No. 06-3107

IN THE UNITED STATES COURT OF APPEALS
FOR THE THIRD CIRCUIT

JOSEPH C. COLACICCO, Individually and as Executor
of the Estate of Lois Ann Colacicco, Deceased,

Plaintiff-Appellant,

v.

APOTEX, INC., APOTEX CORP., as a Subsidiary of Apotex, Inc., and
SMITHKLINE BEECHAM, d/b/a GlaxoSmithKline,

Defendants-Appellees.

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

BRIEF OF PRODUCT LIABILITY ADVISORY COUNCIL, INC. AS *AMICUS CURIAE* IN SUPPORT OF DEFENDANTS-APPELLEES AND IN SUPPORT OF AFFIRMANCE OF THE JUDGMENT

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Pursuant to Rule 29 of the Federal Rules of Appellate Procedure, Product Liability Advisory Council, Inc. ("PLAC"), submits this brief as *amicus curiae* in support of defendants-appellees ("defendants") and in support of affirmance of the district court's dismissal of plaintiff's claims. All parties have consented to the filing of this brief.

INTEREST OF THE *AMICUS CURIAE*

PLAC is a non-profit association with 128 corporate members representing a broad cross-section of American and international product manufacturers. These companies seek to contribute to the improvement and reform of the law in the United States and elsewhere, with emphasis on the law governing the liability of manufacturers of products. PLAC's perspective is derived from the experiences of a corporate membership that spans a diverse group of industries in various facets of the manufacturing sector. In addition, several hundred of the leading product liability defense attorneys in the country are sustaining (non-voting) members of PLAC. Since 1983, PLAC has filed over 725 briefs as *amicus curiae* in both state and federal courts, including this Court, presenting the broad perspective of product manufacturers seeking fairness and balance in the application and development of the law as it affects product liability.

PLAC is well situated to address the issue of preemption raised in this appeal. PLAC's members are engaged in commerce in each of the fifty United

States and are subject in varying degrees to a wide range of federal regulations. Consequently, PLAC's members have often confronted the interplay between the duties imposed by federal law and the state common-law standards applied in product liability cases. Therefore, PLAC not only is uniquely suited to offer a broader perspective on preemption than the parties may provide, but it also is keenly interested in ensuring that the regulatory environment in which its members operate is a rational and consistent one.

INTRODUCTION AND SUMMARY OF ARGUMENT

Plaintiff contends that defendants are liable to him as a matter of state law based on defendants' alleged failure to warn of a purported risk of suicide that is said to accompany the use of Paxil and its generic equivalent, antidepressant drugs that the Food and Drug Administration ("FDA") approved as safe and effective for the treatment of depression and a number of other ailments. *See Colacicco v. Apotex, Inc.*, 432 F. Supp. 2d 514, 518 (E.D. Pa. 2006) (explaining that plaintiff alleges that "the suicide death of his wife, Lois, resulted from the Defendant drug manufacturers' failure to warn of the increased risk of suicidal behavior linked to the anti-depressant Paxil and/or its generic equivalent").

The district court granted defendants' motions to dismiss the complaint under Rule 12(b)(6) of the Federal Rules of Civil Procedure on the ground that plaintiff's claims are impliedly preempted by the federal Food, Drug, and Cosmetic

Act ("FDCA"), 21 U.S.C. § 355(a). Specifically, the district court found that plaintiff's claims are preempted because: (1) when Congress passed the FDCA, "it vested the FDA with authority to regulate the specifics of drug labeling, making important judgments of what is required for safety of the consuming public, what new drugs may appear in the marketplace, and what warnings their instructions and labels must carry" (*Colacicco*, 432 F. Supp. 2d at 518); (2) the FDA unequivocally exercised that congressionally-delegated authority in this case when it approved the labeling for Paxil and repeatedly found no evidence of a nexus between the use of Paxil and suicide (*id.* at 526-29); and (3) a court must defer to the FDA's express determination that its labeling decisions regarding Paxil and the class of drugs to which it belongs – selective serotonin reuptake inhibitors ("SSRIs") – preempt all state-law efforts to require warnings on the label for Paxil that differ from those approved by the FDA (*id.* at 525-26, 529-30, 536).

In their brief to this Court, defendants have amply demonstrated why the district court's judgment with respect to Paxil and its generic version is correct and should be affirmed. In this brief, PLAC uses the issues raised in this action to illustrate a point that has implications beyond the context of the FDA's regulation of pharmaceuticals, namely, that state-law tort litigation can easily upset the delicate regulatory balance struck by any expert federal agency under similar circumstances. It is therefore in the public's interest for a court to defer to the

federal agency's determination that the regulatory scheme for which it is responsible preempts state-law efforts to impose different or additional obligations on the regulated entities.

