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Richard C. Ausness

University of Kentucky College of Law, rausness@uky.edu

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The Impact of *Wyeth v. Levine* on FDA Regulation of Prescription Drugs

RICHARD C. AUSNESS*

I. INTRODUCTION

On March 4, 2009, the United States Supreme Court decided *Wyeth v. Levine*.¹ In that case, the Court concluded that the plaintiff's failure to warn claim against the makers of the drug Phenergan was not impliedly preempted by the Food, Drug and Cosmetic Act (FDCA).² In doing so, the Court rejected the argument of the U.S. Food and Drug Administration (FDA) that tort claims of this nature stand as an obstacle to federal regulatory objectives.³ This article evaluates the Court's opinion in *Wyeth* and examines that decision's impact on subsequent litigation in the area of prescription drug labeling. In particular, the article considers two issues: 1) what effect will the *Wyeth* decision have on cases where FDA has concluded that there is insufficient scientific evidence to justify strengthening a warning and 2) are failure to warn claims against manufacturers of generic drugs preempted on actual conflict grounds because FDA does not permit them to change unilaterally change product labeling? A survey of FDA preemption cases decided in the past year indicates that the *Wyeth* decision has had a profound effect on lower federal courts and has led most of them to conclude that failure to warn claims against drug manufacturers are normally not preempted.

Part II discusses the preemption doctrine and its application to state law tort claims against product manufacturers. Part III examines the history of implied preemption of tort claims against manufacturers of FDA-approved prescription drugs prior to *Wyeth*. Part IV discusses the *Wyeth* decisions in the Vermont Supreme Court and the United States Supreme Court. Part V evaluates some of the prescription drug preemption cases that have been decided in the lower federal courts since *Wyeth* and concludes that these courts are now reluctant to preempt failure to warn claims unless a manufacturer affirmatively seeks permission from FDA to change a drug's labeling.

II. FEDERAL PREEMPTION OF STATE TORT LAW

A. *The Doctrine of Federal Preemption*

Although states are treated as sovereign entities within the American federal system,⁴ Congress can preempt state regulation in certain areas if it chooses to do so.⁵ According to the Supreme Court, the power to preempt state law derives from

* Mr. Ausness is Warrant, Tarrant & Combs Professor of Law at the University of Kentucky College of Law.

¹ 129 S. Ct. 1187 (2009).

² *Id.* at 1204.

³ *Wyeth*, 129 S. Ct. at 1204. FDA's position at the time the *Wyeth* case came before the Court constituted a reversal of earlier statements refusing to assert that the FDCA preempted tort claims against manufacturers of FDA-approved drugs on actual conflict grounds. *Id.* at 1201.

⁴ See *Gregory v. Ashcroft*, 501 U.S. 452, 457 (1991) (declaring that the Constitution "establishes a system of dual sovereignty between the States and the Federal Government").

⁵ See Viet D. Dinh, *Reassessing the Law of Preemption*, 88 Geo. L.J. 2085, 2085 (2000).

the Supremacy Clause of the United States Constitution.⁶ The principle of federal preemption enables federal law to prevail over conflicting state statutes,⁷ local ordinances⁸ and even state common-law doctrines.⁹ At the same time, the Supreme Court sometimes applies a so-called “presumption against preemption”¹⁰ in such traditional areas of state concern as public health and safety unless Congress makes its intent to preempt “clear and manifest.”¹¹

Courts traditionally classify preemption as either express or implied, and further divide the latter category into field preemption and conflict preemption.¹² Express preemption occurs when a federal statute specifically excludes state regulation in a particular area.¹³ Federal agencies, when acting within the scope of their delegated authority, may also expressly preempt state law by regulation.¹⁴ In addition, Congress may impliedly preempt state law. One form of implied preemption is field preemption, which occurs when federal regulations are so pervasive that they

⁶ See *Maryland v. Louisiana*, 451 U.S. 725, 746 (1981); *Hines v. Davidowitz*, 312 U.S. 52, 63 (1941); see also Mary J. Davis, *On Restating Products Liability Preemption*, 74 *Brooklyn L. Rev.* 759, 761 (2009).

⁷ See, e.g., *Gade v. Nat'l Solid Waster Mgt. Ass'n*, 505 U.S. 88, 99 (1992) (declaring that the Occupational Health and Safety Act (OHSA) preempts state occupational and safety standards unless they receive federal approval); *Schneidewind v. ANR Pipeline Co.*, 485 U.S. 293, 300 (1988) (ruling that the federal Natural Gas Act preempts state statute purporting to regulate issuance of long-term securities by natural gas pipeline companies); *Michigan Canners & Freezers Ass'n v. Agricultural Mktg. & Bargaining Bd.*, 467 U.S. 461, 478 (1984) (holding state agricultural marketing statute preempted by federal Agricultural Fair Practices Act).

⁸ See *City of Burbank v. Lockheed Air Terminal, Inc.*, 411 U.S. 624, 640 (1973) (holding municipal airport curfew preempted by Federal Aviation Administration (FAA) regulations).

⁹ See, e.g., *International Paper Co. v. Ouellette*, 479 U.S. 481, 491 (1987) (holding that Clean Water Act bars private nuisance actions against out-of-state polluters); *Arkansas La. Gas Co. v. Hall*, 453 U.S. 571, 582-584 (1981) (holding Natural Gas Act preempts calculation of damages under state contract doctrines); *Chicago & N.W. Transp. Co. v. Kalo Brick & Tile Co.*, 450 U.S. 311, 331 (1981) (ruling Interstate Commerce Act preempts state tort claim based on abandonment of service); *Old Dominion Branch No. 496, Nat'l Ass'n of Letter Carriers v. Austin*, 418 U.S. 264, 270-273 (1974) (noting National Labor Relations Act preempts certain state-law libel claims).

¹⁰ See, e.g., *Wyeth v. Levine*, 129 S. Ct. 1187, 1194-1195 (2009); *Altria Group, Inc. v. Good*, 129 S. Ct. 538, 543 (2008); *Bates v. Dow Agrosciences LLC*, 544 U.S. 431, 449 (2005); *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 485 (1996); *Cipollone v. Liggett Group, Inc.*, 505 U.S. 504, 518 (1992).

¹¹ See *Rice v. Santa Fe Elevator Corp.*, 331 U.S. 218, 230 (1947).

¹² See, e.g., *English v. General Electric Co.*, 496 U.S. 72, 78-79 (1990); *Hillsborough County v. Automated Med. Labs., Inc.*, 471 U.S. 707, 712-713 (1985).

¹³ See, e.g., *Morales v. Trans World Airlines, Inc.*, 504 U.S. 374, 383 (1992) (holding that airline fare advertising guidelines were expressly preempted by Airline Deregulation Act); *Shaw v. Delta Air Lines, Inc.*, 463 U.S. 85, 106-108 (1983) (finding that New York Human Rights Law was preempted by the Employee Retirement Income Security Act (ERISA) insofar as it prohibited practices with respect to benefit plans that were lawful under the federal act); *Railway Employees' Dep't v. Hanson*, 351 U.S. 225, 232 (1956) (concluding that union shop agreements authorized by Railway Labor Act were valid even if they were prohibited by state law).

¹⁴ See *Capital Cities Cable, Inc. v. Crisp*, 467 U.S. 691, 700 (1984) (ruling that Federal Communications Commission (FCC) regulations preempt state prohibition against the broadcasting of advertisements for alcoholic beverages by cable television companies); *Fidelity Federal Savings & Loan Ass'n v. de la Cuesta*, 458 U.S. 141, 170 (1982) (holding that Federal Home loan Bank Board regulation permitting financial institutions to include “due on sale” clauses in home mortgages preempts state prohibition against such provisions); *Free v. Bland*, 369 U.S. 663, 667-668 (1962) (concluding that state community property law is preempted to the extent that it conflicts with Treasury Regulations relating to survivorship rights in U.S. savings bonds); *Public Utilities Comm'n v. United States*, 355 U.S. 534, 544-545 (1958) (declaring that state law authorizing Public Utilities Commission to determine rates for the transportation of federal property is preempted because it limits the ability of federal procurement officers to negotiate such rates); *Leslie Miller, Inc. v. Arkansas*, 352 U.S. 187, 189-190 (1956) (preempting law requiring building contractors to obtain license from state Contractors Licensing Board because it was inconsistent with federal procurement regulations).

leave no room for state regulations.¹⁵ A more common form of implied preemption, known as conflict preemption, occurs either when it is impossible to comply with both state and federal law or when state law stands as an obstacle to the achievement of federal regulatory objectives.¹⁶

B. *The Preemption of Common-Law Tort Claims.*

Product manufacturers have invoked federal preemption as a defense to state tort liability with increasing frequency in recent years.¹⁷ One of the first products liability preemption cases was *Cipollone v. Liggett Group, Inc.*¹⁸ decided in 1992. The *Cipollone* Court declared that it must construe the statute's preemptive language "in light of the presumption against the pre-emption of state police power regulations."¹⁹ However, the Court also determined that common-law tort doctrines could have the same coercive effect as statutes, ordinances and administrative regulations.²⁰ The Court then concluded that the 1969 Federal Cigarette Labeling and Advertising Act expressly preempted the plaintiff's failure to warn claims against cigarette manufacturers.²¹

