in 2003; they merely contend that it should now pay damages for failing to have done so.

*Natural Res. Def. Council*, 467 U.S. 837 (1984). And the preamble lacks the thoroughness, validity of reasoning, and consistency with earlier FDA pronouncements that would give it the “power to persuade” under *United States v. Mead Corp.*, 533 U.S. 218 (2001), and *Skidmore v. Swift & Co.*, 323 U.S. 134 (1994).

#### **A. The Preamble Does Not Apply to This Case.**

As a threshold matter, it appears that the FDA’s discussion of preemption in the Preamble does not cover the Perrys’ claims in this case. The Preamble does assert, as Novartis notes, that “FDA approval of labeling under the act, whether it be in the old or new format, preempts conflicting or contrary State law.” 71 Fed. Reg. at 3934. However, the Preamble then goes on to identify six specific claims that the agency believes would be preempted by its regulation of prescription drug labeling. *Id.* at 3935-36.<sup>16</sup> The Perrys’ claims do not fit in any of these six categories.

The only one that even arguably applies is the third: “claims that a sponsor breached an obligation to warn by failing to include contraindications or warnings that are not supported by evidence that meets the standards set forth in this rule . . . .” But, as

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<sup>16</sup> The six claims are: “(1) Claims that a drug sponsor breached an obligation to warn by failing to put in Highlights or otherwise emphasize any information the substance of which appears anywhere in the labeling; (2) claims that a drug sponsor breached an obligation to warn by failing to include in an advertisement any information the substance of which appears anywhere in the labeling, in those cases where a drug’s sponsor has used Highlights consistently with FDA draft guidance regarding the ‘brief summary’ in direct-to-consumer advertising; (3) claims that a sponsor breached an obligation to warn by failing to include contraindications or warnings that are not supported by evidence that meets the standards set forth in this rule, including § 201.57(c)(5) (requiring that contraindications reflect ‘[k]nown hazards and not theoretical possibilities’) and (c)(7); (4) claims that a drug sponsor breached an obligation to warn by failing to include a statement in labeling or advertising, the substance of which had been proposed to FDA for inclusion in labeling, if that statement was not required by FDA at the time plaintiff claims the sponsor had an obligation to warn (unless FDA has made a finding that the sponsor withheld material information relating to the proposed warning before plaintiff claims the sponsor had the obligation to warn); (5) claims that a drug sponsor breached an obligation to warn by failing to include in labeling or in advertising a statement the substance of which FDA has prohibited in labeling or advertising; and (6) claims that a drug’s sponsor breached an obligation to plaintiff by making statements that FDA approved for inclusion in the drug’s label (unless FDA has made a finding that the sponsor withheld material information relating to the statement).” *Id.* at 3936 (citation omitted).

discussed above, the Perrys contend that Novartis' obligation to warn of Elidel's cancer risk, even in 2003, was "supported by evidence that meets the standards set forth in this rule," and the FDA itself never concluded otherwise. (To the contrary, it eventually required the very warning advocated by Plaintiffs.) *See* 21 C.F.R. § 201.57(e) [now redesignated 21 C.F.R. § 201.80(e)] (requiring a drug label to be revised "to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug").

Thus, even if this Court were to consider the FDA's views on preemption, the plaintiffs' claims should be permitted to proceed, because they do not fall within any of the preempted categories listed in the Preamble. *Compare Medtronic*, 518 U.S. at 495 ("Nothing in [the express preemption provision of the Medical Device Amendments] denies Florida the right to provide a traditional damages remedy for violations of common-law duties when those duties parallel federal requirements. . . . The presence of a damages remedy does not amount to the additional or different 'requirement' that is necessary under the statute; rather, it merely provides another reason for manufacturers to comply with identical existing 'requirements' under federal law"). In any event, as we now explain, those views are not entitled to deference.

