No. 06-3107

IN THE UNITED STATES COURT OF APPEALS
FOR THE THIRD CIRCUIT

JOSEPH C. COLACICCO,

Plaintiff-Appellant,

v.

APOTEX, INC., AND GLAXOSMITHKLINE,

Defendants-Appellees.

On Appeal from the United States District Court
for the Eastern District of Pennsylvania

BRIEF OF AMICI CURIAE PUBLIC CITIZEN, TRIAL LAWYERS FOR PUBLIC JUSTICE AND ASSOCIATION OF TRIAL LAWYERS OF AMERICA IN SUPPORT OF APPELLANT SEEKING REVERSAL

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CORPORATE DISCLOSURE STATEMENT
(Federal Rule of Appellate Procedure 26.1)

Pursuant to Federal Rule of Civil Procedure 26.1, amici Public Citizen, the Association of Trial Lawyers of America ("ATLA"), and Trial Lawyers for Public Justice ("TLPJ") state that none of the three organizations has a parent company or issues stock to the public, and that no publicly-held company has an ownership interest (such as stock or partnership shares) in Public Citizen, ATLA, or TLPJ.

/s/
Allison M. Zieve

TABLE OF CONTENTS

TABLE OF AUTHORITIES

CASES Pages

STATUTES

REGULATORY MATERIALS

MISCELLANEOUS

INTRODUCTION

Damages actions for personal injuries caused by prescription drugs have co-existed with federal regulation of drugs since the early 1900s. Without identifying a single instance in which a verdict for a plaintiff injured by a drug undermined federal regulation, the court below accepted the argument of defendants-appellees Apotex and GlaxoSmithKline that the Food, Drug, and Cosmetic Act ("FDCA") impliedly preempts Mr. Colacicco's damages claims based on the death of his wife, Lois.

The companies' preemption argument is based on the theory that the Food and Drug Administration's ("FDA") regulation of prescription drugs cannot peacefully co-exist with state common-law regimes for compensation of patients injured as a result of inadequate warnings. That argument is both wrong as a matter of law and based on a misunderstanding of the scope and purpose of FDA regulation. Moreover, it is particularly ill-timed.

Recently, two independent government reports have described the dangerous shortcomings in FDA oversight of drug safety. In a report issued last March, the General Accounting Office concluded:

> FDA lacks clear and effective processes for making decisions about, and providing management oversight of, postmarket safety issues. The process has been limited by a lack of clarity about how decisions are made and about organizational roles, insufficient oversight by management, and data constraints.

GAO, *Improvement Needed in FDA's Postmarket Decision-making and Oversight Process*, Highlights (GAO-06-402 March 2006), *available at* www.gao.gov/cgi-bin/getrpt?GAO-06-402.

A National Academies' Institute of Medicine ("IOM") report released last week mirrors these conclusions. The IOM report, which was prepared at FDA's request, found that the nation's drug safety system is impaired by "serious resource constraints that weaken the quality and quantity of the science that is brought to bear on drug safety; an organizational culture in [FDA] that is not optimally functional; and unclear and insufficient regulatory authorities particularly with respect to enforcement." IOM, *The Future of Drug Safety: Promoting and Protecting the Health of the Public* at S-4 (Sept. 22, 2006), *available at* http://newton.nap.edu/execsumm_pdf/11750 ("IOM Report").

FDA employees report similar problems. Responding to two recent surveys, employees expressed discomfort with the pressure they feel to approve new drugs. In a survey released this summer, 60 percent of FDA employees who responded knew of cases "where commercial interests have inappropriately induced or attempted to induce the reversal, withdrawal or modification of FDA determinations or actions." Union of Concerned Scientists, *Summary of FDA Scientists Survey* (July 2006), *available at* www.ucsusa.org/scientific_integrity/interference/fda-scientists-survey-

summary.html. And 18 percent responded, "I have been asked, for non-scientific reasons, to inappropriately exclude or alter technical information or my conclusions in an FDA scientific document." *Id*. Similarly, in a 2003 survey by FDA's parent, the Department of Health and Human Services, 18 percent of FDA physicians and scientists who responded reported pressure to recommend that drugs be approved, even when they had reservations about safety, effectiveness or quality, and 66 percent lacked some or all confidence that the agency "adequately monitors the safety of prescription drugs once they are on the market." HHS, Office of Inspector General, *FDA's Review Process for New Drug Applications* at 12, 19 (March 2003), link *available at* www.ucsusa.org/news/press_release/fda-scientists-issued-early-warnings-on-drug-approvals.html.

Experience suggests that FDA's shortcomings undermine public health. In recent years, several drugs have been forced from the market for safety reasons—in some cases, long after FDA became aware that the drug was causing serious harm. For example, before the diabetes drug Rezulin was removed from the market in 2002, FDA and the drug's manufacturer experimented with labeling changes for several years, unsuccessfully trying to warn of the drug's risk of severe liver damage rather than eliminating the risk by removing the drug. The pain reliever Vioxx provides

another well-known example. *See* www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4090B1_04_E-FDA-TAB-C.htm; *see also* examples discussed *infra* pp. 26, 30.