A few years later, in *Geier v. American Honda*,²² the Court held that Federal Motor Vehicle Safety Standard 208 (FMVSS 208), promulgated by the Department of Transportation (DOT) under the authority of the National Transportation Motor Vehicle Safety Act (NTMVSA),²³ impliedly preempted design defect claims based on a failure to equip motor vehicles with airbags.²⁴ A provision of NTMVSA expressly preempted "any safety standard" established by a state that was "applicable to the same aspect of performance of a motor vehicle or motor vehicle equipment" unless it was identical to the federal standard.²⁵ At the same time, NTMVSA also contained a "saving clause" which declared that compliance with federal safety standards would not "exempt a person from liability [under] common law."²⁶

Acting under the authority of NTMVSA, DOT adopted a regulation, FMVSS 208, which provided for the gradual phase-in of airbags by requiring automobile manufacturers to equip some, but not all, of their vehicles with airbags each year.²⁷ Honda contended that FMVSS 208 preempted the plaintiff's "no airbag" claim. The

¹⁵ See *Schneidewind v. ANR Pipeline Co.*, 485 U.S. 293, 300 (1988) (holding that state laws regulating the issuance of securities by natural gas pipeline companies was preempted by Natural Gas Act which also regulated the issuance of such securities).

¹⁶ See, e.g., *Geier v. American Honda Motor Co., Inc.*, 529 U.S. 861, 899 (2000) (concluding that "no airbag" design defect claims were preempted by Department of Transportation vehicle safety standards); *United States v. Locke*, 529 U.S. 89, 109 (2000) (preempting state regulations relating to the design, construction and operation of oil tankers); *Michigan Canners & Freezers Ass'n v. Agricultural Marketing & Bargaining Board*, 467 U.S. 461, 478 (1984) (holding that federal Agricultural Fair Prices Act preempted Michigan Agricultural Marketing and Bargaining Act to the extent that state requirements conflicted with federal regulatory scheme relating to the marketing of agricultural products).

¹⁷ See Mary J. Davis, *On Restating Products Liability Preemption*, 74 *Brooklyn L. Rev.* 759, 760-761 (2009).

¹⁸ 505 U.S. 504 (1992).

¹⁹ *Id.* at 518.

²⁰ See Susan Raeker-Jordan, *The Pre-emption Presumption That Never Was: Pre-emption Doctrine Swallows the Rule*, 40 *Ariz. L. Rev.* 1379, 1412 (1998).

²¹ *Cipollone*, 505 U.S. at 524.

²² 529 U.S. 861 (2000).

²³ NTMVSA, 80 Stat. 718 (1966) codified in various sections of 49 U.S.C. (2004).

²⁴ *Geier*, 529 U.S. at 865.

²⁵ 15 U.S.C. § 1392(d) (1988) (current version is located at 49 U.S.C. § 30,103(b) (2004)).

²⁶ *Id.* § 1397(k) (current version is located at 49 U.S.C. § 30,103(e) (2004)).

²⁷ *Geier*, 529 U.S. at 864-865.

Court first determined that the savings clause required it to interpret the preemption clause narrowly and, therefore, concluded that the federal safety standard would not expressly preempt the plaintiff's design defect claim.²⁸ However, the Court then ruled that the "no airbag" claim was impliedly preempted because it conflicted with DOT's policy of providing automobile manufacturer's with "a range of choices among different passive restraint devices."²⁹

The first case to consider the possible preemptive effect of FDA regulation on state tort claims was *Medtronic, Inc. v. Lohr*.³⁰ The issue before the Court in that case was whether § 521 (a) of the Medical Device Amendments,³¹ now codified as 21 U.S.C. § 360k(a), expressly preempted design defect claims against a Class III medical device manufacturer whose product had undergone what is known as a § 510(k) notification process instead of FDA's more rigorous premarket approval (PMA) review.³² In a plurality opinion, Justice Stevens concluded that § 360k(a) did not necessarily preempt common-law tort claims.³³ The plurality opinion noted that an FDA regulation, 21 C.F.R. § 808.1(d), provided that § 360k(a) would preempt state and local requirements only when FDA had established *specific counterpart regulations* or other regulations that are *specific to a particular device*.³⁴ In addition, only state and local requirements that were *applicable to the device* would be preempted and only if they were *different from or in addition to* FDA's specific requirements.³⁵

The plurality opinion also found that the § 510(k) process was more concerned with equivalence than safety. Therefore, since FDA's requirements were not related to the safety of the product's design, there was no overlap between them and the standards applicable to manufacturers under state tort law.³⁶ Thus, the Court concluded that none of the plaintiffs' claims based on defective manufacturing, design or labeling were preempted.³⁷ Justice Breyer concurred in the judgment, agreeing that § 360k(a) would not preempt this particular plaintiff's design defect claims.³⁸ However, he indicated that tort claims might be preempted in other cases.³⁹

In *Buckman Co. v. Plaintiffs' Legal Committee*⁴⁰ the Court considered whether "fraud on the FDA" claims were preempted. The plaintiffs, who were injured by surgical bone screws, alleged that the manufacturer and its consultant, the Buckman Company, had made fraudulent representations to FDA in order to obtain agency approval to market its product as a Class III medical device.⁴¹ According to

²⁸ *Id.* at 868.

²⁹ *Id.* at 875.

³⁰ 518 U.S. 470 (1996).

³¹ 90 Stat. 539 (1976), now codified as amended in 21 U.S.C. §§ 301-360 (2000).

³² In the case of original medical devices, § 360e declares that the manufacturer must provide reasonable assurance to FDA that the device is both "safe and effective." 21 U.S.C. § 360e(d)(2) (2000). For example, under the PMA process, the applicant must provide a full report of any clinical investigations that concern the safety or effectiveness of the proposed device. *See* 21 U.S.C. § 360e(a) (2000). However, a different standard applies to medical devices that are "substantially equivalent" to devices that were marketed prior to the enactment of the MDA. 21 U.S.C. § 360c(f)(1)(A)(ii) (2000). In such cases, the manufacturer of the proposed device can bypass the PMA requirements and obtain an FDA finding of substantial equivalence by submitting a premarket notification to the agency. *See* 21 U.S.C. §§ 360(k), 360c(f)(4) (2000). This is known as §510(k) notification after the number of the section in the original Act. *See Lohr*, 518 U.S. at 478.

³³ *Lohr*, 518 U.S. at 503.

³⁴ 21 C.F.R. § 808.1(d) (1995) (emphasis added).

³⁵ *Id.* (emphasis added).

³⁶ *Lohr*, 518 U.S. at 492-494.

³⁷ *Id.* at 513-14.

³⁸ *Id.* at 508 (Breyer, J., concurring).

³⁹ *Id.* at 503-05.

⁴⁰ 531 U.S. 341 (2001).

⁴¹ *Id.* at 343.

the plaintiffs, the manufacturer obtained FDA approval by claiming that the bone screws would be used in the long bones of the arms and legs when, in reality, the company intended to market them principally for use in spinal fusion surgery.⁴²

The *Buckman* Court held that the plaintiffs' fraud-on-the-agency claims were impliedly preempted by the Medical Device Amendments to the FDCA.⁴³ In contrast to its approach in *Geier*, the Court acknowledged the existence of a presumption against preemption.⁴⁴ However, it concluded that issue involved in *Buckman* was inherently federal in character and that the states had no interest in protecting FDA against fraudulent representations by license applicants.⁴⁵ Consequently, the Court concluded that the presumption against preemption was not applicable in this case.⁴⁶

Although the plaintiffs argued that the Court should not consider implied preemption when the statute in question contained an express preemption provision, the Court affirmed the position adopted in *Geier* that neither an express preemption provision nor a savings clause would prevent the "ordinary working of conflict preemption principles."⁴⁷ The Court then determined that a conflict did exist between common-law tort claims like the plaintiffs' and FDA's need to balance a number of regulatory objectives.⁴⁸ While one of these objectives was to protect the integrity of the licensing process, another was to ensure that the licensing process did not slow down the introduction of new medical products into the market or interfere with the judgment of healthcare professionals.⁴⁹ In the Court's view, allowing private persons to bring fraud-on-the-agency claims against manufacturers of medical devices would greatly increase the cost of licensing for both applicants and FDA.⁵⁰

In *Sprietsma v. Mercury Marine*,⁵¹ the plaintiff argued that a boat engine manufactured by the defendant was defective because it did not have a shroud or guard around its propeller. The Federal Boat Safety Act⁵² authorized the Secretary of Transportation to establish safety standards for recreational boats and equipment.⁵³ The Act expressly prohibited the states from establishing safety standards that were not identical to the federal standards,⁵⁴ but also contained a saving clause.⁵⁵ In its analysis of the preemption issue, the Court pointed out that a Coast Guard advisory committee had studied the question of propeller guards, but had declined to recommend that they be required.⁵⁶ Because of the existence of the savings clause, the Court interpreted the Act's preemption provision narrowly and concluded that it did not expressly preempt state common law.⁵⁷ The Court also rejected the argument that the Act impliedly preempted the plaintiff's tort claims.⁵⁸

⁴² *Id.* at 346.