**B. The FDA's Opinion Regarding Preemption Is Not Entitled to *Chevron* Deference Because It Does Not Possess the Force of Law.**

Certain agency actions are entitled to heightened deference from the courts under *Chevron*, 467 U.S. 837. Such deference, however, "is warranted only 'when it appears that Congress delegated authority to the agency generally to make rules carrying the force of law, and that the *agency interpretation claiming deference was promulgated in the exercise of that authority.*'" *Gonzales v. Oregon*, \_\_\_ U.S. \_\_\_, 126 S. Ct. 904, 915

(2006) (quoting *U.S. v. Mead Corp.*, 533 U.S. at 226-27) (emphasis added). Although Congress has conferred rulemaking authority on the FDA, the Preamble was not “promulgated in the exercise of that authority,” because it is merely the preamble to a rule and not part of the rule itself.

FDA regulations make clear that a regulatory preamble is not itself part of the rule, and lacks the force of law. 21 C.F.R. § 10.85 expressly provides that “[a]ny portion of a Federal Register notice other than the text of a proposed or final regulation, *e.g.*, a notice to manufacturers or a *preamble to a proposed or final regulation*” constitutes only an advisory opinion. *Id.* (emphasis added). And, the regulations continue, such an advisory opinion may not be used in court proceedings as “a legal requirement.” 21 C.F.R. § 10.85(j).<sup>17</sup> Thus, the Preamble at issue here is *not* entitled to *Chevron* deference. *See Christensen v. Harris County*, 529 U.S. 576, 587 (2000) (“Interpretations such as those in opinion letters—like interpretations contained in policy statements, agency manuals, and enforcement guidelines, all of which lack the force of law—do not warrant *Chevron*-style deference”).

**C. The FDA’s Position Regarding Preemption Is Not Entitled to This Court’s Respect Under *Skidmore* and *Mead* Because It Lacks the “Power to Persuade.”**

Where an agency interpretation is not entitled to *Chevron* deference, it is “‘entitled to respect’ only to the extent it has the ‘power to persuade.’” *Gonzalez*, 126 S. Ct. at 915 (quoting *Skidmore v. Swift & Co.*, 323 U.S. 134, 140 (1994)). As the Supreme Court recently explained,

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<sup>17</sup> See Jennifer Corbett Dooren, *UPDATE: FDA To Require Simpler Drug Labels*, Wall Street Journal Online, Jan. 18, 2006, at [http://online.wsj.com/article\\_print/BT-CO-200600118-008819.htm](http://online.wsj.com/article_print/BT-CO-200600118-008819.htm) (“Dr. Scott Gottlieb, the FDA’s deputy commissioner for medical and scientific affairs, noted that the provision is in the rule’s preamble, meaning it will not be codified into federal law. He said the courts could decide to ignore the FDA’s opinions.”).

‘the weight [accorded to an administrative] judgment in a particular case will depend upon the thoroughness evident in its consideration, the validity of its reasoning, its consistency with earlier and later pronouncements, and all those factors which give the power to persuade, if lacking power to control.’

*United States v. Mead*, 533 U.S. 218, 228 (2001) (quoting *Skidmore*, 323 U.S. at 140).

Judged by these factors – thoroughness, consistency, and validity – the FDA statement on preemption lacks the power to persuade and is not entitled to any judicial deference.

**Thoroughness of Consideration.** The FDA preamble does not reflect a thorough agency consideration of both sides of the legal arguments for and against preemption. Rather, it reads like an advocacy brief for one side of the question, which is not surprising given that the agency derived the preamble from arguments it had recently advanced in *amicus* briefs supporting preemption.