In this case, the FDA mandated both the language and location of the suicidality warnings on Paxil's labeling, repeatedly reviewed those warnings prior to the death of plaintiff's wife, and in each instance reaffirmed that the warnings it required best served the agency's interest in promoting and preserving public health. If private litigants are permitted to hold manufacturers liable on an *ad hoc* basis for failing to include risk warnings that are contrary to those mandated by the expert federal agency, not only would manufacturers have strong incentives to "overwarn," but the goal of national uniformity in product regulation would be seriously undermined and substantial burdens would be imposed on interstate commerce. Accordingly, the district court was correct in finding that it owed deference to the FDA's determination that its labeling decisions regarding Paxil and other SSRIs preempt plaintiff's failure-to-warn claims, and the judgment for the defendants should therefore be affirmed.

ARGUMENT

A. The FDA's Determination That Its Labeling Decisions Preempt State-Law Failure-To-Warn Claims Is Entitled To *Chevron* Deference.

Under the Supremacy Clause of the United States Constitution, Congress may preempt state statutory or common law through federal legislation. *See* U.S.

CONST. art. VI, cl. 2; *Chicago & N.W. Transp. Co. v. Kalo Brick & Tile Co.*, 450 U.S. 311, 326-27 (1981). It is well settled that federal regulations implementing such statutes "have no less pre-emptive effect than federal statutes" themselves. *Fid. Fed. Sav. & Loan Ass'n v. de la Cuesta*, 458 U.S. 141, 153 (1982).

In the course of delineating the circumstances in which preemption exists, the Supreme Court has held that a federal statute or regulation impliedly preempts any state law (including any state common law) that would "prevent or frustrate the accomplishment of a federal objective." *Geier v. Am. Honda Motor Co.*, 529 U.S. 861, 873-74 (2000); *see also United States v. Locke*, 529 U.S. 89, 109 (2000) (preemption is implied "when the state law stands as an obstacle to the accomplishment and execution of the full purposes and objective of Congress") (internal quotation marks and citation omitted). When, as in the case of the FDA, Congress has delegated authority to an expert federal agency to implement and enforce a federal regulatory scheme, the agency's determination that state law threatens to upset federal objectives "is dispositive . . . unless either the agency's position is inconsistent with clearly expressed congressional intent, . . . or subsequent developments reveal a change in that position." *Hillsborough County v. Automated Med. Labs., Inc.*, 471 U.S. 707, 714-15 (1985) (citation omitted).

This deference to an agency's interpretation of the preemptive scope of a federal statute or regulation that the agency administers derives from the seminal

decision in *Chevron U.S.A. Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837 (1984). As the Supreme Court explained in *Chevron*, administrative deference inheres in the congressional decision to delegate powers to the agency:

> The power of an administrative agency to administer a congressionally created . . . program necessarily requires the formulation of policy and the making of rules to fill any gap left, implicitly or explicitly, by Congress. If Congress has explicitly left a gap for the agency to fill, there is an express delegation of authority to the agency to elucidate a specific provision of the statute by regulation. Such legislative regulations are given controlling weight unless they are arbitrary, capricious, or manifestly contrary to the statute. Sometimes the legislative delegation to an agency on a particular question is implicit rather than explicit. *In such a case, a court may not substitute its own construction of a statutory provision for a reasonable interpretation made by the administrator of an agency.*

Id. at 843-44 (citations and internal quotation marks omitted; emphasis added). Thus, under *Chevron*, "a court must give effect to an agency's regulation containing a reasonable interpretation of an ambiguous statute." *Christensen v. Harris County*, 529 U.S. 576, 586-87 (2000). That same absolute deference is accorded to "an agency's [reasonable] construction of its own regulations." *Martin v. Occupational Safety And Health Review Comm'n*, 499 U.S. 144, 150 (1991) (citation omitted).

The key to *Chevron* deference is the nature of the authority that Congress has delegated to the agency.

> [A]dministrative implementation of a particular statutory provision qualifies for *Chevron* deference 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. Delegation of such authority may be shown in a variety of ways, as by an agency's power to engage in adjudication or notice-and-comment rulemaking, or by some other indication of a comparable congressional intent.

United States v. Mead Corp., 533 U.S. 218, 226-27 (2001). There can be no serious question that the authority over prescription drug labeling that Congress delegated to the FDA satisfies the *Chevron* test for deference.

As the district court explained (*see Colacicco*, 432 F. Supp. 2d at 522-23) and as plaintiff concedes (*see* Appellant's Br. at 33), the FDA is the expert federal agency charged by Congress with ensuring that drugs are safe and effective. To that end, the FDCA mandates that drug manufacturers obtain FDA approval to market prescription drugs, and the agency makes those approval decisions based "on a comprehensive scientific evaluation of the product's risks and benefits under the conditions of use prescribed, recommended, or suggested *in the labeling*." Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922, 3934 (Jan. 24, 2006) (to be codified at 21 C.F.R. Parts 201, 314, and 601) (citing 21 U.S.C. § 355(d)) (emphasis added). Indeed,

> [t]he *centerpiece* of risk management for prescription drugs generally is the labeling which reflects thorough FDA review of the pertinent scientific evidence and communicates to health care practitioners the agency's formal, authoritative conclusions regarding the conditions under which the product can be used safely and effectively. FDA

> carefully controls the content of labeling for a prescription drug, because such *labeling is FDA's principal tool for educating health care professionals about the risks and benefits of the approved product to help ensure safe and effective use*.