⁴³ *Id.*

⁴⁴ *Id.* at 347-348.

⁴⁵ *Id.*

⁴⁶ *Id.* at 348.

⁴⁷ *Id.* at 352 (quoting *Geier v. Honda Motor Co.*, 529 U.S. 861, 869 (2000)).

⁴⁸ *Id.* at 348.

⁴⁹ *Id.* at 349.

⁵⁰ *Id.* at 350-351.

⁵¹ 537 U.S. 51 (2002).

⁵² 46 U.S.C. §§ 4301-4311 (2007).

⁵³ Federal Boat Safety Act of 1971, Pub. L. No. 92-75, § 2, 85 Stat. 213-214 (codified as amended in scattered sections of 46 U.S.C. §§ 4301-4311 (2007)).

⁵⁴ 46 U.S.C. § 4306 (2007).

⁵⁵ *Id.*, § 4311(g). A "saving" or "savings" clause is an exception to the general operation of a statute. See *Stafford v. Wessel*, 52 N.E.2d 605, 605-606 (Ct. App. Ill. 1943).

⁵⁶ *Sprietsma*, 537 U.S. at 60-61.

⁵⁷ *Id.* at 64.

⁵⁸ *Id.* at 69-70.

In *Bates v. Dow Agrosciences LLC*,⁵⁹ the Court again refused to preempt a tort claim. *Bates* involved a suit by a group of Texas peanut farmers against the manufacturer of a weed killer that was registered by the EPA under the provisions of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA).⁶⁰ The product's original label claimed that it could be used "in all areas where peanuts are grown."⁶¹ In fact, the product was unsuitable for use in soil which had a pH of 7.2 or more and it damaged the plaintiffs' peanut crops.⁶² The plaintiffs sued the manufacturer alleging negligence, strict products liability, fraud, breach of express warranty and violation of the Texas Deceptive Trade Practices-Consumer Protection Act.⁶³ The manufacturer attempted to defend against these claims by contending that they were expressly and impliedly preempted by FIFRA.⁶⁴

FIFRA contained an express preemption clause, § 136v(b), which prohibited states from imposing "any requirements for labeling or packaging in addition to or different from" those required by FIFRA.⁶⁵ However, the Court held that the term "requirements" as used in § 136v(b) did not preempt the plaintiffs' common-law tort claims.⁶⁶ The Court rejected the lower court's conclusion that tort liability was a "requirement" because it could induce the manufacturer to alter its label,⁶⁷ finding instead, that § 136v(b) permitted the state to impose "parallel requirements" and different or additional remedies than FIFRA.⁶⁸ The Court also invoked the presumption against preemption to justify its narrow reading of § 136v(b)⁶⁹ and rejected the defendant's contention that FIFRA intended to impose a high degree of centralization and uniformity on pesticide labeling.⁷⁰

Finally, in *Riegel v. Medtronic, Inc.*, the Court concluded that the plaintiff's design defect claim against the manufacturer of the Evergreen Balloon Catheter, a Class III medical device used for opening clogged arteries during angioplasty operations, was expressly preempted.⁷¹ The defendant's catheter had been approved for marketing by FDA in 1994 pursuant to its PMA process.⁷² The plaintiff alleged that the manufacturer was negligent with respect to the design, testing, inspection, manufacture, distribution, labeling, marketing and sale of its Evergreen Balloon Catheters.⁷³ The complaint also sought damages based on strict liability, breach of express warranty and breach of implied warranty.⁷⁴ In response, Medtronic alleged that the plaintiff's claims were preempted by § 360k(a) of the FDCA.⁷⁵ The lower court later dismissed all of the plaintiff's claims.⁷⁶ On appeal, the Second Circuit Court of Appeals concluded that the Evergreen Balloon Catheter was subject to the federal device-specific requirement of complying with the particular standards set forth in Medtronic's approved PMA application.⁷⁷

⁵⁹ 544 U.S. 431 (2005).

⁶⁰ *Id.* at 434.

⁶¹ *Id.* at 435.

⁶² *Id.*

⁶³ *Id.*

⁶⁴ *Id.*

⁶⁵ 7 U.S.C. § 136v(b) (2006).

⁶⁶ *Bates*, 544 U.S. at 452.

⁶⁷ *Bates v. Dow Agrosciences LLC*, 332 F.3d 323, 332 (5th Cir. 2003).

⁶⁸ *Bates*, 544 U.S. at 447-448.

⁶⁹ *Id.* at 449.

⁷⁰ *Id.* at 450-451.

⁷¹ *See Riegel v. Medtronic, Inc.*, 451 F.3d 104, 106-107 (2d Cir. 2006).

⁷² *Id.*

⁷³ *Id.*

⁷⁴ *Id.*

⁷⁵ *Id.*

⁷⁶ *Id.* at 107-108.

⁷⁷ *Id.*

On appeal, the Court considered whether the federal government had “established requirements applicable to Medtronic’s catheter” and, if so, whether the plaintiffs’ tort claims were based upon state law requirements with respect to that device that were “‘different from, or in addition to’ the federal ones, and that related to safety and effectiveness.”⁷⁸ First, the Court determined that the requirements contained in FDA’s premarket approval of the Medtronic catheter were federal requirements specific to that device.⁷⁹ Next, the Court considered whether any of the plaintiffs’ claims relied upon “any requirement” that was “different from, or in addition to” federal requirements applicable to the Medtronic catheter.⁸⁰ The Court first determined that negligence and strict liability doctrines could impose state “requirements” that were subject to preemption by federal requirements that were specific to a particular medical device.⁸¹ The Court then responded to the plaintiffs’ contention that state law negligence or strict liability doctrines should not be preempted because they were not specific to the defendant’s catheter or even to medical devices in general.⁸² Citing its opinion in *Lohr*, the Court pointed out that nothing in § 360k(a) suggested that it would preempt only state requirements that applied specifically to medical devices.⁸³ Furthermore, the Court rejected the plaintiffs’ contention that § 360k(a) did not apply to “state or local requirements of general applicability.”⁸⁴ The Court concluded by reaffirming that § 360k(a) did not preempt all tort claims against medical device manufacturers, but only those that were “different from, or in addition to” requirements imposed by federal law.⁸⁵ Thus, § 360k(a) would not preempt parallel claims, including claims based on violation of state law requirements that paralleled federal requirements.⁸⁶

III. PREEMPTION LITIGATION PRIOR TO *WYETH*

Prior to the Supreme Court’s decision in *Wyeth*, there was a split of authority among the lower courts as to whether the FDCA impliedly preempted failure to warn claims against pharmaceutical companies.⁸⁷ *In re Zyprexa Products Liability Litigation*⁸⁸ is illustrative of the majority position finding no preemption, while

⁷⁸ *Id.* at 1006.

⁷⁹ *Id.* at 1006-1007.

⁸⁰ *Id.*

⁸¹ *Id.* at 1007-1008.

⁸² *Id.* at 1009-1010.

⁸³ *Id.* at 1010.

⁸⁴ *Id.*

⁸⁵ *Id.*

⁸⁶ *Id.*

⁸⁷ The following cases failed to find preemption: *In re Zyprexa Prods. Liab. Litig.*, 489 F. Supp. 2d 230 (E.D.N.Y. 2007) (*Zyprexa*); *Perry v. Novartis Pharm. Corp.*, 456 F. Supp. 2d 678 (E.D. Pa. 2006) (*Elidel*); *Adesina v. Aladan Corp.*, 438 F. Supp.2d 329 (S.D.N.Y. 2006); *Jackson v. Pfizer, Inc.*, 432 F. Supp. 2d 964 (D. Neb. 2006) (*Zolofit*); *Laisure-Radke v. Par Pharm., Inc.*, 426 F. Supp. 2d 1168 (W.D. Wash. 2006) (*Prozac*); *Peters v. Astrazenica, L.P.S.E.2d 417 F. Supp. 2d 1051 (W.D. Wis. 2006) (Prilosec); Witczak v. Pfizer, Inc.*, 377 F. Supp. 2d 726 (D. Minn. 2005) (*Zolofit*); *Caraker v. Sandoz Pharm. Corp.*, 172 F. Supp. 2d 1018 (S.D. Ill. 2001) (*Parlodel*); *Motus v. Pfizer, Inc.*, 127 F. Supp. 2d 1085 (C.D. Cal. 2000), rev’d on other grounds, 358 F.3d 659 (9th Cir. 2004) (*Zolofit*); *Bryant v. Hoffmann-LaRoche, Inc.*, 585 S.E.2d 723 (Ga. Ct. App. 2003) (heart medication); *Bell v. Lollar*, 791 N.E.2d 849 (Ind. Ct. App. 2003) (pain medication); *Levine v. Wyeth*, 944 A.2d 179 (Vt. 2006) (*Phenergan*); *Kurer v. Park, Davis & Co.*, 679 N.W.2d 867 (Wis. Ct. App. 2004) (oral contraceptive). The following cases did find preemption: *Horne v. Novartis Pharmaceuticals Corp.*, 541 F. Supp. 2d 768 (W.D.N.C. 2008); *Sykes v. Glaxo-SmithKline*, 484 F. Supp. 2d 289 (E.D. Pa. 2007) (*HypRho-D immune globulin*); *Colacicco v. Apotex, Inc.*, 432 F. Supp. 2d 514 (E.D. Pa. 2006), aff’d, 521 F.3d 253 (3d Cir. 2008), vacated 129 U.S. 1578 (2009); *Ehllis v. Shire Richwood, Inc.*, 233 F. Supp. 2d 1189 (D.N.J. 2002) (*Adderall*).