Thorough agency consideration of an issue, as in formal notice-and-comment rulemaking, compels an agency to solicit comments from and weigh the arguments of all interested parties. The FDA did not do that here. When the FDA first proposed its new labeling rules in 2000, it explicitly stated that the regulations would *not* have preemptive effect. *See* 65 Fed. Reg. 81082, 81103 (proposed Dec. 22, 2000). The FDA did not request comments on the appropriate preemptive effect of the proposed new labeling requirements, nor did FDA officials consult with state and local officials about the potential preemptive effect of the proposed regulation, or provide them with specific notice and an opportunity to comment, as required by Executive Order 13132. Exec. Ord. 13132, § 4(d) & (e) (1999). Thus, the agency reached its views on preemption expressed in the Preamble without due consideration of the arguments against preemption.<sup>18</sup>

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<sup>18</sup> If the Preamble were a substantive rule possessing the force of law, the promulgation of the Preamble would have violated the notice-and-comment requirements for rulemaking under the Administrative Procedures Act. 5 U.S.C. §§ 553(b), (c); *see also Solid Waste Agency of N. Cook County v. U.S. Army Corps of Eng’rs*, 531 U.S. 159, 164 n.1 (2001) (stating that “the Corps issued the ‘Migratory Bird Rule’ without following the notice and comment procedures outlined in the Administrative Procedure Act”). Comments were not sought on preemption; rather, the Proposed Rule specifically disclaimed any preemptive effect. Because the Preamble is not a “logical outgrowth” of the Proposed Rule, it likely

**Consistency with Earlier Pronouncements.** Where an agency changes its mind and reverses position, its views are not entitled to deference. Just last year, for example, in *Bates*, the U.S. Supreme Court rejected the Environmental Protection Agency’s argument, set forth in an *amicus* brief to the Court, that federal law preempts tort claims against a pesticide manufacturer alleging design defect and failure to warn. The Court noted that the agency’s pro-preemption argument was “particularly dubious given that just five years ago the United States advocated the [opposite] interpretation.” 544 U.S. at 449 & n. 24 (citations omitted); *see also Norfolk South. R.R. Co. v. Shanklin*, 529 U.S. 344, 356 (2000) (stating that an agency’s construction of its own regulations is not entitled to deference when that construction “contradicts the agency’s own prior construction”).<sup>19</sup>

The FDA’s recent pronouncement on preemption is equally “dubious,” because of its inconsistency with earlier agency pronouncements. As just discussed, when the FDA first proposed its labeling rules in 2000, it explicitly stated that “this proposed rule does not contain policies that have federalism implications or that preempt state law.” *See* 65 Fed. Reg. at 81103.

This position was consistent with prior FDA statements. For example, the preamble to the FDA’s 1979 labeling rule explained (in response to comments on liability): “It is *not* the intent of FDA to influence the civil tort liability of the manufacturer.” 44 Fed. Reg. 37434, 37437 (1979) (emphasis added). Likewise, in a final labeling rule published in 1998, the FDA rejected manufacturers’ calls to preempt state tort claims and stated unequivocally that “FDA’s regulations establish the minimal

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violates notice-and-comment rulemaking. *See, e.g., Am. Water Works Ass’n v. EPA*, 40 F.3d 1266, 1274 (D.C. Cir. 1994) (holding that agency failed to provide adequate notice that it would adopt a novel definition of the term and thus vacating the rule).

<sup>19</sup> By contrast, in those recent cases where the Supreme Court has given deference to an agency’s views on preemption, there was no evidence of any prior inconsistent positions on the agency’s part. *See, e.g., Geier v. Am. Honda Motor Co., Inc.*, 529 U.S. 861, 863 (2000); *Medtronic*, 518 U.S. at 496; *Sprietsma v. Mercury Marine Co.*, 537 U.S. 51, 68 (2002). To the contrary, in all of those cases, the agency views accorded deference had been consistently stated over time, both in *amicus* briefs and in regulatory preambles. Plainly, that is not this case.

standards necessary, *but were not intended to preclude the states from imposing additional labeling standards.*” 63 Fed. Reg. 66378, 66384 (1998) (emphasis added). Because the FDA’s current pro-preemption stance is plainly a reversal of its previous position, it is not entitled to the Court’s respect.<sup>20</sup>

Ironically, the *Colacicco* court acknowledged the manifest inconsistency in the FDA’s prior positions on preemption. In fact, the district court admitted that the FDA’s 2006 Preamble is directly contrary to what the agency stated in the 2000 preamble to the proposed version of *those very same rules*, and noted that the FDA’s *amicus* brief in *Colacicco* was “completely silent” on the issue, despite having been specifically asked to address this very point. *See* 2006 WL 1443357 at \*12.