Id. (emphasis added); *see also id.* at 3967-69; New Drug and Antibiotic Regulations, 50 Fed. Reg. 7452, 7470 (Feb. 22, 1985) ("Drug labeling serves as the standard under which FDA determines whether a product is safe and effective.").

The Supreme Court has recognized that state law cannot be allowed to disrupt FDA efforts to achieve "a somewhat delicate balance of statutory objectives," and held on that basis that the FDCA impliedly preempts state-law claims of fraud on the FDA. *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 348 (2001). The FDA argued in favor of this result in *Buckman*, because fraud-on-the-FDA claims would allow courts applying state law to ignore actual federal agency actions if deemed "fraudulently" obtained.[1]

Applying that same rationale – that courts applying state law cannot ignore the actions of the agency – the FDA, in an *amicus* brief filed at the request of the district court below, unequivocally stated its conclusion that,

> [t]o base a tort judgment on drug manufacturers' failure to warn in October 2003 of an association between adult use of [Paxil] and

[1] *See* Brief For United States As *Amicus Curiae* Supporting Petitioner, *Buckman Co. v. Plaintiffs' Legal Committee*, No. 98-1768 (U.S. Sept. 13, 2000) (arguing at the merits stage that fraud-on-the-FDA claims are preempted); Brief For United States As *Amicus Curiae*, *Buckman Co. v. Plaintiffs' Legal Committee*, No. 98-1768 (U.S. June 7, 2000) (same argument on petition for certiorari).

> suicide or suicidality, despite FDA's judgment at that time that there was not reasonable evidence of such an association, would be to demand a warning statement that would have been false and misleading, and thus contrary to federal law. In such a case, federal law must prevail.

Brief For *Amicus Curiae* The United States Of America at 1, *Colacicco v. Apotex, Inc.*, No. 05-CV-05500-MMB (E.D. Pa. May 10, 2006) (hereinafter "FDA *Amicus* Br."). That determination is reiterated in the preamble to the agency's final rules governing the content and format of labeling for all human prescription drug and biological products (hereinafter the "Preemption Preamble").[2] The agency unequivocally declared that "FDA approval of labeling under the [FDCA], whether it be in the old or new format, preempts conflicting or contrary State law" (71 Fed. Reg. at 3934), and specifically identified as preempted all claims that a drug manufacturer "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," or "by failing to include a statement in labeling or in 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 [manufacturer] had an obligation to warn" (*id.* at 3935-36).

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[2] The Supreme Court has held that a federal agency's determination that federal law preempts state law may properly be communicated in "regulations, *preambles*, interpretive statements and responses to comments" (*Hillsborough County,* 471 U.S. at 718 (emphasis added)), as well as in *amicus* briefs (*see, e.g.*, *Geier*, 529 U.S. at 883).

As we next show, the FDA is correct that, as in *Buckman*, claims such as those made by plaintiff pose a threat to the FDA's ability to achieve the delicate balance between ensuring public access to lifesaving drugs and informing the health-care community about potential dangers posed by those drugs. Accordingly, consistent with the principles elucidated in *Chevron* and its progeny, the district court properly deferred to the FDA's reasonable determination that state-law failure-to-warn claims are preempted by the agency's labeling decisions made pursuant to the FDCA. Moreover, because other federal agencies are engaged, or may be asked to engage, in a similar balancing of interests with respect to other types of products marketed nationwide, the decision in this case could have an impact well beyond the labeling of Paxil and its generic competitors.

B. State-Law Failure-To-Warn Liability Conflicts With The FDA's Goals Of Preventing Overwarning And Patchwork Regulation.

The FDA's overarching goal in regulating the warning labels of pharmaceuticals is to strike the right balance between providing adequate information to drug users and providing too many, or the wrong kind of, warnings. "FDA seeks to encourage the optimal level of use in light of reasonable safety concerns, by requiring scientific evidence of an association between a drug and a particular hazard before warning of that association on a drug's labeling." FDA *Amicus* Br. at 14 (citing 21 C.F.R. § 201.57(e)). To achieve that goal, "FDA considers not only complex clinical issues related to the use of the product in study

populations, but also important and practical public health issues pertaining to use of the product in day-to-day clinical practice . . . ." 71 Fed. Reg. at 3968. Through careful consideration of these factors, "appropriate warnings are drafted that identify established risks while avoiding inadequately substantiated risks, mention of which could improperly deter use of the drug to the detriment of the very patients it is designed to benefit." FDA *Amicus* Br. at 5.

In the Preemption Preamble, the FDA emphasized how delicate and important this balance is, and how overwarning can harm patients and interfere with regulatory goals:

> Given the comprehensiveness of FDA regulation of drug safety, effectiveness, and labeling under the act, additional requirements for the disclosure of risk information are not necessarily more protective of patients. Instead, they can erode and disrupt the careful and truthful representation of benefits and risks that prescribers need to make appropriate judgments about drug use.