⁸⁸ 489 F. Supp. 2d 230 (E.D.N.Y. 2007).

*Horne v. Novartis Pharmaceuticals Corporation*⁸⁹ exemplifies the reasoning of those courts that concluded that such claims were preempted.

A. *In re Zyprexa Products Liability Litigation*

In 2004, the plaintiff, who was treated with the antipsychotic drug, Zyprexa, brought a products liability action against the drug's manufacturer, Eli Lilly in a New York federal district court.⁹⁰ Later, that year, thousands of similar cases were transferred to that court by the Judicial Panel on Multidistrict Litigation.⁹¹ Some 8000 of these claims were eventually settled in November, 2005 and a large number of newly transferred cases were settled in January, 2007.⁹² However, approximately 1000 of these cases were not disposed of and were scheduled for trial later that year.⁹³ Prior to trial, Eli Lilly moved for summary judgment in four of these cases, arguing that federal law preempted the plaintiffs' failure to warn claims against it.⁹⁴ In a lengthy opinion, Judge Jack Weinstein denied the defendant's motion.⁹⁵

Zyprexa was approved by the FDA in 1996 for treating schizophrenia and acute manic episodes associated with bipolar disorder.⁹⁶ In May, 2000, FDA investigated whether patients who took atypical antipsychotic drugs, such as Zyprexa, might be subject to an increased risk of diabetes and hyperglycemia.⁹⁷ As a result of this inquiry, in September, 2003, FDA directed the manufacturers of such drugs to warn about the possible connection between antipsychotic drugs and these conditions.⁹⁸ Shortly thereafter, Eli Lilly added the required warning to Zyprexa's product labeling.⁹⁹ Two of the plaintiffs were diagnosed as diabetic after being treated with Zyprexa, another plaintiff claimed that Zyprexa caused his existing diabetic condition to worsen, and a fourth plaintiff contended that Zyprexa was responsible for her hyperglycemia.¹⁰⁰ Each of these plaintiffs argued that the FDA-approved warnings on Zyprexa did not adequately inform their physicians about the risks of diabetes and hyperglycemia. The defendant, on the other hand, maintained that the plaintiffs should not be allowed to claim that warnings approved by FDA pursuant to its premarket approval process were inadequate.

The court's opinion focused on two issues: the presumption against preemption and FDA's claim of preemption in the Preamble of its final rule on product labeling. Finding that there was ambiguity about the preemptive effect of FDA labeling requirements in failure to warn cases, the court declared that "a federal court should take the law's default position, honoring the traditional state control of tort law."¹⁰¹ To overcome this presumption against preemption, the court declared that the party asserting preemption as a defense must show: 1) express preemption by Congress or, when statutorily authorized, by the regulatory agency; 2) that Congress intended to occupy the field; or 3) that state law would conflict with federal objec-

⁸⁹ 541 F. Supp. 2d 768 (W.D.N.C. 2008).

⁹⁰ *In re Zyprexa*, 489 F. Supp. 2d at 236.

⁹¹ *Id.* at 236-237.

⁹² *Id.* at 237-238.

⁹³ *Id.* at 238.

⁹⁴ *Id.* at 271.

⁹⁵ *Id.* at 291.

⁹⁶ *Id.* at 248.

⁹⁷ *Id.*

⁹⁸ *Id.*

⁹⁹ *Id.* at 249.

¹⁰⁰ *Id.* at 253-262.

¹⁰¹ *Id.* at 240.

tives to such a great extent that coexistence was not possible.¹⁰² The second issue before the court was whether it should defer to FDA's position, notwithstanding the presumption against preemption. FDA's position on preemption appeared in the Preamble to a final rule on prescription drug labeling that it promulgated in January, 2006.¹⁰³ In this Preamble, FDA warned that state tort actions threatened its role as the federal agency responsible for evaluating and regulating drugs.¹⁰⁴ Consequently, FDA declared that failure to warn claims should be preempted on conflict grounds when the warning in question was approved by the agency as part of its premarket approval process.¹⁰⁵

The court found that the greatest deference should be given when Congress had expressly delegated authority to the agency to make rules having the force of law and that the agency interpretation at issue was promulgated in the exercise of that authority.¹⁰⁶ According to the Supreme Court's decision in *Chevron*, in such cases a court should accept the agency's interpretation of its statute as long as the interpretation was reasonable.¹⁰⁷ In addition, according to the Court's holding in *Auer v. Robbins*,¹⁰⁸ a court should treat an agency's statement clarifying ambiguities in its own regulations as controlling unless it is "plainly erroneous or inconsistent with the regulation."¹⁰⁹ Finally, the Court's holding in *Skidmore*, provided that agency interpretations that did not qualify for deference under the *Chevron* or *Auer* standard would be accepted by courts only if they have the "power to persuade."¹¹⁰ After describing these various forms of deference, the court determined that the Preamble to the FDA's Final Rule was not entitled to deference under either *Chevron* or *Auer* and, therefore, would be binding only if it had the "power to persuade" as required under *Skidmore*.¹¹¹ After setting forth these principles of agency deference, the court concluded that the defendant's preemption by preamble claim was not persuasive.¹¹² First of all, the court pointed out that the Preamble was inconsistent with FDA's prior interpretations of the FDCA.¹¹³ The court also observed that most other courts had rejected the contention that FDA's labeling approval process preempted failure to warn claims.¹¹⁴ Finally, the court noted that the Preamble was nothing more than an advisory opinion, which purported to bind only the agency and which could be changed at any time without notice or opportunity for public comment.¹¹⁵ Therefore, the court found that FDA's guidelines were only entitled to "some deference."¹¹⁶

¹⁰² *Id.* at 272-273.

¹⁰³ See FDA, Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922 (Jan. 24, 2006), see also Cristina Rodriguez, The FDA Preamble: A Backdoor to Federalization of Prescription Warning Labels?, 41 JOHN MARSHALL L. REV. 161 (2007); Catherine M. Sharkey, Preemption by Preamble: Federal Agencies and the Federalization of Tort Law, 56 DEPAUL L. REV. 227 (2007); Katherine M. Glaser, Comment, A Step Toward Preemption: The Effect of the FDA's 2006 Preamble, 80 TEMPLE L. REV. 871 (2007)..

¹⁰⁴ *Id.* at 3935.

¹⁰⁵ *Id.* at 3935-3936.

¹⁰⁶ *In re Zeprexa*, 489 F. Supp. 2d at 272.

¹⁰⁷ See *Chevron USA, Inc. v. Nat'l Res. Def. Council, Inc.*, 467 U.S. 837 (1984). This is known as "Chevron Deference." See, e.g., Richard C. Ausness, "After You, My Dear Alphonse!": Should the Courts Defer to the FDA's New Interpretation of § 360k(a) of the Medical Device Amendments?, 80 TUL. L. REV. 727, 759 (2006).

¹⁰⁸ 519 U.S. 452 (1997).

¹⁰⁹ *Id.* at 461.

¹¹⁰ See *Skidmore v. Swift & Co.*, 323 U.S. 134, 140 (1944).

¹¹¹ *In re Zeprexa*, 489 F. Supp. 2d at 273.

¹¹² *Id.*

¹¹³ *Id.*

¹¹⁴ *Id.* at 274.

¹¹⁵ *Id.*

¹¹⁶ See *Reno v. Koray*, 515 U.S. 50, 61 (1995).