Nonetheless, believing that recent statements from FDA about the scope of preemption were "dispositive," the district court stated that FDA regulation of drug labels preempts Mr. Colacicco's claims. App. A15, A33; *see also* A20, A23. Below, amici explain briefly why common-law claims are consistent with federal regulation. We then discuss why the district court's deference to FDA reflects a misunderstanding of Supreme Court case law on the weight to be accorded an agency's views and how, properly applied, that case law supports reversal.

INTEREST OF AMICI[1]

Public Citizen, a national non-profit consumer advocacy organization founded in 1971, does research, education, advocacy, and litigation on a broad range of consumer issues. In particular, through the work of its Health Research Group, Public Citizen has extensive knowledge of federal regulation of drugs. Public Citizen lawyers have represented plaintiffs on appeal, *see*, *e.g.*, *Medtronic ,Inc. v. Lohr*, 518 U.S. 470 (1996), and Public Citizen has participated as amicus curiae, *see*, *e.g.*, *Motus v. Pfizer*, 358 F.3d 659 (9th Cir. 2002), in many cases presenting the question whether the FDCA preempts state-law claims.

[1] All parties have consented to the filing of this amicus brief.

Trial Lawyers for Public Justice ("TLPJ") is a national public interest law firm that marshals the skills and resources of trial lawyers to create a more just society. TLPJ has pioneered cases advancing consumers' rights, preserving the environment, upholding civil rights, and safeguarding the civil justice system. TLPJ also has represented plaintiffs on appeal and participated as amicus curiae in numerous cases involving the question of preemption of state-law tort claims. *See*, *e.g.*, *Bates v. Dow AgroSciences*, 125 S. Ct. 1788 (2005) (amicus); *Sprietsma v. Mercury Marine*, 537 U.S. 51 (2002) (counsel of record).

The Association of Trial Lawyers of America ("ATLA") is an international coalition of attorneys, law professors, paralegals, and law students. As the world's largest trial bar, ATLA promotes justice and fairness for injured people and works to safeguard victims' rights—particularly the right to trial by jury—and to strengthen the civil justice system through education and disclosure of information critical to public health and safety.

Amici are concerned about a trend in the lower courts toward immunizing defendants from tort liability by holding that federal statutes preempt the claims of tort plaintiffs. These holdings have often been rejected by the Supreme Court. *See*, *e.g.*, *Bates*, 125 S. Ct. 1788; *Sprietsma*, 537 U.S. 51; *Medtronic,* 518 U.S. 470. Nonetheless, drug manufacturers are increasingly making preemption arguments in

products liability cases. The decision in this case will likely be the first circuit court decision to address a drug manufacturer's preemption argument since the development of the Supreme Court's tort preemption jurisprudence in the 1990s. Accordingly, this appeal is important to consumers around the country.

REGULATORY BACKGROUND

Since 1938, all prescription drugs must first be approved by FDA before they are marketed. To obtain permission to market a new product, a drug company must first submit a "new drug application" ("NDA") for 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, after reviewing the application, FDA finds that the drug is safe and effective for its intended use or uses and that the labeling is not false or misleading, FDA will send an approval letter to the applicant. *Id*. § 355(c)(1)(A).

FDA approval includes approval of the labeling, which must include several sections, including contraindications, warnings, precautions, and adverse reactions. 21 C.F.R. §§ 201.56, 201.57, 201.80. After approval, the manufacturer cannot make certain labeling changes without first obtaining FDA approval. *Id*. § 314.70(b). However, without prior approval, the company may make some changes, *id*. §§ 314.70(c), (d), including changes "[t]o add or strengthen a contra-indication,

warning, precaution, or adverse reaction." *Id.* § 314.70(c)(6)(iii). 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. 21 C.F.R. §§ 201.57(c)(6), 201.80(e). Indeed, FDA has advised that its labeling requirements "do not prohibit" manufacturers from warning—through labeling, advertising, or "Dear Doctor" letters—as soon as they discover harmful adverse effects not stated in the labeling. 44 Fed. Reg. 37434, 37447 (1979).

ARGUMENT

I. DAMAGES SUITS ARE CONSISTENT WITH FEDERAL REGULATION OF PRESCRIPTION DRUGS.

Suits seeking damages for injuries caused by drugs generally are based on theories of negligence and/or strict liability for product defects and/or inadequate warnings. Below, the district court accepted FDA's argument that compliance with both federal requirements and the state-law requirements on which this lawsuit is based will frustrate the purposes of federal regulation and, perhaps, that compliance with both federal and state requirements would be impossible. Under FDA's preemption theory, products liability actions could rarely be maintained against a pharmaceutical company for injuries caused by prescription drugs.

FDA's position runs contrary to Congress's purpose in enacting the FDCA: to protect public health. As one court stated in rejecting the preemption argument:

> FDA's and [defendant]'s position 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, *cf. Medtronic, Inc. v. Lohr*, 518 U.S. 470, 487 (1996), and the Court declines the invitation.