71 Fed. Reg. at 3935; *accord* FDA *Amicus* Br. at 13 ("In considering the agency's views on drug labeling, it is critical to understand that, where warnings are concerned, more is not always better."). Among other dangers, "[e]xaggeration of risk could discourage appropriate use of a beneficial drug." 71 Fed. Reg. at 3935. Moreover, "labeling that includes theoretical hazards not well-grounded in scientific evidence can cause meaningful risk information to 'lose its significance.'" *Id.* (quoting 44 Fed. Reg. 37,434, 37,447 (June 26, 1979)). Thus, "State-law attempts to impose additional warnings can lead to labeling that does

not accurately portray a product's risks, thereby potentially discouraging safe and effective use of approved products or encouraging inappropriate use and undermining the objectives of the act." *Id.*; *see also, e.g.*, Brief For *Amicus Curiae* The United States Of America at 23-24, *Motus v. Pfizer, Inc.*, 358 F.3d 659 (9th Cir. 2004) (Nos. 02-55372 & 02-55498) ("*Motus Amicus* Br.") (explaining that "[u]nder-utilization of a drug based on dissemination of scientifically unsubstantiated warnings, so as to deprive patients of beneficial, possibly life-saving treatment, could well frustrate the purposes of federal regulation as much as over-utilization resulting from a failure to disclose a drug's scientifically demonstrable adverse effects").[3]

[3] The *Motus* brief is one of a number of FDA *amicus* briefs supporting implied preemption filed since 2000. In each case, the FDA was concerned about some aspect of civil litigation that posed a specific threat to its authority. *See Amicus* Brief For The United States, *Kallas v. Pfizer, Inc.*, No. 2:04CV0998 PGC (D. Utah. Sept. 15, 2005) (arguing, as here, that suicidality warning claim was preempted by FDA rejection of scientific basis for warning); *Amicus Curiae* Brief Of The United States Of America, *Dowhal v. SmithKline Beecham Consumer Healthcare, LP*, No. A094460 (Cal. July 18, 2003) (state mandated teratogenicity statement on smoking cessation product preempted where FDA had concluded that statement should not appear); Statement Of Interest Of The United States Of America, *Murphee v. Pacesetter*, Civ. No. ct-005429-00-3 (Tenn. Cir. 30th Dist. Dec. 12, 2003) (claim based on misstatements of nature of FDA medical device approval preempted); Brief Of The United States, *In re Paxil Litig.*, No. CV 01-07937 MRP (C.D. Cal. Sept. 5, 2002) (state-law injunction against FDA-approved advertising preempted); Statement Of Interest Of The United States, *Bernhardt v. Pfizer, Inc.*, 00 Civ. 4042 (LLM) (S.D.N.Y. Nov. 13, 2000) (state-law injunctive relief to force changes in drug labeling and issuance of "Dear Doctor" letters preempted).

These concerns were echoed not long ago in a letter entered in the *Congressional Record* from five former Chief Counsel of the FDA, whose tenures date back to 1972. That letter debunked allegations that the FDA had gone "'in a radical new direction'" by arguing in its *amicus* brief in *Motus*, *supra*, that failure-to-warn claims are preempted by the FDCA. 150 Cong. Rec. S8657 (daily ed. July 22, 2004) (quoting 150 Cong. Rec. H5598-5599 (July 13, 2004)); *accord* 150 Cong. Rec. E1505 (July 22, 2004). These former FDA Chief Counsel explained that, in arguing for preemption, the "amicus curiae briefs filed by [the United States] . . . protect FDA's jurisdiction and the integrity of the federal regulatory process" because, "[i]f every state judge and jury could fashion their own labeling requirements for drugs and medical devices, there would be regulatory chaos for these two industries that are so vital to the public health, and FDA's ability to advance the public health by allocating scarce space in product labeling to the most important information would be seriously eroded." 150 Cong. Rec. S8657.

This is not mere political rhetoric, as the FDA's preemption stance has been maintained under both Democratic and Republican administrations. Courts and commentators alike acknowledge the wisdom of preserving FDA primacy in reviewing and approving labeling for products over which it has regulatory authority. Indeed, when this Court held in *Horn v. Thoratec Corp.*, 376 F.3d 163 (3d Cir. 2004), that the federal pre-market approval process for medical devices

preempts state common-law claims alleging defective design and manufacture, the Court relied upon the FDA's conclusion that "'State common law tort actions threaten the statutory framework for the regulation of medical devices, *particularly with regard to FDA's review and approval of product labeling*.'" *Id.* at 178 (quoting the Letter Brief Of *Amicus Curiae* The United States Of America at 25) (emphasis added). Similarly, in *Brooks v. Howmedica, Inc.*, 273 F.3d 785 (8th Cir. 2001) (en banc) – a failure-to-warn case involving the labeling of a medical device approved by the FDA – the Eighth Circuit identified

> a number of sound reasons why the FDA may prefer to limit warnings on product labels. Warnings about dangers with less basis in science or fewer hazards could take attention away from those that present confirmed, higher risks. A label with many varied warnings may not deliver the desired information to users. Space on product labeling is also a factor, and the most effective labels are those with large, bold warnings and a simple design.