The court concluded by holding that the presumption against preemption had not been overcome. According to the court, there was no clear statement of congressional intent to preempt.¹¹⁷ Furthermore, the Preamble did not amount to a regulation expressly identifying a congressional intent to preempt.¹¹⁸ In addition, the court concluded that there was no actual conflict between the plaintiffs' failure to warn claims and federal law.¹¹⁹ The court noted that a jury verdict holding Eli Lilly liable for failing to warn of Zyprexa's risks would not actually compel it to change its labeling.¹²⁰ The court also suggested that FDA's Preamble may not even apply to the plaintiffs' claims in this case, but may only apply to warnings that had been expressly rejected by FDA.¹²¹ Finally, the court endorsed the argument that tort law can complement FDA's mandate to promote drug safety by providing an additional incentive to manufacturers to ensure that their products are safe before they are marketed to consumers.¹²²

B. *Horne v. Novartis Pharmaceuticals Corporation*

*Horne v. Novartis Pharmaceuticals Corp.*¹²³ is illustrative of the pre-*Wyeth* cases holding that failure to warn cases against prescription drug manufacturers could be impliedly preempted. The plaintiff in that case brought suit against the manufacturer of Lotensin HCT, an angiotensin-converting-enzyme (ACE) inhibitor, which was prescribed to treat hypertension.¹²⁴ The plaintiff took Lotensin while pregnant until her doctor switched her prescription to another form of hypertension medicine.¹²⁵ According to the plaintiff, Lotensin caused her son to be born with heart and kidney defects which resulted in death 19 days later.¹²⁶ She contended that Lotensin's labeling should have warned that fetal injuries might occur to women who took the product in the first trimester of their pregnancy.¹²⁷ The FDA-approved labeling warned of the danger of fetal injury from ACE inhibitors like Lotensin if taken in the second or third trimester, but asserted that no link between Lotensin and fetal injuries had been established when the drug was used during the first trimester of pregnancy.¹²⁸ The defendant brought suit against Novartis, the drug's manufacturer, alleging negligence, wantonness, failure to warn, breach of warranty and fraudulent misrepresentation and concealment.¹²⁹

In response, the defendant moved to dismiss, arguing that the plaintiff's claims "directly conflicted with the pregnancy category classifications and warnings approved and mandated by the FDA for products containing ACE inhibitors, such as Lotensin HCT."¹³⁰ The court agreed with this contention and ruled that the

¹¹⁷ *Id.*

¹¹⁸ *Id.*

¹¹⁹ *Id.* at 276.

¹²⁰ *Id.* at 276-277.

¹²¹ *Id.* at 277.

¹²² *Id.* at 277-778 (quoting Jonathan V. O'Steen & Van O'Steen, The FDA Defense: Vioxx and the Argument Against Federal Preemption of State Claims for Injuries Resulting from Defective Drugs, 48 *Ariz. L. Rev.* 67, 94 (2006)).

¹²³ 541 F. Supp. 2d 768 (W.D.N.C. 2008).

¹²⁴ *Id.* at 772.

¹²⁵ *Id.*

¹²⁶ *Id.*

¹²⁷ *Id.* at 772-773.

¹²⁸ *Id.* at 773-775.

¹²⁹ *Id.* at 775.

¹³⁰ *Id.*

plaintiff's failure to warn claims were preempted.¹³¹ One issue before the court was how much deference should be given to FDA's Preamble on Preemption.¹³² The court observed that a number of courts had ruled that it was appropriate to give considerable deference to the Preamble.¹³³ However, the plaintiff argued that the court should look to the intent of Congress, not FDA, to determine whether conflict preemption was applicable.¹³⁴ The plaintiff pointed out that Congress had expressed an intent that state law not be preempted by the FDCA. For example, when Congress amended the Act in 1962, it declared that the FDCA should not be construed to preempt state law "unless there is a direct and positive conflict" between the two.¹³⁵ Furthermore, when Congress amended the FDCA again in 1997, it did not place any statement in the law regarding its preemptive effect.¹³⁶ According to the plaintiff, in light of its silence on the issue of preemption, the court should presume that Congress did not intend to preempt state law tort claims against drug manufacturers.¹³⁷

The court conceded that the issue of preemption normally would require it to examine the intent of Congress and in the absence of express preemption language, a court would ordinarily presume that Congress did not intend to supplant state law.¹³⁸ However, the court observed that state law might be preempted on actual conflict grounds even when Congress did not specifically intend to preempt it.¹³⁹ Therefore, in conflict preemption cases, a court should look beyond the stated intent of Congress and FDA to determine whether the plaintiff's failure to warn claims would actually conflict with the FDCA or FDA's drug labeling regulations.¹⁴⁰

The court in *Horne* observed that *Sykes v. Glaxo-SmithKline* also involved drug labeling that had been expressly considered and approved by FDA and the court in that case concluded that the warning that the plaintiff proposed would directly conflict with the FDA-approved warnings.¹⁴¹ According to the court in *Horne*, the situation was very similar to the situation in *Sykes*.¹⁴² In *Sykes*, the plaintiff argued that the defendant failed to provide an adequate warning about mercury levels in thimerosal, a preservative used in an immune globulin that was administered to the plaintiff while she was pregnant.¹⁴³ The FDA-approved package insert disclosed the presence of mercury in the product and declared that it was not known whether it could cause fetal harm when administered to pregnant women.¹⁴⁴ The court concluded that any affirmative statement made by the manufacturer that thimerosal was toxic to fetuses would directly contradict FDA's finding that such toxicity had not been established.¹⁴⁵ Furthermore, the change in the labeling advocated by the

¹³¹ *Id.* at 783.

¹³² *Id.* at 780.

¹³³ *Id.* at 780 (citing *Colacicco v. Apotex, Inc.*, 432 F. Supp. 2d 514, 529 (E.D. Pa. 2006); *Dobbs v. Wyeth Pharm.*, 530 F. Supp. 2d 1275, 1287-1289 (W.D. Okla. 2008)).

¹³⁴ *Id.* at 781.

¹³⁵ *Id.* (citing Drug Amendments of 1962 § 202, 52 Stat. 1040, 21 U.S.C. § 301 (2000)).

¹³⁶ *Id.*

¹³⁷ *Id.*

¹³⁸ *Id.* (quoting *New York State Conf. v. Travelers Ins. Co.*, 514 U.S. 645, 654 (1995)).

¹³⁹ *Id.*

¹⁴⁰ *Id.*

¹⁴¹ 484 F. Supp. 2d 289 (E.D. Pa. 2007).

¹⁴² *Horne*, 541 F. Supp. 2d at 782.

¹⁴³ *Sykes*, 484 F. Supp. 2d at 292.

¹⁴⁴ *Id.* at 311.

¹⁴⁵ *Id.*

plaintiff would violate FDA requirements that such statements be substantiated by “reasonable evidence of an association of a serious hazard with a drug.”¹⁴⁶

According to the court in *Horne*, the plaintiff in that case was making a similar claim to the one that was made in *Sykes*.¹⁴⁷ In her complaint, the plaintiff contended that the defendant should have changed the drug’s labeling to declare that there were “dangerous” and “significant” risks of birth defects and fetal injury if pregnant women used Lotensin HCT during the first trimester of pregnancy.¹⁴⁸ However, the FDA-approved labeling stated that FDA had affirmatively considered the medical and scientific proof available at the time the drug was approved for sale and had concluded that the risks of birth were apparently not associated with use of the drug during the first trimester of pregnancy.¹⁴⁹

Furthermore, the plaintiff had failed to identify any studies in existence at the time of her pregnancy that indicated that birth defects might be caused by the use of Lotensin HCT or any other ACE inhibitor during the first trimester.¹⁵⁰ Nor did the plaintiff allege that the defendant has any “reasonable evidence” at the time of her pregnancy that would require a revision of the labeling in accordance with 21 C.F.R. § 201.57 (c)(6).¹⁵¹ The only evidence the plaintiff presented this issue was the Cooper Study, published after the birth of her child, which suggested a possible link between exposure to ACE inhibitors during the first trimester and the occurrence of birth defects.¹⁵² Moreover, the court observed, FDA in a 2006 Public Health Advisory declared that the Cooper Study’s evidence was the first to suggest that women who took ACE inhibitors during the first trimester of pregnancy might suffer birth defects.¹⁵³ FDA also pointed out that the results of “this one observational study” were not sufficient to justify any change to the pregnancy categories or any additional warning for ACE inhibitors.¹⁵⁴ Therefore, the court determined that:¹⁵⁵

Given the lack of scientific evidence of an association of birth defects and the use of ACE inhibitors during the first trimester, during the relevant period, if Defendant had added the additional warnings advocated by the Plaintiff, the label content would not have been substantiated by “reasonable evidence of a causal association” between the serious hazard claimed and the drug.

For this reason, the defendant could not have utilized the CBE supplement process to unilaterally add additional warnings to Lotensin HCT’s labeling, nor would it have been successful in asking FDA to do so by filing a supplemental NDA.

¹⁴⁶ *Id.* (citing 21 C.F.R. § 201.57(c)(6) (2009)). Generally, before a drug manufacturer can make a change in the approved labeling, it must submit a supplemental New Drug Application to FDA describing the proposed change and obtain FDA approval. 21 C.F.R. § 314.70(b) (2009). However, under the “changes being effected” or CBE process, a manufacturer may “add or strengthen a contraindication, warning, precaution or adverse reaction” without obtaining prior FDA approval by filing a supplemental application with the agency. 21 C.F.R. § 314.70 (c)(2)(i) (2009). See also *Bartlett v. Mutual Pharmaceutical Co.*, 659 F. Supp. 2d 279, 287-289 (D.N.H. 2009).

¹⁴⁷ *Horne*, 541 F. Supp. 2d at 782.

¹⁴⁸ *Id.*

¹⁴⁹ *Id.*

¹⁵⁰ *Id.* at 782-783.

¹⁵¹ *Id.* 783.