In re Paxil Litig., 2002 WL 31375497, at *1 (C.D. Cal. 2002).

After a drug is approved, "FDA cannot unilaterally compel label changes . . . or change the content of other documents intended for the public." IOM Report at 5-6. Because "knowledge of a drug's risk-benefit profile is never complete at the time of approval," *id.*, the limitations on FDA post-approval authority are significant here. Products liability lawsuits help to protect patients from drugs with undisclosed risks because the potential for being held liable for harm caused by their products provides a powerful incentive for drug companies to make their products as safe and effective as possible and to revise labels as soon as new risks become apparent.

Furthermore, because FDA lacks authority to subpoena documents from the companies it regulates, products liability lawsuits help to uncover information that can lead to safer products. Accordingly, such lawsuits are consistent with the FDCA's primary purpose of protecting public health.

Moreover, in a products liability suit, a verdict awarding money damages does not require a drug company to change its product's label or otherwise alter any obligation imposed on the company by the regulatory system. In some circumstances, a drug manufacturer may choose to revise a label in response to an adverse jury verdict. However, as the Supreme Court recently stated, "[a] requirement is a rule of law that must be obeyed; an event, such as a jury verdict, that merely motivates an optional decision, is not a requirement." *Bates*, 125 S. Ct. at 1799.[2] And "there is no general inherent conflict between federal pre-emption of state [regulatory] requirements and the continued vitality of state common law damages actions." *Cipollone v. Liggett Group*, 505 U.S. 504, 518 (1992) (plurality); *id.* at 533-34 (Blackmun, J., concurring). In other words, a verdict ordering the payment of damages does not require a drug manufacturer to do anything inconsistent with any FDA requirement. *See generally Eve v. Sandoz Pharm. Corp*., 2002 WL181972 (S.D. Ind. 2002*); Caraker v. Sandoz Pharm. Corp*., 172 F. Supp. 2d 1018 (S.D. Ill. 2001). Indeed, a core principle of strict products liability is that, although some potentially dangerous products will cause harm on occasion, it is beneficial to society as a whole

[2]*See also Sprietsma*, 537 U.S. at 64 (unanimous opinion) ("perfectly rational" for Congress to preempt state positive law, but not "common-law claims, which—unlike most administrative and legislative regulations—necessarily perform an important remedial role in compensating accident victims").

to keep them on the market *and* to compensate injured parties through the tort system. *See Prosser & Keeton on Torts* 536-57, 692-93 (5th ed. 1984).

II. FDA'S POSITION ON PREEMPTION OF TORT CLAIMS IS NOT ENTITLED TO DEFERENCE.

The district court held that an FDA amicus brief and the preemption discussion in the preamble to a revised labeling regulation issued in January were "dispositive to [the court's] determination" that Mr. Colacicco's claims are preempted. App. A33. However, a proper understanding and application of the Supreme Court's jurisprudence on deference to an agency's views shows that the court erred in giving such weight to FDA's position.

A. FDA Lacks Authority To Override State Tort Law.

Deference is premised on the assumptions that an ambiguity in the statute at issue reflects a gap within which Congress intended to delegate lawmaking discretion to an agency and that the agency's reasonable interpretation reflects a lawful exercise of that delegated discretion. *See United States v. Mead Corp*., 533 U.S. 218, 227, 229 (2001); *Chevron, USA v. Natural Res. Def. Council*, 467 U.S. 837, 843 (1984). Thus, the starting point for considering whether deference is warranted is the statute that provides the basis for the agency's authority. As the Supreme Court recently explained:

> Deference in accordance with *Chevron* . . . is warranted only "when it appears that Congress delegated authority to the agency to make rules carrying the force of law, *and* that the agency interpretation claiming deference was promulgated in the exercise of that authority."

Gonzalez v. Oregon, 126 S. Ct. 904, 915 (2006) (quoting *Mead*, 533 U.S. at 226-27) (emphasis added). In other words, "*Chevron* deference . . . is not accorded merely because the statute is ambiguous and an administrative official is involved. To begin with, the rule must be promulgated pursuant to authority Congress has delegated to the official." *Id.* at 916 (citing *Mead*, 533 U.S. at 226-27).

With respect to drugs, Congress has not delegated to FDA the authority to determine the preemptive effect of drug labeling rules on state damages actions. To be sure, FDA has authority to issue labeling rules, *see* 21 U.S.C. §§ 352, 355, but nowhere does the FDCA even imply an ancillary power to patrol the border between federal substantive rulemaking authority regarding drug labeling and the state's historic power to compensate its citizens through the tort system for harms caused by undisclosed hazards of prescription drugs.[3] Because the FDCA contains no delegation on the topic for which preemption is sought, no basis for deference exists.

The principle that no deference is owed to an agency's position on a topic outside the agency's delegated authority is illustrated by *Adams Fruit Co. v. Barrett*,

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[3] *Cf. FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 160 (2000) ("[W]e are confident that Congress could not have intended to delegate a decision of such economic and political importance to an agency in so cryptic a fashion.").