Id. at 796.

None of these concerns is likely, however, to motivate – or even be considered by – a jury that is asked to decide a state failure-to-warn claim. All such a jury would be called upon to determine is whether the content of the defendant's label satisfied the defendant's state-law duty to warn the *particular* plaintiffs of the *particular* risk at issue. If the jury answers that question in the negative, liability is almost certain to attach, regardless of the potential impact that

the addition of that warning might have on *other* consumers' ability or willingness to use the product.

This problem is exacerbated by the case-by-case process of common-law adjudication. Later judges or juries cannot reconsider outcomes reached in earlier cases. Thus, a trier of fact cannot deem unnecessary or inappropriate a warning added in response to an earlier verdict. Nor do judges and juries know how many warnings will be vying for limited reader attention.

That is precisely the role of the FDA. As the Eighth Circuit emphasized, "[i]t would be difficult for a jury focused on a single case to take into account 'the cumulative, systemic effects' of a series of verdicts. In contrast, the FDA possesses a broader perspective." *Brooks*, 273 F.3d at 797 (quoting Richard B. Stewart, *Regulatory Compliance Preclusion of Tort Liability: Limiting the Dual-Track System*, 88 Geo. L.J. 2167, 2175 (2000)). Even where a judge or jury is aware of potential overwarning, it can do little to prevent the problem. *See* James A. Henderson, Jr. & Aaron D. Twerski, *Doctrinal Collapse in Products Liability: The Empty Shell of Failure to Warn*, 65 N.Y.U. L. Rev. 265, 302 (1990).

In light of these widely-recognized risks, the FDA has reasonably determined that "State law actions . . . threaten FDA's statutorily prescribed role as the expert Federal agency responsible for evaluating and regulating drugs." 71 Fed. Reg. at 3935. As the agency summarized in the Preemption Preamble:

> State actions are not characterized by centralized expert evaluation of drug regulatory issues. Instead, they encourage, and in fact require, lay judges and juries to second-guess the assessment of benefits versus risks of a specific drug to the general public – the central role of FDA – sometimes on behalf of a single individual or group of individuals. That individualized reevaluation of the benefits and risks of a product can result in relief – including the threat of significant damage awards or penalties – that creates pressure on manufacturers to attempt to add warnings that FDA has neither approved nor found to be scientifically required. This could encourage manufacturers to propose "defensive labeling" to avoid State liability, which, if implemented, could result in scientifically unsubstantiated warnings and underutilization of beneficial treatments.

Id. Only comprehensive, exclusive regulation by an expert agency, such as the FDA, can solve the problem of overwarning by permitting an overall evaluation of risk and a rational decision about what risks are sufficiently serious to warrant inclusion on a label, how those warnings should be phrased, and where they should be placed. This is especially true where, as here, the intended readership consists not of ordinary consumers, but, under the learned-intermediary doctrine, highly-trained physicians who make judgments based on scientific data and information.

In addition to the danger of overwarning created when states require warnings not approved by the FDA, state regulation via failure-to-warn claims undermines "the need for national uniformity in product regulation." *Brooks*, 273 F.3d at 797. The FDA explained in another *amicus* brief that, if judgments under state law were allowed to trump the FDA's assessment of what may appear in drug advertisements, "the public undoubtedly would receive inconsistent information

from region to region." *Amicus Curiae* Brief of the United States at 5, *In re Paxil Litig.*, No. CV 01-07937 MRP (C.D. Cal. Sept. 5, 2002).

The Supreme Court likewise recognized in the context of another federal labeling regime – the Federal Cigarette Labeling and Advertising Act of 1965 – that the national economy can be greatly burdened if manufacturers of a product sold around the country are subjected to "diverse, nonuniform, and confusing . . . labeling and advertising regulations." *Cipollone v. Liggett Group, Inc.*, 505 U.S. 504, 514 (1992). Congress, in the legislative history of the Medical Device Amendments to the FDCA ("MDA"), observed that, "if a substantial number of differing requirements applicable to a medical device are imposed by jurisdictions other than the Federal government, interstate commerce would be unduly burdened." H.R. Rep. No. 853, 45 (1976) (quoted in *Brooks*, 273 F.3d at 797). For these reasons, it was reasonable for the FDA to conclude that,

> [i]f State authorities, including judges and juries applying State law, were permitted to reach conclusions about the safety and effectiveness information disseminated with respect to drugs for which FDA has already made a series of regulatory determinations based on its considerable institutional expertise and comprehensive statutory authority, the federal system for regulation of drugs would be disrupted.

71 Fed. Reg. at 3969. Not only would allowing plaintiff's claims to proceed in this case open the door to the burdening of interstate commerce in prescription drugs,

but it also would set a precedent that could affect other federally-regulated industries.

C. The Dangers Posed By Overwarning Are Widely Recognized.

Drug manufacturers facing tort liability for using FDA-approved product labels would have strong incentives to warn against any and all conceivable harms. Although a defendant in a particular case might be liable only for failing to include one specific warning, that defendant would then be forced to decide whether all risks of similar probability and magnitude of harm also should be acknowledged, lest other courts in other cases find other omissions unlawful.