¹⁵² *Id.*

¹⁵³ *Id.* (citing FDA Public Health Advisory, Angiotensin-Converting Enzyme Inhibitor (ACE Inhibitor) Drugs and Pregnancy, Doc. 11-3 (2006)).

¹⁵⁴ *Id.* (citing FDA Public Health Advisory, Angiotensin-Converting Enzyme Inhibitor (ACE Inhibitor) Drugs and Pregnancy, Doc. 11-3 (2006)).

¹⁵⁵ *Id.*

This led the court in *Horne* to conclude that:¹⁵⁶

To hold the Defendant liable for failing to provide an additional warning to the effect that use of Lotensin HCT during the first trimester poses risks of birth defect and fetal injury when the FDA has already determined that such risks do not appear to result from use of the drug in the first trimester would create a direct conflict between the requirements of federal law and the requirements of state law and would place the Defendant in an impossible situation whereby the Defendant could not comply with federal law and state law at the same time.

Consequently, the court held that the plaintiff's failure to warn claims were preempted.¹⁵⁷

IV. THE *WYETH* DECISION

A. *Levine v. Wyeth*

The plaintiff in *Wyeth* received two injections of the defendant's drug, Phenergan, an antihistamine, in order to treat nausea resulting from a migraine headache.¹⁵⁸ The first dose was administered by intramuscular injection and when that failed to stop the plaintiff's nausea, a second dose was administered by intravenous injection into her arm.¹⁵⁹ Using a procedure known as IV push, the drug was mistakenly injected into the patient's artery instead of her vein, resulting in damage to her artery and eventual amputation of her arm.¹⁶⁰ The plaintiff brought suit against Wyeth, the manufacturer of Phenergan, in a Vermont state court, relying on both negligence and strict products liability theories.¹⁶¹ The plaintiff alleged that the drug's FDA-approved labeling was inadequate because it did not instruct health care professionals to use the IV-drip method of intravenous administration instead of the more risky IV-push method.¹⁶² In addition, the plaintiff claimed that Phenergan was not reasonably safe for intravenous administration because the risks of gangrene were greater than the therapeutic benefits of this method of administering the drug.¹⁶³

The trial court rejected the defendant's preemption claim and the jury awarded almost \$7 million in damages.¹⁶⁴ In its appeal to the Vermont Supreme Court, Wyeth continued to argue that the FDCA impliedly preempted the plaintiff's failure to warn claim.¹⁶⁵ The drug manufacturer contended that because FDA had ordered it to use

¹⁵⁶ *Id.* at 782.

¹⁵⁷ *Id.* at 783. However, the court refused to dismiss the plaintiff's negligence and breach of warranty claims insofar as they were based on defective design or manufacture or inadequate research, development or testing. *Id.* at 785-7 87.

¹⁵⁸ *Levine v. Wyeth*, 944 A.2d 179, 182 (Vt. 2006).

¹⁵⁹ *Id.* at 182.

¹⁶⁰ *Levine*, 944 A.2d at 182.

¹⁶¹ *Wyeth*, 129 S. Ct. at 1191.

¹⁶² *Levine*, 944 A.2d at 1191-1192. There are two ways to administer the injectable form of Phenergan intravenously. The first is the IV-push method, in which the drug is injected directly into the patient's vein; the second is the IV-drip method, whereby the drug is inserted into the patient's vein in a saline solution which slowly descends from a hanging intravenous bag. *Wyeth*, 129 S. Ct. 1191.

¹⁶³ *Id.* at 1192.

¹⁶⁴ *Levine*, 944 A.2d at 182-183.

¹⁶⁵ *Id.* at 183-184.

the warning language in question on its labeling, notwithstanding the agency's awareness of the risks of administration by the IV-push procedure, it would be impossible for Wyeth to comply with the requirements of both state and federal law.¹⁶⁶ In addition, Wyeth claimed that state tort doctrines undermined FDA's labeling scheme by allowing consumers to recover damages against drug companies even though they used FDA-approved labeling on their products.¹⁶⁷

The defendant's impossibility argument was reminiscent of *McDermott v. Wisconsin*,¹⁶⁸ where a purveyor of syrup successfully claimed that he could not comply with both federal labeling requirements and those of the state of Wisconsin because they were inconsistent.¹⁶⁹ The defendant in *Wyeth* argued that its situation was similar because FDA had prohibited it from providing a stronger warning about IV-push administration of Phenergan.¹⁷⁰ The Vermont court, however, responded that FDA had not expressly prohibited Wyeth from changing Phenergan's labeling and that the company was free to do so without prior FDA approval under § 314.70(c). In addition, the defendant contended that FDA had expressed its opinion about the adequacy of the drug's labeling when it reviewed the label for use in a different version of Phenergan and directed the manufacturer to "[r]etain verbiage in current label."¹⁷¹ However, the Vermont court did not agree that this directive indicated that FDA would necessarily refuse to permit Wyeth to provide a stronger warning.¹⁷² Since Wyeth could strengthen its warning pursuant to § 314.70(c), the court concluded that it was not impossible for the drug manufacturer to comply with both state and federal law.¹⁷³

The defendant also argued that liability under state tort law for use of FDA-approved labeling stood as an obstacle to federal regulatory objectives.¹⁷⁴ However, the court determined that FDA labeling requirements created a floor, not a ceiling for state regulation.¹⁷⁵ According to the court, this conclusion was consistent with the FDCA's principal goal of protecting consumers from dangerous products.¹⁷⁶ The court also declared that its position was supported by 1962 amendments to the FDCA that expressly limited the preemptive effect of the statute.¹⁷⁷ In the court's view, this provision indicated that Congress wished to leave state law, including common law tort principles, in place unless they created a "direct and positive conflict" between state and federal law.¹⁷⁸

Finally, the Vermont court considered FDA's Preamble on Preemption. While acknowledging that it would ordinarily defer to an agency's interpretation of a statute that it administers,¹⁷⁹ the court concluded that FDA's interpretation was not entitled to any deference because it was inconsistent with the 1962 Amendments.¹⁸⁰ As the court pointed out, FDA's statement was neither an authoritative interpretation of

¹⁶⁶ *Id.* at 185.

¹⁶⁷ *Id.*

¹⁶⁸ 228 U.S. 115 (1913).

¹⁶⁹ *Id.* at 137.

¹⁷⁰ *Wyeth*, 944 A.2d at 188.

¹⁷¹ *Id.*

¹⁷² *Id.* at 189.

¹⁷³ *Id.*

¹⁷⁴ *Id.* at 190.

¹⁷⁵ *Id.*

¹⁷⁶ *Id.*

¹⁷⁷ *Id.* (citing Drug Amendments of 1962 (Harris-Kefauver Act), Pub. L. No. 87-781, § 202, 76 Stat. 780, 793 (1962)).

¹⁷⁸ *Id.* at 190-191.

¹⁷⁹ *Id.* at 192 (citing *Chevron, U.S.A., Inc. v. Natural Res. Def. Council*, 467 U.S. 837, 844 (1984)).

¹⁸⁰ *Id.* at 192-193.

an ambiguous statutory provision, nor was it a persuasive policy statement.¹⁸¹ Since Congress had expressed an unambiguous intent to preserve state laws that did not create a “direct and positive” conflict with federal law, the court concluded that FDA’s views on preemption could not trump those of Congress.¹⁸²

B. *Wyeth v. Levine*

On March 4, 2009, the United States Supreme Court affirmed the Vermont court’s decision in *Wyeth*.¹⁸³ Justice Stevens, joined by four other Justices,¹⁸⁴ wrote the majority opinion.¹⁸⁵ Justice Thomas concurred in the judgment, but filed a separate concurring opinion,¹⁸⁶ while Justice Alito, joined by Chief Justice Roberts and Justice Scalia, dissented.¹⁸⁷ The Court addressed both of Wyeth’s preemption arguments: 1) that it would have been impossible for the company to modify existing FDA-approved labeling without violating federal law; and 2) that the plaintiff’s state law failure to warn claims would constitute an obstacle to federal regulatory policy because it would allow lay jurors to substitute their judgment for that of FDA as to the adequacy of FDA-approved drug labeling.¹⁸⁸

As a preliminary matter, the Court made it clear that the jury in *Wyeth* had not concluded that the IV-push procedure should be contraindicated or that Wyeth should have placed any particular warning language on its labeling; rather, according to the Court, the jury had simply determined that the language that Wyeth did place on its Phenergan labeling did not adequately warn about the risks of injection by the IV-push method.¹⁸⁹ The issue in *Wyeth*, therefore, was whether federal law impliedly preempted the claim that Wyeth failed to provide an adequate warning about the risks of using the IV-push procedure.¹⁹⁰ To answer that question, the Court declared, it must be guided by “two cornerstones of our pre-emption jurisprudence:” First, that “the purpose of Congress is the ultimate touchstone in every pre-emption case” and, second, “that the historic police powers of the States were not to be superseded by the Federal Act unless that was the clear and manifest purpose of Congress.”¹⁹¹

In response to the defendant’s “impossibility” argument, the Court pointed out that FDA’s “changes being effected” (CBE) regulation¹⁹² permitted a drug manufacturer to strengthen an existing warning or add an additional warning or contraindication to FDA-approved labeling without seeking prior approval from FDA.¹⁹³ Wyeth contended that this CBE regulation was not applicable because it only allowed a manufacturer to change its label “to reflect newly acquired information.”¹⁹⁴ For this reason, Wyeth maintained, it could not have changed Phenergan’s labeling pursuant to the CBE regulation unless new information subsequently became available that had not already been considered by FDA.¹⁹⁵ However, the

¹⁸¹ *Id.* at 194.