**Validity of Reasoning.** Even if the FDA’s new preemption position did not expressly contradict its prior statements on the matter, the Preamble still would not be entitled to this Court’s respect because of the invalidity of its reasoning. As Plaintiffs discussed at length in Section I, the legal arguments against preemption are compelling. In order to reach a contrary conclusion, the FDA’s discussion of preemption in the Preamble, among other things, ignores the presumption against preemption, discounts

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<sup>20</sup> In an attempt to create the impression that its position on preemption “is not new,” the FDA in the Preamble cited four earlier occasions in which the FDA had asserted that “State law requirements relating to drugs” were preempted by federal regulations. *See* 71 Fed. Reg. 3935. But none of these regulations concerned the labeling of prescription pharmaceuticals and each of these preemption claims appear to have been “directed at state positive laws that specifically regulated the particular matter at issue;” none “suggested that common-law claims would be preempted.” *See* Allison M. Zieve and Brian Wolfman, *The FDA’s Argument for Eradicating State Tort Law: Why It Is Wrong and Warrants No Deference*, 34 Prod. Safety & Liab. Rep. (BNA) 12, 308-16 (Mar. 27, 2006) (reprint attached as ex. 4). Indeed, the preamble to one of these regulations expressly “recognize[d] that product liability plays an important role in consumer protection” and made clear that “the proposed preemption action is not intended to frustrate or impede tort litigation in this area.” 59 Fed. Reg. 3944, 3948 (1994).

The Preamble also cites four *amicus* briefs that the FDA had filed in cases prior to the present administration. *See* 71 Fed. Reg. 3935. Three of those briefs, however, did not address preemption of damages claims at all and the fourth, *Buckman v. Plaintiffs’ Legal Committee*, 531 U.S. 341 (2001), involved an unusual “fraud on the FDA” claim, which was held to be preempted because it intruded on a preeminent federal concern, the relationship between the federal government and the entities it regulates. The FDA brief in *Buckman* carefully distinguished this claim from traditional products liability claims such as failure to warn, which the agency conceded “implicate[] core areas of traditional state concern” and carry a strong presumption against preemption. Brief for the United States as *Amicus Curiae*, 2000 WL 1364441, at \*17 (filed Sept. 13, 2000).

adverse legislative language, describes the regulations that govern labeling in a misleading manner, disregards the legislative purpose of the FDCA, and overlooks or mischaracterizes prior agency statements on preemption. Most importantly, to reach its conclusions, the Preamble wrongly presumes that virtually any warning not approved by the FDA must be false or misleading. It is a piece of advocacy, not of legal analysis, that does not withstand even the mildest form of scrutiny. This court should have no reservations about rejecting it outright.

**D. The *Colacicco* Court Erred By Treating the FDA’s Views on Preemption as Dispositive.**

As Novartis notes, the *Colacicco* court did not merely show deference to the FDA’s position on preemption, but treated it as “dispositive.” Novartis Mem. at 4 (*citing Colacicco* at \*7).<sup>21</sup> The court held that it was inappropriate “to substitute its judgment for the FDA’s about these medical [*sic*] issues.” *Colacicco* at \*11.

This was clear error. To reach this conclusion, the *Colacicco* court relied heavily on *Chevron*, 467 U.S. 837 (1984), and on language from *Hillsborough County v. Automated Medical Labs., Inc.*, 471 U.S. 707, 714 (1985), that applied *Chevron* and treated an FDA statement on preemption as “dispositive.” *Colacicco* at \*7. The *Colacicco* court simply ignored more recent Supreme Court precedent that places limits on *Chevron* and on judicial deference to administrative agencies. One will search in vain through the *Colacicco* opinion for any reference to *Skidmore*, *Mead*, or *Gonzales* on this topic.