> As one moves from more important warnings to those of lesser urgency, the number of warnings that must be supplied increases exponentially at each descending level. The plaintiff typically asks for only one warning — the one precisely relating to the risk that materialized in his injury. But the defendant has the right to insist that other, equally important warnings also not be obscured as a result.

Henderson & Twerski, 65 N.Y.U. L. Rev. at 307-08.

Indeed, "[t]rials of tort claims pose incentives to overwarn" because, although "'the visible monetary costs of additional warnings are typically quite low – a few pennies for a bit more paper and a little more ink'" (*Brooks*, 273 F.3d at 797 (quoting Henderson & Twerski, 65 N.Y.U. L. Rev. at 297)), the consequences of failing to include a particular warning later required under state law could be devastating. *See* Lars Noah, *The Imperative to Warn: Disentangling the "Right to Know" From the "Need to Know" About Consumer Product Hazards*, 11 Yale J.

On Reg. 293, 375 (1994). It is easy for a single judge or jury to conclude that an additional warning should have been given. However, the combined effect of individual suits is an overloaded warning label, and the negative impact on the public health of such a blunderbuss approach can be pronounced.

Lengthy warning labels listing every conceivable risk might help to insulate drug manufacturers from tort lawsuits, but they are highly detrimental to users and prescribers of drugs. As the FDA explained in the Preemption Preamble, "liability concerns [can] creat[e] pressure on manufacturers to expand labeling warnings to include speculative risks and, thus, to limit physician appreciation of potentially far more significant contraindications and side effects." 71 Fed. Reg. at 3935 (citation omitted); *see also* FDA, Centers for Drug Evaluation and Research and Biologics Evaluation and Research, *Draft Guidance for Industry: Brief Summary: Disclosing Risk Information in Consumer-Directed Print Advertisements*, at 2 (January 2004), *available at* www.fda.gov/cber/gdlns/consumad.htm (last visited Nov. 14, 2006) ("exhaustive lists of minor risks detract from and make it difficult to comprehend and retain information on the more important risks," because "the volume of the material, coupled with the format in which it is presented (*i.e.*, very small print and sophisticated medical terminology) discourages its use and makes the information less comprehensible to consumers"); *id.* at 4 ("We believe that omitting less

serious, infrequent risks from patient labeling may actually increase the usefulness of this labeling for its audience by making the more important risks stand out more clearly."); *Motus Amicus* Br. at 23-24 ("allowing unsubstantiated warnings may also diminish the impact of valid warnings by creating an unnecessary distraction and making even valid warnings less credible"). Thus, the FDA has urged that manufacturers avoid the use of "[e]xhaustive lists of every reported adverse event, including those that are infrequent and minor, commonly observed in the absence of drug therapy or not plausibly related to drug therapy . . . ." FDA, Centers for Drug Evaluation and Research and Biologics Evaluation and Research, *Guidance for Industry: Adverse Reactions Section of Labeling for Human Prescription Drug and Biological Products — Content and Format*, at 2 (January 2006), *available at* www.fda.gov/cber/gdlns/cfadvers.htm (last visited Nov. 14, 2006).

The wisdom of the FDA's judicious approach to labeling has been echoed by numerous courts and commentators. For example, the California Supreme Court concluded:

> Both common sense and experience suggest that if every report of a possible risk, no matter how speculative, conjectural, or tentative, imposed an affirmative duty to give some warning, a manufacturer would be required to inundate physicians indiscriminately with notice of any and every hint of danger, thereby inevitably diluting the force of any specific warning given.

Finn v. G.D. Searle & Co., 35 Cal.3d 691, 701 (1984); *see also, e.g.*, *Thomas v. Hoffman-LaRoche, Inc.*, 949 F.2d 806, 815 (5th Cir. 1992) ("To be reasonable, the

warning should neither understate nor overstate the known risks associated with the use of a particular product."); *Doe v. Miles Labs., Inc.*, 927 F.2d 187, 194 (4th Cir. 1991) ("If pharmaceutical companies were required to warn of every suspected risk that could *possibly* attend the use of a drug, the consuming public would be so barraged with warnings that it would undermine the effectiveness of these warnings."); W. Kip Viscusi, *Individual Rationality, Hazard Warnings, and the Foundations of Tort Law*, 48 Rutgers L. Rev. 625, 632 (1996); Noah, 11 Yale J. On Reg. at 297 ("additional warnings about relatively inconsequential hazards may cause [users] to become less attentive to labels as a whole," diminishing the impact of even succinct warnings). Congress has likewise acknowledged the danger posed by overwarning:

> If labeling were required to caution against the risk of even the most trifling indisposition, there would hardly be any substance . . . which would not have to bear cautionary labeling, so that consumers would tend more and more to disregard label warnings, thus inviting indifference to cautionary statements on packages of substances presenting a real hazard of substantial injury or illness.