¹⁸² *Id.*

¹⁸³ 129 S.Ct. 1187, 1191 (2009).

¹⁸⁴ Justices Breyer, Ginsburg, Kennedy and Souter.

¹⁸⁵ *Id.* at 1190.

¹⁸⁶ *Id.* at 1204-1217. Justice Breyer also wrote a concurring opinion. *Id.* at 1204.

¹⁸⁷ *Id.* at 1217-1231.

¹⁸⁸ *Id.* at 1193-1194.

¹⁸⁹ *Id.* at 1194.

¹⁹⁰ *Id.*

¹⁹¹ *Id.* at 1194-1195.

¹⁹² 21 C.F.R. § 314.70(c)(6)(iii)(A), (C) (2009).

¹⁹³ *Wyeth*, 129 S. Ct. at 1196.

¹⁹⁴ *Id.* at 1197.

¹⁹⁵ *Id.*

Court observed that FDA had expressly stated that “newly acquired information” included not only new data, but also encompassed “new analyses of previously submitted data.”¹⁹⁶ Thus, the requirements of the CBE regulation could be satisfied if new analyses of existing data showed that the existence of greater risks or different risks than had previously been disclosed to FDA.¹⁹⁷ While there was little evidence of new information about the risks of IV-push administration of Phenergan, the Court suggested that Wyeth could have reevaluated post-approval reporting of amputations from this procedure and formulated a stronger warning on the basis of this new data.¹⁹⁸

Wyeth also claimed that it would be liable for unauthorized distribution and misbranding if it marketed Phenergan without first obtaining FDA approval for any revised labeling.¹⁹⁹ According to Wyeth, if the manufacturer made an unauthorized labeling change to Phenergan, FDA would treat it as an unapproved new drug.²⁰⁰ Any marketing without FDA approval would constitute an unauthorized distribution of the drug. Furthermore, altering the approved labeling would cause FDA to classify Phenergan as misbranded.²⁰¹ However, the Court rejected both of these contentions. First, it concluded that changing the labeling would not cause Phenergan to be considered a new drug under the statutory definition of that term.²⁰² In addition, the Court expressed skepticism that FDA would bring an enforcement action against the manufacturer for misbranding simply because it had strengthened Phenergan’s warning.²⁰³

Moreover, the Court also took issue with Wyeth’s implicit assumption that FDA, rather than the manufacturer, was primarily responsible for the drug labeling.²⁰⁴ In the Court’s view, “it has remained a central premise of federal drug regulation that the manufacturer bears responsibility for the content of its label at all times.”²⁰⁵ Indeed, prior to 2007, FDA lacked legal authority to require a drug manufacturer to modify its label.²⁰⁶ When Congress did grant this power to FDA, it reaffirmed the manufacturer’s responsibilities with respect to drug warnings and referred specifically to the CBE regulation.²⁰⁷ Finally, the Court distinguished between a situation in which FDA had affirmatively prohibited a drug company from changing a product’s labeling and a present situation where FDA had not taken a position on the issue of stronger warnings. Since Wyeth had presented no evidence that FDA had concluded that stronger warning was not needed,²⁰⁸ the Court concluded that Wyeth had failed to prove “that it was impossible for it to comply with both federal and state requirements.”²⁰⁹

Wyeth’s second preemption argument reasoned that an obligation, imposed under state tort law, to provide a stronger warning about the risks of the IV-push

¹⁹⁶ *Id.*, citing Rules and Regulations, Department of Health and Human Services (HHS), FDA, 21 CFR Parts 314, 601 and 814, Supplemental Applications Proposing Labeling Changes for Approved Drugs, biologics and Medical Devices, 73 Fed. Reg. 49,603, 49,604 (Aug. 22, 2008).

¹⁹⁷ *Id.*

¹⁹⁸ *Id.*

¹⁹⁹ *Id.*

²⁰⁰ *Id.*

²⁰¹ *Id.*

²⁰² *Id.* (citing 21 U.S.C. § 321(p)(1) (2000) and 21 C.F.R. § 310.3(h) (2009)).

²⁰³ *Id.*

²⁰⁴ *Id.* at 1197-1198.

²⁰⁵ *Id.*

²⁰⁶ *Id.* at 1198.

²⁰⁷ *Id.*

²⁰⁸ *Id.* at 1198-1199.

²⁰⁹ *Id.* at 1199.

procedure would “obstruct the purposes and objectives of federal drug labeling regulations.”²¹⁰ According to Wyeth, Congress intended that FDA make “drug labeling decisions that strike a balance between competing objectives.”²¹¹ In effect, the FDCA established “both a floor and a ceiling for drug regulation” which precluded juries in tort cases from finding FDA-approved labeling to be inadequate.²¹² The Court, however, declared that this argument relied on “an untenable interpretation of congressional intent and an overbroad view of an agency’s power to preempt state law.”²¹³ In the Court’s view, the failure of Congress to provide a federal remedy in the 1938 FDCA or any of its subsequent amendments indicated that it expected state tort law to provide adequate relief for consumers who were injured by unsafe drugs.²¹⁴ Furthermore, the Court reasoned, if Congress believed that tort litigation threatened federal regulatory objectives, it would have added an express preemption provision to the FDCA at some point in its history.²¹⁵

The Court also distinguished its decision in *Geier*, which held that DOT’s passive restraint regulation impliedly preempted “no airbag” lawsuits by accident victims.²¹⁶ Wyeth had claimed that FDA’s regulatory scheme was similar to that in *Geier*.²¹⁷ However, the Court disagreed. Not only had DOT conducted a formal rulemaking before adopting a regulation that allowed automobile companies to phase in airbags,²¹⁸ but there was also ample evidence that DOT had considered a variety of factors in the formulation of its regulatory scheme.²¹⁹ Finally, the Court in *Geier* took into account DOT’s explanation of how no-airbag lawsuits would interfere with its decision to phase in airbags rather than requiring automakers to provide them in all of their cars immediately.²²⁰ In contrast, FDA approval of Phenergan’s labeling was not the product of a formal rulemaking procedure, nor was there any evidence that it represented some sort of explicit policy choice on the part of the agency.²²¹ Indeed, the FDCA’s regulatory history revealed a “long-standing coexistence of state and federal law and FDA’s traditional recognition of state-law remedies—a recognition in place each time the agency reviewed Wyeth’s Phenergan label.”²²² Thus, the Court concluded that it was not impossible for Wyeth to comply with both state and federal obligations, nor did the plaintiff’s failure to warn claims stand as an obstacle to the accomplishment of congressional purposes as reflected in the FDCA.²²³

Both Justice Breyer and Justice Thomas wrote concurring opinions. Although he agreed that FDA’s approval of the Phenergan labeling did not impliedly preempt Levine’s failure to warn claim, Justice Breyer acknowledged that such claims might be preempted in other circumstances.²²⁴ For example, state tort law might be preempted on actual conflict grounds if it interfered with “FDA’s desire to create

²¹⁰ *Id.*

²¹¹ *Id.*

²¹² *Id.*

²¹³ *Id.*

²¹⁴ *Id.* at 1199-1200.

²¹⁵ *Id.* at 1200.

²¹⁶ *Id.* at 1203.

²¹⁷ *Id.*

²¹⁸ *Id.*

²¹⁹ *Id.*

²²⁰ *Id.*

²²¹ *Id.*

²²² *Id.*

²²³ *Id.* at 1204.