494 U.S. 638 (1990). There, a migrant worker sued under the federal private right of action established by the Migrant and Seasonal Agricultural Worker Protection Act ("AWPA"), seeking compensation for injuries he sustained while being transported in a van owned by his employer. In an amicus brief, the Secretary of Labor argued that the federal remedy was unavailable because state workers' compensation law provided a remedy to migrant workers. The Supreme Court declined to give deference to the Secretary's view because Congress had not given the agency authority to determine the preemptive scope of the AWPA's right of action. The Court held that the Secretary could not premise its call for deference on the statute's delegation to the agency of the authority to issue safety standards for employers' vehicles. To the contrary, the delegation did "not empower the Secretary to regulate the scope of the judicial power vested by the statute. Although agency determinations within the scope of delegated authority are entitled to deference, it is fundamental 'that an agency may not bootstrap itself into an area in which it has no jurisdiction.'" 494 U.S. at 650 (quotation omitted).

Just as the agency's authority to issue vehicle safety standards in *Adams Fruit* did not extend to determining the scope of civil remedies available to plaintiffs injured in vehicles, FDA's authority to issue drug labeling regulations does not extend to the question of civil remedies for failure to warn. Indeed, the claim to authority here is

even weaker than in *Adams Fruit*. There, Congress had at least contemplated the issue of remedies, and it had supplied a federal remedy at the same time it authorized the agency to issue vehicle safety standards. Here, Congress declined to provide a federal damages remedy in the FDCA precisely because state-law damages remedies were available. Adler & Mann, *Preemption and Medical Devices: The Courts Run Amok*, 59 Mo. L. Rev. 895, 924 & n. 130 (1995) ("Congress rejected a provision in a draft of the original FD&C providing a federal cause of action for damages because 'a common law right of action [already] exists.'") (quoting legislative history). Having made no effort to legislate on the topic of drug-related damages remedies, Congress can hardly be said to have authorized FDA to supersede the damages remedies traditionally provided by the states.

This point distinguishes FDA's recent preemption statements from the statement considered by the Supreme Court in *Hillsborough County v. Automated Medical Laboratories*, 471 U.S. 707, 714 (1985). In that case, the operator of a blood plasma center sued Hillsborough County, arguing that county ordinances and regulations governing blood plasma centers were preempted by FDA regulations on the same topic. When FDA had issued its regulations, it had expressly stated that the regulations did not preempt state and local authorities from regulating the same subject matter in their jurisdictions. The Supreme Court found that FDA's statement

was dispositive on the question of implicit intent to preempt, unless inconsistent with clearly expressed congressional intent or unless subsequent developments showed a change in the agency's position. *Id*. at 714-15.

In *Hillsborough County*, FDA's preemption statement went to a matter within the scope of the authority delegated to it by Congress—regulation of blood plasma centers. That is, FDA's authority to regulate blood plasma centers carried with it authority to address the preemptive effect of its regulation on state and local regulation of that same area. In contrast, here, FDA's statement regarding preemption goes to a matter outside the scope of the authority delegated to FDA—common-law claims. The authority to regulate drug labeling may carry with it the authority to address state drug labeling regulations, but it does not carry with it authority to determine the preemptive effect of federal regulation on state common-law compensation systems. *See also Medtronic*, 518 U.S. at 496 (FDA's view on scope of express preemption under Medical Device Amendments entitled to weight because "Congress explicitly delegated to FDA the authority to exempt state regulations from the pre-emptive effect of the MDA—an authority that necessarily requires the FDA to assess the pre-emptive effect that the Act and its own regulations will have on state laws").

Tellingly, in discussing the preemptive scope of the new labeling rules, FDA does not claim any congressional delegation. In fact, the January preamble suggests just the opposite. Tucked in a footnote, FDA quotes from the Drug Amendments of 1962, which amended the FDCA to require applications for approval of new drugs to demonstrate effectiveness, as well as safety, as follows: "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." Pub. L. No. 87-781, Title II, § 202, 76 Stat. 793 (Oct. 10, 1962) (emphasis added). At most, FDA's preemption discussion describes an *indirect* and attenuated conflict. Moreover, duty-to-warn cases often involve drugs whose hazards have become well known. Where the drug manufacturer has, prior to the plaintiff's suit, revised the label to warn of the relevant harm, or removed the product from the market altogether, the claim even to an indirect conflict is nonsensical.[4]

[4]The Controlled Substances Act contains similar anti-preemption language, stating that Congress has no intent to preempt state law "unless there is a positive conflict" between the Act and the state law "so that the two cannot consistently stand together." 21 U.S.C. § 903. The Supreme Court recently cited this language in rejecting a different preemption argument. *Gonzalez*, 126 S. Ct. at 923.