H.R. Rep. No. 86-1861 (1960), *reprinted in* 1960 U.S.C.C.A.N. 2833, 2837.

Apart from the possibility that the users of prescription drugs will simply ignore too-lengthy warnings, there is a real possibility that overwarning will confuse users. Studies have shown that some consumers

> believe that a product whose label discloses several small risks is more hazardous than a product whose label warns of a single serious risk. Conversely, one study found the perverse effect that consumers

> viewed products with warning labels as more desirable than those without them, perhaps because products accompanied by warnings were perceived as containing more powerful ingredients.

Noah, 11 Yale J. On Reg. at 384 (footnotes omitted). Other users "become preoccupied with information about trivial hazards." *Id.* at 297. Users may forego using a drug or other product, or choose to use a different one, in response to lengthy warning statements – even if these alternatives "pose greater (though perhaps less alarming) risks." *Id.* Even if medical personnel are not misled by a warning label, "they may nonetheless avoid using perfectly safe and effective [drugs] for fear of malpractice liability if they disregard a warning." *Id.* at 390. Thus, "[t]he full costs of overwarning would only be known if legal actions were available to people deterred from taking needed therapy by excessive warnings." Richard A. Epstein, *Legal Liability for Medical Innovation*, 8 Cardozo L. Rev. 1139, 1150 (1987).

Furthermore, in what can fairly be called a Catch-22, overwarning might even increase vulnerability to tort liability. As one commentator has suggested, "[i]t seems to be only a matter of time before a plaintiff succeeds in bringing an inadequate warning claim premised on the argument that, although a completely accurate statement of the risk had been provided, the pertinent warning lacked sufficient prominence because it was lost among the clutter of too many other

cautionary statements on the label." Noah, 11 Yale J. On Reg. at 379-80; *see also id.* at 380 n.435 (describing similar cases).

These adverse consequences of overwarning are all sharply at odds with the FDA's regulatory goals. They result from the misguided notion that FDA-approved warning labels are minimal warnings that can and should be supplemented by state-law failure-to-warn actions. *See* Final Rule, 71 Fed. Reg. at 3934-35 ("Another misunderstanding of the act encouraged by State law actions is that FDA labeling requirements represent a minimum safety standard. . . . In fact, FDA interprets the act to establish both a 'floor' and a 'ceiling' . . . ."); Henderson & Twerski, 65 N.Y.U. L. Rev. at 320; *see also* Appellant's Br. at 24-25. In light of the substantial benefits to be gained by standardization and rationalization of prescription drug warnings, and the significant harms caused by piecemeal evaluation by lay jurors of the adequacy of warnings, a court should be extremely reluctant to conclude that failure-to-warn claims are a useful supplement to expert federal agency regulation. And where, as here, the additional warning sought by the plaintiff is in direct conflict with the warning that the FDA directed the manufacturer to include, the plaintiff's failure-to-warn claims should be preempted.

D. Even If The FDA's Determination That Its Drug Labeling Decisions Preempt Failure-To-Warn Claims Reflects A Change In The Agency's Position, That Interpretation Is Entitled To *Chevron* Deference.

The district court and defendants have amply demonstrated that the FDA has consistently and repeatedly declared that its drug labeling decisions preempt state efforts to require additional or different warnings for Paxil and its generic competitors. *See Colacicco*, 432 F. Supp. 2d at 526-29, 531-32; Joint Brief For Appellees at 69-71. But even if the FDA's statements in the Preemption Preamble and its *amicus* brief below were viewed as the result of a change in the agency's position regarding the preemptive force of its labeling determinations, that change is more than reasonable in the circumstances currently facing both drug manufacturers and health care professionals, and therefore is entitled to the same deference due to any reasonable agency interpretation of its own regulations under *Chevron*.

In *Horn*, this Court had no difficulty in affording deference to the FDA's revised determination that its approval of a medical device pursuant to the MDA pre-market approval process preempted state common-law tort claims alleging defective design and manufacture. *See Horn*, 376 F.3d at 171, 179. Similarly, the Supreme Court has explained that the fact "that the agency has from time to time changed its interpretation . . . does not . . . lead us to conclude that no deference should be accorded the agency's interpretation of the statute," because "[a]n initial

agency interpretation is not instantly carved in stone." *Chevron*, 467 U.S. at 863-64. Administrative agencies "must be given ample latitude to 'adapt their rules and policies to the demands of changing circumstances.'" *Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 42 (1983). For that reason, the Supreme Court "has rejected the argument that an agency's interpretation is not entitled to deference because it represents a sharp break with prior interpretations of the statute in question." *Rust v. Sullivan*, 500 U.S. 173, 186 (1991) (citation and quotation marks omitted). Unless a past position has been "ratified" through congressional legislation, the FDA retains the prerogative to change its mind. *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 157-59 (2000). There can be no serious dispute that the FDA has provided, in both the Preemption Preamble and its *amicus* brief filed below, a well-reasoned and "authoritative"[4] explanation of its determination that the agency's labeling decisions for prescription drugs preempt state-law failure-to-warn claims regarding those same products.