Those decisions provide a context for the Supreme Court’s more recent discussions of the weight to be given an agency’s views on preemption in cases such as

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<sup>21</sup> Novartis also correctly observes that, while the FDA submitted an *amicus* brief in *Colacicco*, the court made clear that it was deferring to the preamble as well as the brief. *Id.* at \*10-\*11. This was striking because the FDA itself had emphasized in its brief that “the basis for federal preemption in this litigation is not the preamble itself.” Brief for the United States as *Amicus Curiae* Supporting Defendant, *Colacicco v. Apotex, Inc.*, at 2 (filed May 10, 2006); *see also id.* at 18.

*Bates*, *Geier*, and *Medtronic*.<sup>22</sup> Of course, an agency can communicate its “intentions” about the preemptive effect of its regulations “through statements in ‘regulations, preambles, interpretive statements, and responses to comments,’” *Medtronic*, 518 U.S. at 506 (Breyer, J., concurring in part and concurring in judgment) (quoting *Hillsborough*, 471 U.S. at 718), and those agency views may be entitled to “some weight.” *Geier*, 529 U.S. at 883. But the weight those views receive from a court, under *Skidmore* and *Mead*, depends entirely on their “power to persuade.” *Mead*, 533 U.S. at 228 (quoting *Skidmore*, 323 U.S. at 140). They have no “power to control” the court’s judgment on preemption. Thus, the *Colacicco* court erred by simply accepting the FDA’s views on preemption and not conducting its own independent analysis. *See Colacicco* at \*16 (“This Court has concluded . . . that it is improper for a federal district judge to engage in this analysis in the first place”).<sup>23</sup>

### III. COLACICCO IS DISTINGUISHABLE.

Thus, the *Colacicco* case was wrongly decided as a matter of law. The *Colacicco* court did not consider the compelling legal arguments against preemption; it simply, and incorrectly, deferred to the FDA’s assertion of preemption in that case. But even if the preemption holding in *Colacicco* had been correct on the facts of that case, it would still not be applicable here.

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<sup>22</sup> *Bates*, which affirmatively rejected a federal agency’s views on preemption, is not even mentioned in *Colacicco*.

<sup>23</sup> *Horn v. Thoratec Corp.*, 376 F.3d 163 (3d Cir. 2004), the Third Circuit’s recent discussion of FDA preemption cited in *Colacicco*, confirms this analysis. *Horn* involved a claim of express preemption under § 360k(a) of the Medical Device Amendments (MDA) to the FDCA. In *Medtronic*, the Supreme Court had instructed that the FDA’s views on preemption under the MDA were entitled to “substantial weight,” because “Congress has given the FDA a unique role in determining the scope of § 360k’s preemptive effect.” 518 U.S. at 495-96. Following *Medtronic*, the Third Circuit in *Horn* treated the FDA’s preemption determination, as expressed in an *amicus* brief, as “significant,” but not “dispositive.” 376 F.3d at 171. Although the FDA’s position had changed from prior cases, the Court of Appeals concluded that it was still entitled to respect under the *Mead* standard because the agency had justified its change of position with a “reasoned analysis.” *Id.* at 179 and n. 25. The court conducted its own analysis of the preemption issue informed by the FDA’s views. *See, e.g., id.* at 177 (“Our preemption conclusion is reinforced by the informed analysis found in the FDA’s *amicus curiae* brief”).

**A. *Colacicco* Has No Bearing Here Because This Case Involves a Brand-Name Drug, Rather Than a Generic.**

*Colacicco* involved a woman who committed suicide after taking a generic version of Paxil, a selective serotonin reuptake inhibitor (“SSRI”). Her husband sued both Apotex, the manufacturer of the generic drug she had taken, and also GlaxoSmithKline, the maker of Paxil, which the victim never took.