B. FDA's Current Position On Preemption Is Not Entitled To Substantial Weight.

Even apart from the absence of congressional delegation to FDA of authority to override state common law, FDA's preamble and the amicus briefs on which it is based, *see* 71 Fed. Reg. 3922, 3934 (2006) (preamble discussion of preemption intended to set forth arguments made in amicus briefs), warrant no weight. The degree of weight due to an executive agency depends, among other things, on the formality, consistency, thoroughness, and persuasiveness of the agency's view. *Mead*, 533 U.S. at 228. Consideration of these factors shows that the district court erred in deferring to FDA.

Formality: FDA's position on preemption, stated in a regulatory preamble and an amicus brief, lacks the formality that would warrant substantial weight. Although the preamble accompanied issuance of a rule promulgated through notice-and-comment rulemaking, it is not part of the regulation: It will not appear in the Code of Federal Regulations and does not have the force of law. In fact, a longstanding FDA regulation provides that a statement in a regulatory preamble constitutes only an "advisory opinion." 21 C.F.R. § 10.85(d)(1) (originally issued in 1979). Although FDA has "obligated" itself to follow its own advisory opinions, *id*. § 10.85(e), the agency recognizes that, in court proceedings seeking to bind a member of the public, an advisory opinion may be used to "illustrate acceptable . . . procedures or standard,

but not as a legal requirement." *Id*. § 10.85(j) (emphasis added). Thus, FDA's own regulations acknowledge that regulatory preambles are not statements of law and caution that preambles should not be presented as such in legal proceedings.

Even without issuing a regulation, agencies at times use notice-and-comment rulemaking to issue "interpretive rules"—rules without the force of law that set forth the agency's understanding of a statute that Congress has authorized the agency to interpret or enforce. These rules, too, sometimes receive deference from the courts. *See Gonzalez*, 125 S. Ct. at 914-16 (discussing deference to interpretative rules). However, FDA has not purported to issue an interpretative rule regarding preemption of state-law damages actions. Rather, the agency stated its "belief" on a legal question. *See* 71 Fed. Reg. at 3934 ("FDA believes . . ."); *id*. at 3969 (same).

Moreover, when FDA issued its proposed labeling rule in December 2000, it stated that "this proposed rule does not preempt State law." 65 Fed. Reg. 81082, 81103 (2000). The rule requested comment on products liability issues, but only by asking whether the new "Highlights" section of drug labeling raised liability concerns and, if so, how FDA might alleviate those concerns without eliminating the Highlights section. *Id*. at 81086. This request cannot be called "notice" of the broad preemption statement that followed, particularly given the agency's express statement that the rule would "not preempt state law." *Id*. at 81103. Thus, although presented in a Federal

Register notice in the course of issuing a regulation, FDA's preemption statement lacks the formality necessary to justify special weight.

Below, the district court cited *Geier v. American Honda Motor Corp*., 529 U.S. 861 (2000), for the proposition that informal statements such as amicus briefs and preambles may warrant deference. In *Geier*, the Supreme Court considered the preemptive effect of a 1984 Department of Transportation regulation regarding passive restraint systems. The regulation set a five-year phase-in period for required use of airbags and gave automakers a choice of passive restraints to install during that period. It did not address preemption. The Court concluded that the regulation preempted a claim that Honda was negligent for failing to install an airbag in the plaintiff's 1987 vehicle based on its reading of the purpose and substantive requirements of the regulation itself, as expressed by the agency at the time it formulated the regulation. *See Geier*, 529 U.S. at 877-81. Only after independently deciding that the plaintiff's claim would stand as an obstacle to the purposes of the regulation did the Court address the agency's amicus brief. Even then, the Court did not find that the agency's view was entitled to deference. Rather, consistent with its opinion the following term in *Mead*, the Court stated that the brief was entitled to "some weight," given considerations such as the agency's expertise and the

consistency of its views. *Id*. at 883. Thus, *Geier* does not support the "dispositive" weight that the district court gave to FDA's view.

Consistency: FDA's preemption statement also lacks the "consistency" needed to warrant any degree of deference. Prior to 2002, and since its inception in 1906, FDA's consistent view was that state common law was not preempted by federal drug regulation. For example, in both 1979 and 1998, in preambles accompanying various drug regulations, FDA stated that state tort law did *not* interfere with federal regulation. *See* 63 Fed. Reg. 66378, 66384 (1998) (regulation addressing Medication Guides, issued pursuant to FDA's authority over drug labeling) ("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."); 44 Fed. Reg. at 37437 ("It is not the intent of the FDA to influence the civil tort liability of the manufacturer."); *cf*. *Geier*, 529 U.S. at 883 (giving "some weight" to agency's view on preemptive effect of 1984 regulation, given consistent statements by agency in 1989, 1994, and 2000).

Similarly, although, as described above, FDA now argues that its requirements are not "minimum" requirements but rather impose both a floor and a ceiling, the agency stated the opposite in 1998 when issuing regulations addressing pharmacists' provision of written patient information in the form of "Medication Guides" for certain drugs. Manufacturers are required to obtain FDA approval of the Medication

Guides, 21 C.F.R. § 208.24(a), and FDA has prescribed numerous specific requirements as to both form and content. *See id*. § 208.20. Nonetheless, when issuing the final rule, FDA rejected comments calling for FDA to express an intent to preempt state regulation of labeling requirements:

> FDA regulations establish minimal standards necessary, but were not intended to preclude states from imposing additional labeling requirements. States may authorize additional labeling but they cannot reduce, alter, or eliminate FDA-required labeling.