Specifically, the agency noted that, "[i]n recent years, there has been an increase in the length, detail, and complexity of prescription drug labeling, making it harder for health care practitioners to find specific information and to discern the most critical information." 71 Fed. Reg. at 3922. Accordingly, it has become even

[4] *See Sprietsma v. Mercury Marine*, 537 U.S. 51, 66-67 (2002) (federal agencies should "convey an 'authoritative' message of a federal policy" when intending a refusal to require a product change to have preemptive effect).

more important that prescription drug labels maintain the delicate balance discussed in the preceding sections between warning of scientifically substantiated risks and encouraging the safe and effective use of those medications. At the same time, the FDA found this balance increasingly endangered by the proliferation of "product liability lawsuits [that] have directly threatened the agency's ability to regulate manufacturer dissemination of risk information for prescription drugs in accordance with the act." *Id.* at 3934 & nn.4-7 (citing *Ehlis v. Shire Richwood, Inc.*, 233 F. Supp. 2d 1189, 1198 (D.N.D. 2002), *aff'd*, 367 F.3d 1013 (8th Cir. 2004); *Bernhardt v. Pfizer, Inc.*, Nos. 00-Civ.-4042 (LMM), 00-Civ.-4379 (LMM), 2000 U.S. Dist. LEXIS 16963 (S.D.N.Y. Nov. 16, 2000); *In re Paxil Litig.*, No. CV 01-07937 MRP, 2002 U.S. Dist. LEXIS 16221 (C.D. Cal. August 16, 2002), *transferred*, 296 F. Supp. 2d 1374 (J.P.M.L. 2003); and *Dowhal v. SmithKline Beecham Consumer Healthcare*, No. A094460, 2002 Cal. App. LEXIS 4384 (Cal. Ct. App. 2002), *rev'd*, 2004 Cal. LEXIS 3040 (Cal. April 15, 2004)); *see also id.* at 3934-35 (citing, *inter alia*, *Eve v. Sandoz Pharm. Corp.*, No. IP 98-1429-C-Y/S, 2002 U.S. Dist. LEXIS 23965 (S.D. Ind. Jan. 28, 2002); *Ohler v. Purdue Pharma, L.P.*, No. 01-3061 Section "N" (2), 2002 U.S. Dist. LEXIS 2368 (E.D. La. Jan. 22, 2002); *Caraker v. Sandoz Pharm. Corp.*, 172 F. Supp. 2d 1018 (S.D. Ill. 2001); *Motus v. Pfizer Inc.*, 127 F. Supp. 2d 1085 (C.D. Cal. 2000)).

In fact, this Court need look no further than the briefs filed by the plaintiff and his *amici* in this case to appreciate how a state tort suit can be little more than an attack on the FDA's decisionmaking. Prior to the suicide of plaintiff's wife in October 2003, the FDA had conducted a number of reevaluations of the suicide-related warnings in the labeling of Paxil and other SSRIs. In each instance the FDA had determined that adequate scientific evidence was lacking of any association between use of these drugs by adults and a risk of suicide that would justify the type of warning demanded here. *See* FDA Amicus Br. at 7-10. Thus, although plaintiff seeks to impose liability only on the defendants for failing to warn of this purported risk, his claims are unmistakably an attack on the FDA's expert decision not to mandate the warnings, because, as the district court found below, that decision belonged exclusively to the agency. *See Colacicco*, 432 F. Supp. 2d at 522-23, 528.

The Supreme Court has made clear, albeit in different contexts, that state-law causes of action that require a court to second-guess the decision of a federal entity having exclusive jurisdiction to make that decision are preempted by federal law. *See Buckman*, 531 U.S. at 354 (Stevens, J., concurring) (explaining that a state common-law claim alleging that the defendant had obtained FDA approval of a medical device through fraud was preempted because it required "speculation as to the FDA's behavior in a counterfactual situation"); *Kalo Brick*, 450 U.S. at 324

(holding that state tort claims were preempted because they were "little more than an attempt by a disappointed [plaintiff] to gain from the [state] courts the relief it was denied by the [federal agency]" that had plenary authority over the matter). Because that is precisely what the plaintiff seeks to do under the guise of state tort law, the FDA's determination that those tort claims are preempted is fully justified and entitled to *Chevron* deference.

CONCLUSION

The judgment of the district court should be affirmed.

Respectfully submitted,

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November 29, 2006

CERTIFICATE OF ADMISSION TO BAR

I, Kenneth S. Geller, counsel for *Amicus Curiae* Product Liability Advisory Council, Inc., do hereby certify that I am a member in good standing of the bar of the United States Court of Appeals for the Third Circuit.

Pursuant to 28 U.S.C. § 1746, I certify under penalty of perjury that the foregoing is true and correct.

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CERTIFICATE OF SERVICE

I hereby certify that on this 29th day of November, 2006, the foregoing Brief Of Product Liability Advisory Council, Inc. As *Amicus Curiae* In Support Of Defendants-Appellees And In Support Of Affirmance Of The Judgment was filed and served on the following in the numbers and manner indicated:

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