Central to the preemption arguments advanced by both Apotex and the FDA in its *amicus* brief in *Colacicco* was the fact that the victim had taken a generic drug. Both Apotex and the FDA contended, and the court agreed, that a generic pharmaceutical manufacturer is *prohibited* by FDA regulations from strengthening warnings on a product’s label without prior FDA approval, and therefore that the plaintiff’s failure-to-warn claims “inherently conflict[ed]” with federal law. *See Colacicco, supra*, at \*17. In fact, apart from misguided deference to the FDA, this purported regulatory prohibition against strengthening warnings was the sole reason cited by the court in support of preemption. *Id.* at \*18.<sup>24</sup>

The *Colacicco* court’s determination that generic manufacturers are precluded from unilaterally strengthening warnings was incorrect, *see, e.g., Laisure-Radke v. Par Pharm., Inc.*, No. C03-3654RSM, slip op. (W.D. Wash. Mar. 29, 2006) (manufacturers of generic drugs may alter labeling to add or strengthen a warning without prior FDA approval) (attached as ex. 2); *Foster v. American Home Prods. Corp.*, 29 F.3d 165, 169 (4th Cir. 1994) (same), but it is in any event wholly irrelevant to the present case. Novartis is the name-brand manufacturer of Elidel and, as such, was free under 21 C.F.R.

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<sup>24</sup> It is true, as Novartis notes in its memorandum, at p. 9, n. 6, that the *Colacicco* court also dismissed plaintiff’s claims against GlaxoSmithKline on preemption grounds, but it did so purely on the basis of deference to the FDA. *Id.*

§§ 314.70(c) and 201.57(e) to add or strengthen warnings on the product label without prior FDA approval.<sup>25</sup> For this reason, *Colacicco* is distinguishable and much of its reasoning irrelevant to this case.

**B. *Colacicco* Has No Bearing Here Because the FDA Never Rejected a Stronger Warning for Elidel.**

There is a second significant factual difference between the present case and *Colacicco*: the drug involved. *Colacicco* involved generic Paxil, a member of the class of SSRIs. Unlike with Elidel, there was a long history of FDA decisions affirmatively rejecting additional warnings on SSRIs prior to the time that generic Paxil was prescribed to Lois Colacicco.

As summarized by the FDA in its *Colacicco amicus* brief: Paxil was initially approved by the FDA in 1992. Its original approved label reflected that there was a risk of suicide in patients using the drug, noting the “possibility of a suicide attempt inherent in major depressive disorder . . . until significant remission occurs,” and recommended “[c]lose supervision of high-risk patients.” In 1991, the FDA had denied a citizen petition seeking FDA withdrawal of approval for Prozac, another SSRI, because “[t]he data and information available at this time do not indicate that Prozac causes suicidality or violent behavior,” and, in 1992 and 1997, the FDA denied citizen petitions requesting that the agency revise the approved labeling for Prozac to include a warning of suicide or suicidal thought. In 2002, the FDA conducted a review of SSRIs to evaluate the state of scientific knowledge regarding their connection with suicide and again concluded that

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<sup>25</sup> The FDA’s assertion, cited by Novartis, that “the determination whether labeling revisions are necessary is, in the end, *squarely and solely the FDA’s* under the act,” 71 Fed. Reg. at 3934, refers only to the fact that the FDA can reject a CBE label change if it finds that the change renders the product misbranded. As discussed above, *supra* p. 21, given the FDA’s longstanding concerns about an association between Elidel and cancer and the 2005 decision to require a black box cancer warning, it is hard to imagine that the FDA would ever have challenged such a labeling change as misbranding.

“the scientific evidence did not show an association between the use of anti-depressants, including SSRIs, and suicide.” In the government’s words, prior to the time Ms.