63 Fed. Reg. at 66384.

The January preamble lists four instances in which an FDA preamble accompanying issuance of a new rule has stated that the rule would be preemptive. 71 Fed. Reg. at 3935. None of the prior statements, however, suggested that common-law claims would be preempted. Three were directed at state positive laws that specifically regulated the particular matter at issue. For example, in expressing its view that the federal requirement for a Reyes syndrome warning on over-the-counter products containing aspirin preempted state requirements, FDA noted that it was "unaware of any such requirements at this time." 51 Fed. Reg. 5180, 5181 (1986). FDA was not, of course, unaware of state common-law failure-to-warn claims, and thus its statement must have been directed at state positive law label requirements concerning Reye's Syndrome. *See also* 47 Fed. Reg. 50442, 50447-48 (1982) (tamper-resistant packaging regulations for over-the-counter drugs intended to

preempt state packaging requirements); 47 Fed. Reg. 54750, 54756-57 (1982) (stating that over-the-counter drug pregnancy-nursing warning requirements preempted by new FDA requirement on that topic and focusing on California law directed specifically to pregnancy-nursing warning requirements).

FDA's fourth citation is to a statement that a regulation providing for confidentiality for those who report adverse events to FDA and for patients identified in the reports is intended to preempt state disclosure requirements. 59 Fed. Reg. 3944, 3949 (1994). Although the preemptive effect of this regulation could affect the availability of certain discovery in damages suits, it has no potential to preempt damages claims, and FDA's discussion with respect to that regulation does not suggest otherwise.

As evidence that its practice of submitting amicus briefs supporting preemption "is not new," FDA's preamble cites briefs it filed in four cases prior to 2002. 71 Fed. Reg. at 3935. Three of those briefs, however, did not address preemption of damages claims at all: Two addressed preemption of state food-labeling laws, which FDA argued were preempted by federal labeling laws. *See Grocery Mfrs. of Am. v. Gerace*, 755 F.2d 993 (2d Cir. 1985); *Jones v. Rath Packing Co.*, 430 U.S. 519 (1977). And one brief concerned a plaintiff's request for discovery of the identities of those who had provided adverse reaction reports to FDA. *Eli Lilly and Co. v. Marshall*, 850

S.W.2d 155 (Tex. 1993). The defendant argued that the request was preempted by an FDA regulation providing that such information would not be disclosed; FDA filed a brief in support of the defendant, but the court rejected the preemption argument. *Id*. at 158-60.

In only one case cited by FDA, *Buckman v. Plaintiffs' Legal Committee*, 531 U.S. 341 (2001), did FDA argue that a damages claim was preempted. The claim at issue in that case, however, was unusual, and FDA's preemption argument was narrow. *Buckman* concerned a so-called "fraud-on-the-FDA claim," the theory of which was that the defendant had defrauded FDA to obtain marketing clearance for a medical device. Observing that the claim did "not focus on the device itself . . . [but] focuses, rather, on the relationship between the federal government and the entity it regulates," Brief for U.S. as Amicus Curiae in *Buckman*, 2000 WL 1364441, at *17-*18 (filed Sept. 13, 2000), the agency argued that the fraud-on-the-FDA claim conflicted with "the strong federal interest in permitting the FDA to decide for itself whether it has been defrauded and, if so, what statutorily authorized remedy to seek." *Id*. at *23. At the same time, FDA emphasized the narrow scope of its view of preemption by explaining that, unlike claims of defective design or failure to warn, the fraud-on-the-FDA claim "does not depend on any claim that the product itself was independently defective under state law or on any claim that the distribution of the

product independently violated any duty owed under state law." *Id*. at *20. Indeed, in contrast to its current position, FDA also acknowledged "the historic primacy of state regulation of matters of health and safety" and the appropriateness of a presumption against preemption where the state-law claims allege defective design, negligent manufacturing, or failure to warn. *Id*. at *17. The Supreme Court's opinion drew this same distinction. 531 U.S. 341, 347-48 (2001).

Thoroughness: The "thoroughness" of FDA's preemption analysis also shows that FDA's views warrant little weight here. As explained in the discussion of "consistency" (above) and "persuasiveness" (below), the preamble glosses over or simply ignores contrary statements made by the agency in the past, and it relies on cases and regulations that do not address preemption of common law to try to support a historical FDA view that does not exist.

Persuasiveness: Finally, the "persuasiveness" of FDA's preamble does not justify substantial weight.