Colacicco was prescribed Paxil, the “FDA had repeatedly determined . . . that there was inadequate evidence of an association between use of Paxil or other SSRIs by adult patients and a risk of suicide or suicidality to support a specific warning” on the drug’s label. Brief for the United States as *Amicus Curiae* Supporting Defendant, *Colacicco v. Apotex, Inc.*, at 6-10. Under these specific circumstances, in which the plaintiff’s tort claim arose out of an alleged failure to provide a warning that the FDA “had determined was not scientifically supported,” *id.* at 13, the FDA contended—and the court agreed—that plaintiff’s claims were preempted because they conflicted with federal law.<sup>26</sup>

There are good reasons to reject the FDA’s arguments concerning preemption of failure-to-warn claims involving SSRIs and, indeed, the vast majority of courts to consider the issue have ruled against preemption in those cases.<sup>27</sup> But, again, the issue is irrelevant to this case. There were no citizen petitions seeking stronger warnings for Elidel rejected by the FDA and no determination by the agency that a warning of an association between use of the drug and cancer would not be scientifically supported. To

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<sup>26</sup> Indeed, in its *Colacicco* brief, the FDA expressly disclaimed reliance on the January 2006 preamble as a basis for federal preemption in that case. *Id.* at 2, 18. And, it is striking to note that virtually every pharmaceutical tort suit in which the FDA has submitted a brief in support of preemption has involved an SSRI. See Briefs for the United States as *Amicus Curiae* Supporting Defendants, *Motus v. Pfizer, Inc.*; *Kallas v. Pfizer, Inc.*; and *Colacicco v. Apotex, Inc.* (attached as Exs. C, E, and F to Novartis’ motion and concerning Zoloft and generic Paxil, respectively). (The *Amicus* Brief for the United States in *Dowhal v. SmithKline Beecham Consumer Health Care, LP*, attached as Exhibit D to Novartis’ motion, addressed a conflict between the FDCA and a state statute, California Proposition 65.)

<sup>27</sup> See, e.g., *Laisure-Radke v. Par Pharmaceutical, Inc.*, No. C03-3654RSM, slip op. (W.D. Wash. Mar. 29, 2006) (attached as ex. 2); *Jackson v. Pfizer, Inc.*, \_\_\_ F. Supp. 2d \_\_\_, 2006 WL 1506886 (D. Neb. May 31, 2006) (denying preemption motion by manufacturers of Zoloft and Effexor); *Motus v. Pfizer, Inc.*, 127 F. Supp. 2d 1085, 1099-1100 (C.D. Cal); *Cloud v. Pfizer, Inc.*, No. CV 99-627-TUC-WDB, slip op. (D. Ariz. 2001); *Miles v. Pfizer, Inc.*, No. 03-731-C (M.D. La. March 30, 2005); *Cartwright v. Pfizer, Inc.*, 369 F. Supp. 2d 876, 882 (E.D. Tex. 2005); *Zikis v. Pfizer, Inc.*, No. 04 C 8104, 2005 WL 1126909 (N.D. Ill. May 9, 2005); *Witczak v. Pfizer, Inc.*, 377 F. Supp. 2d 726, 732 (D. Minn. 2005); *McNellis v. Pfizer, Inc.*, No. 05-1286 (D.N.J. 2005); *Szybinski v. Pfizer, Inc.*, No. YC047439 (Super. Ct. Cty of Los Angeles).

the contrary, from the time of Novartis' initial application for approval the FDA was concerned about an association with cancer. The FDA placed restrictions on the product's use, insisted upon further post-approval studies of cancer risk, and eventually both issued a public health advisory and required a black box warning. There is no conflict whatsoever between the regulatory history of Elidel and the Perrys' tort claims. For this reason as well, *Colacicco* is distinguishable from and irrelevant to this Court's consideration of the present motion.

### **Conclusion**

For all of the foregoing reasons, Plaintiffs urge this Court to deny Defendant Novartis' Motion to Dismiss Plaintiffs' Claims on Federal Preemption Grounds. Plaintiffs hereby request oral argument on this motion.

Respectfully submitted,

July 24, 2006  
Date

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**CERTIFICATE OF SERVICE**

I certify that on the 24 day of July, 2006 the foregoing document was electronically filed with the Court and is available for viewing and downloading from the Court's ECF system. The document was also served on all counsel of record in accordance with the Federal Rules of Civil Procedure and Local Rules for the Eastern District of Pennsylvania as indicated below:

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