1. The agency's view is unsupported by evidence that products liability lawsuits interfere with federal regulation, despite the many decades in which the two have co-existed. The preamble cites a handful of lawsuits and purports to explain how recent products liability lawsuits have "threatened the agency's ability to regulate risk information for prescription drugs in accordance with the [FDCA]." 71 Fed. Reg. at

3934. Notably, the only specific example that the agency offers was not a products liability case, but a case seeking to enforce a state labeling law, California's Proposition 65. *Dowhal v. SmithKline Beecham*, 32 Cal. 4th 910, 88 P.3d 1 (2004). Of five other cases cited in the preamble as illustrating the threat to federal regulation posed by products liability suits, three sought injunctive relief under state law to effect a labeling change. 71 Fed. Reg. at 3934 nn. 5-7. Only two of the listed cases were suits seeking only damages—which is the only relief sought in most products liability cases.[5] About those two, FDA says nothing in particular. It does not describe the cases or in any way explain how they posed a potential threat to FDA authority.

Significantly, the two cases were no different from typical products liability suits brought against drug companies for more than a century: The only relief sought in the lawsuits was damages for injuries caused by a drug, and no design or labeling changes were requested. Therefore, if the claims in the two damages cases cited in the preamble were preempted, the claims in all products liability cases against pharmaceutical companies since 1906 (when the first drug laws were enacted) or at least since 1938 (when new drugs were first required to be safe before they entered

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[5]71 Fed. Reg. at 3934 nn. 5 & 7 (citing *Ehlis v. Shire Richwood*, 233 F. Supp. 2d 1189, 1198 (D.N.D. 2002) (decision finding preemption), *aff'd on other grounds*, 367 F.3d 1013 (8th Cir. 2004); *Motus v. Pfizer*, 127 F. Supp. 2d 1085 (2000) (decision rejecting preemption), *subsequent dismissal on other grounds aff'd*, 358 F.3d 659 (9th Cir. 2004)).

the market) should have been preempted. Yet the Supreme Court has often reiterated the principle that state law "is superseded only where the repugnance or conflict is so 'direct and positive' that the two acts cannot be reconciled or consistently stand together." *Jones v. Rath Packing Co.*, 430 U.S. 519, 544 (1977) (citation omitted); *Amalgamated Ass'n of Street, Elec., Ry. & Motor Coach Employees v. Wisconsin Employment Relations Bd.*, 340 U.S. 383, 403 (1951). Surely, if so direct and positive a conflict existed, it would have repeatedly manifested itself over the years, and FDA should have been able to give numerous specific examples of verdicts that hampered the agency's ability to regulate or forced the defendant company to misbrand a product. The preamble does not offer a single example.

The reason for FDA's inability to cite cases in which an inadequate-warning claim actually threatened to interfere with federal regulatory authority is that a damages claim does not challenge FDA's decision to allow marketing of a product or its decision that the product can be labeled for certain indications. Instead, it challenges *the company's* decision not to include—either initially or later—a warning about a particular risk. *See* 21 C.F.R. §§ 201.57(c)(6), 201.80(e) (manufacturers' must revise label as soon as there is reasonable evidence of association with significant hazard); 21 C.F.R. § 314.70(c) (manufacturer may add warning without prior agency approval).

Further, a failure-to-warn claim is consistent with the fact that warnings set forth in the original FDA-approved labeling are not necessarily adequate. In many instances, neither the manufacturer nor FDA initially determine that a certain warning should appear on a drug label, and one or both later decide a warning is needed based on reports of adverse events in patients. Rezulin, Lotronex, Celebrex, Vioxx, Zoloft, Prozac, and Accutane are just a few examples of the many drugs that required post-approval labeling changes to add or strengthen warnings. In fact, "[m]any serious ADRs [adverse drug reactions] are discovered only after a drug has been on the market for years. Only half of newly discovered serious ADRs are detected and documented in the *Physicians' Desk Reference* within 7 years after drug approval." Lasser, *et al.*, *Timing of New Black Box Warnings and Withdrawals for Prescription Medications*, 287 J. A.M.A. 2215, 2218 (May 1, 2002). Moreover, an association between a drug and an adverse reaction is often identified or identifiable from premarketing trials, but no warning is given until after FDA receives adverse event reports from patients. *Id*. *But see* IOM Report at S-6 ("FDA's Adverse Event Reporting System (AERS) is outdated and inefficient."). As a result, a failure-to-warn claim is often consistent with labeling changes later made.

In fact, here, since at least several months before Mrs. Colacicco's suicide, FDA had been reviewing data about a possible link between SSRIs such as Paxil and

suicidality, and the agency issued a Public Health Advisory on that topic in October 2003—the same month that she died. *See* FDA Talk Paper (March 22, 2004), *available at* www.fda.gov/bbs/topics/ANSWERS/2004/ANS01283.html.

2. The district court held that failure-to-warn claims against the generic manufacturer Apotex would conflict with the FDCA because Apotex was required to use the labeling approved for the name-brand manufacturer. App. 35-36. Central to the court's discussion on this point was its belief that it was "require[d]" to follow the FDA's statement, made in an amicus brief, that generic companies cannot alter products labels without FDA approval. *Id*. at 36. That statement, however, contradicts 21 C.F.R. § 314.70(c)(6)(iii), which allows companies to add warnings to labels without prior FDA approval. *See also* 21 C.F.R. § 201.80(e) (manufacturer must revise label as soon as there is reasonable evidence of an association between its product and a serious hazard). Unlike the FDA's amicus brief, its regulation has the force of law. Moreover, section 314.70 unambiguously applies to generic manufacturers, as well as to name-brand companies.[6] Because the FDA's amicus brief

[6]Both regulations impose requirements on "applicants," which by definition include both name-brand and generic manufacturers. *See* 21 C.F.R. § 314.3(b). Moreover, even if, contrary to the plain language of § 314.70 and § 314.3(b), § 314.70(c)(6)(iii) did not apply to generic manufacturers, the FDA does not disagree that generic companies should bring new safety information to the agency's attention and request permission to revise labeling. Plaintiffs should be able to hold generic manufacturers accountable for failing to do so.

contradicts its own regulations, the court erred in deferring to it. *Cf. Thomas Jefferson Univ. Hosp. v. Shalala*, 512 U.S. 504, 512 (1992) (agency's interpretation of its regulation entitled to "controlling weight unless . . . inconsistent with the regulation").

3. Although FDA cites no concrete examples in which a damages verdict interfered with the agency's authority, the preamble does describe two ways in which some courts have construed federal requirements differently than FDA has. Neither justifies preemption of damages suits. First, FDA cites cases in which courts have rejected preemption on the ground that federal regulations allow companies to add or strengthen label warnings without prior FDA approval. Second, FDA cites opinions stating that federal labeling requirements impose minimum standards that companies are free to exceed.[7] This point is not really distinct from the prior one, for the idea is that the company should strengthen warnings when information justifying a stronger warning becomes available. *Caraker*, 172 F. Supp. 2d at 1033.

Disagreeing with these cases, FDA says that the decision whether to strengthen warnings is FDA's and that, even if the company changes its label as allowed under 21 C.F.R. § 314.70(c), FDA can disagree and take enforcement action against the company. This response ignores the reality that, "unless a case meets the statutory

[7]Although FDA now disagrees with those cases, it has previously stated that FDA labeling requirements set forth only minimum standards, which states are free to supplement. *See* 63 Fed. Reg. at 66384, discussed *supra* at pp. 19-20.

definition of fraud or misbranding or the high threshold for proving imminent hazard to the health of the public, FDA's regulatory and enforcement options" generally consist of "do nothing or precipitate voluntary withdrawal of the drug." IOM Report at 5-5. Thus, in most cases, FDA tries to negotiate the wording of labeling changes, not to dictate whether or not they will occur. And although concern that FDA would disagree with a change could be offered as a defense to a negligence claim, it does not alter the plain text of section 314.70(c)(6), or manufacturers' obligation to revise labeling "to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug," 21 C.F.R. § 201.80(e); *see id.* 201.57(c)(6) (similar obligation for labels of newer drugs), or the fact that manufacturers can warn without altering labeling, for example, through "Dear Doctor" letters. *See* 44 Fed. Reg. at 37447.

FDA also expresses concern that lawsuits can pressure companies to bolster safety warnings, which may cause them to add speculative warnings or to over-warn, which may cause important risk information to "lose its significance." 71 Fed. Reg. at 3935. This concern is addressed by the new Highlights section of the label, through which labels will emphasize "the most important information that is part of a larger body of information" about risks and usage to be communicated through the labeling. 71 Fed. Reg. at 3931. Because FDA has expressly provided that changes to

Highlights must be pre-approved by the agency, *id*. at 3932 (FDA revising 21 C.F.R. § 314.70 to provide that all changes to highlights section need prior approval, "except for editorial changes or similar minor changes"), the agency can ensure that less important warnings do not drown out more significant ones.

Moreover, FDA is not perfect. Too often, as discussed above, *supra* pp. 4-5, 26, new warnings are added only after much delay, and patients are injured as a result. (Consider the deaths and injuries caused by the reflux medication Propulsid, the diabetes drug Rezulin, and the antidepressant Serzone, before those drugs were finally pulled from the market. *See* www.pbs.org/newshour/bb/health/jan-june00/fda_3-28 .html (March 28, 2000 PBS story on Propulsid and Rezulin); www.namiscc.org/News/ 2004/Spring/Serzone.htm (Associated Press article noting that Serzone was pulled from European market more than one year before U.S. market)). In such instances, the "pressure" that lawsuits can put "on manufacturers to attempt to add warnings," 71 Fed. Reg. at 3935, is a productive counter-balance to the limitations of FDA regulation. It further illustrates the complementary roles of regulation and common law, the latter coming into play when the former fails to prevent injury or death.

CONCLUSION

The district court's decision should be reversed.

Respectfully submitted,

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I hereby certify that on this 28th day of September, 2006, I served the foregoing BRIEF OF AMICI CURIAE PUBLIC CITIZEN, *ET AL.*, on the parties listed below by causing two true and correct copies thereof to be placed in the U.S. mail, first-class postage prepaid, addressed as follows:

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