²²⁴ *Id.* (Breyer, J., concurring).

a drug label containing a specific set of cautions or instructions”²²⁵ or if it forced drug manufacturers to “raise prices to a point where those who are sick are unable to obtain the drugs they need.”²²⁶ Justice Thomas concurred in the Court’s judgment, but disagreed with “the majority’s implicit endorsement of far-reaching pre-emption doctrines.”²²⁷ Specifically, Justice Thomas decried the “purposes and objectives” aspect of the preemption doctrine, which he believed, enabled the Court to invalidate state laws “based on perceived conflicts with broad federal policy objectives, legislative history, or generalized notions of congressional purposes that are not embodied within the text of federal law.”²²⁸

Justice Alito wrote the dissenting opinion. To the dissenters, the issue was not whether the defendant had a duty to provide an adequate warning about the risks of injecting Phenergan using the IV-push procedure; rather, it was whether FDA or a lay jury should decide whether the warning in question was adequate.²²⁹ According to the dissent, this decision should be made by FDA alone and not second guessed by juries in products liability lawsuits.²³⁰ The dissent’s argument for preemption was based on the conclusion that FDCA vested FDA with primary responsibility for drug safety.²³¹ There was nothing in the FDCA’s comprehensive regulatory scheme that suggested that Congress had intended for lay juries to exercise some sort of oversight role over FDA and its drug approval process.²³²

The dissent made a number of assertions to support his argument that the plaintiff’s failure to warn claim constituted an obstacle to FDA’s ability to regulate the labeling of Phenergan and other drugs. First, it declared that, contrary to the majority’s claim, FDA “specifically considered and reconsidered the strength of Phenergan’s IV-push related warnings in light of new scientific and medical data.”²³³ The dissent pointed out that in 1987, FDA directed Wyeth to strengthen its warning about the risks of IV-push injections and cited published reports of gangrene caused by this method of administration.²³⁴ In support of its label change order, FDA also cited numerous articles which discussed the enhanced risks of injecting Phenergan and similar drugs in the crook of the elbow, a common injection site.²³⁵ Thus, FDA was well aware of the risks of IV-push injection in a patient’s elbow and while it required Wyeth to provide warnings about this risk, it also refused to prohibit physicians from using this method of administration.²³⁶

Second, the dissent argued that the Court’s reasoning in *Geier* compelled a finding that the plaintiff’s failure to warn claim should be preempted.²³⁷ As in *Geier*, when FDA approved the Phenergan label, it authorized a number of “safe” and “effective” methods of administration, including the IV-push procedure.²³⁸ Even though tort actions did not absolutely prohibit the use of the IV-push option,

²²⁵ *Id.*

²²⁶ *Id.* (citing Louis Lasagna, *The Chilling Effect of Product Liability on New Drug Development*, in *The Liability Maze* 334, 335-336 (Peter W. Huber & Robert E. Litan eds. 1991)).

²²⁷ *Id.* at 1205 (Thomas, J. concurring).

²²⁸ *Id.*

²²⁹ *Id.* at 1218 (Alito, J., dissenting).

²³⁰ *Id.*

²³¹ *Id.* at 1219.

²³² *Id.* at 1220.

²³³ *Id.* at 1222-1227.

²³⁴ *Id.* at 1222-1223.

²³⁵ *Id.* at 1223-1224.

²³⁶ *Id.* at 1225.

²³⁷ *Id.* at 1227.

²³⁸ *Id.*

they created a conflict with federal law if a jury concluded that an FDA-approved method of administration was inappropriate.²³⁹ Finally, the dissent maintained that juries were not well-suited to engage in the sort of cost-benefit analysis that FDA performed.²⁴⁰ While juries tended to focus on the specific design or warning label that allegedly caused the plaintiff's injury, FDA was better equipped to consider the interests of all potential users of the drug.²⁴¹ The dissent also observed that "FDA conveys its warnings with one voice, rather than whipsawing the medical community with 50 (or more) potentially conflicting ones."²⁴² For these reasons, the dissent concluded that the plaintiff's failure to warn claim should be invalidated on conflict preemption grounds.²⁴³

V. LOWER COURT DECISIONS AFTER *WYETH*

There are several federal preemption issues that were not addressed by the *Wyeth* Court and remain unresolved. The first is whether failure to warn claims under state tort law should be preempted on actual conflict grounds when FDA is aware of a risk but does not require a change in the labeling. The second issue is whether failure to warn claims against manufacturers of generic drugs are preempted because FDA does not permit their product to deviate from the labeling of the listed drug upon for which they substitute. In these cases, plaintiffs argued that failure to warn claims should not be preempted because drug manufacturers have the power to change product labeling without FDA advance approval by submitting a CBE supplement. So far, most courts have relied heavily on the reasoning of the *Wyeth* majority to find that these claims are not preempted.

A. SSRI Cases

1. *Colacicco v. Apotex, Inc.*

The first preemption issue is illustrated by *Colacicco v. Apotex, Inc.*²⁴⁴ *Colacicco* was one of several pre-*Wyeth* cases that held that failure to warn claims could be preempted when FDA had determined that there is not enough scientific evidence to justify changing the existing labeling.²⁴⁵ After the *Wyeth* case was decided, the Supreme Court vacated the *Colacicco* decision and remanded the case to the circuit court for further consideration in light of its finding that FDA approval of drug labeling in *Wyeth* did not impliedly preempt state law failure to warn claims.²⁴⁶

Colacicco involved an appeal from two cases where adult patients committed suicide after being treated for depression with selective serotonin uptake inhibitors (SSRIs).²⁴⁷ In the first case, the decedent, Lois Colacicco committed suicide within a month after being treated for depression with a drug containing paroxetine hydro-

²³⁹ *Id.*

²⁴⁰ *Id.* at 1229-1230.

²⁴¹ *Id.*

²⁴² *Id.* at 1230.

²⁴³ *Id.* at 1231.

²⁴⁴ 521 F.3d 253 (3d Cir. 2008), vacated, 129 S. Ct. 1578 (2009).

²⁴⁵ See also *Horne v. Novartis Pharmaceuticals Corp.*, 541 F. Supp. 2d 768 (W.D.N.C. 2008); *Dobbs v. Wyeth Pharm.*, 530 F. Supp. 2d 1275 (W.D. Okla. 2008); *Sykes v. Glaxo-SmithKline*, 484 F. Supp. 2d 289 (E.D. Pa. 2007); but see *Tucker v. SmithKline Beecham Corp.*, 596 F. Supp. 2d 1225 (S.D. Ind. 2008) (finding no preemption).

²⁴⁶ See *Colacicco v. Apotex, Inc.*, 129 S. Ct. 1578 (2009).

²⁴⁷ *Id.* at 256.

chloride, the active ingredient contained in Paxil.²⁴⁸ After her death, the decedent's husband brought suit against Apotex, the manufacturer of a generic version of Paxil, which had actually been prescribed to the decedent, and SmithKline Beecham, the manufacturer of Paxil itself, alleging that the labeling on these products did not sufficiently warn about the increased risk of emergent suicidality in adults who took paroxetine.²⁴⁹ The lower court dismissed the complaint, concluding that the plaintiff's claim was impliedly preempted.²⁵⁰ In a companion case, *McNellis ex rel. DeAngelis v. Pfizer, Inc.*, the decedent, Theodore DeAngelis committed suicide less than two weeks after ingesting Zoloft, which had been prescribed for depression and anxiety.²⁵¹ The decedent's daughter subsequently brought suit against Pfizer, the manufacturer of Zoloft, arguing that the suicide warning on Zoloft's labeling was inadequate.²⁵² When Pfizer asked for a summary judgment on grounds of federal preemption, the trial court denied its motion.²⁵³

On appeal, the Third Circuit Court of Appeals affirmed that state law failure to warn claims could be preempted on actual conflict grounds.²⁵⁴ The court began with a discussion of the presumption against preemption.²⁵⁵ Two of the defendants argued that the presumption was not applicable because the federal government, rather than the states, had traditionally regulated drug labeling.²⁵⁶ However, the court rejected these arguments relying on the fact that the Supreme Court had applied the presumption in *Hillsborough County v. Automated Medical Laboratories*,²⁵⁷ a case which involved a conflict between federal and local regulation of blood plasma centers.²⁵⁸ A third defendant contended that the presumption against preemption should not apply to any implied preemption case.²⁵⁹ The court observed that *Hillsborough County* had applied the presumption against preemption in a conflict preemption situation, but it also conceded that "the extent to which the Court relied on the presumption in the context of its conflict analysis was not clear."²⁶⁰ Ultimately, the court in *Colacicco* recognized that the presumption against preemption was applicable but it also noted the tension between the presumption and implied conflict preemption.²⁶¹ This suggests that it believed that presumption's effect might be weaker in implied preemption cases than in express preemption cases.

The *Colacicco* court went on to observe that instances where it was impossible to comply with both federal and state law were rare.²⁶² Therefore, the court limited its inquiry to whether state law failure to warn claims could "stand as an obstacle to the accomplishment and execution of the full purpose and objectives of Congress."²⁶³ The court first examined FDA's CBE regulation²⁶⁴ which allowed a drug manufacturer to change its product labeling without prior FDA approval when

²⁴⁸ *Id.*

²⁴⁹ *Id.*

²⁵⁰ See *Colacicco v. Apotex, Inc.*, 432 F. Supp. 2d 514, 537-539 (E.D. Pa. 2006).

²⁵¹ *Colacicco*, 521 F.3d at 256-257.

²⁵² *Id.* at 257.

²⁵³ *Id.*

²⁵⁴ *Id.* at 276.

²⁵⁵ *Id.* at 262.

²⁵⁶ *Id.* at 263.

²⁵⁷ 471 U.S. 707, 715 (1985)

²⁵⁸ *Colacicco*, 521 F.3d at 263.

²⁵⁹ *Id.*

²⁶⁰ *Id.* at 265.

²⁶¹ *Id.*

²⁶² *Id.* at 266.

²⁶³ *Id.* at 266 (quoting *Hillsborough County v. Automated Med. Labs, Inc.*, 471 U.S. 707, 713 (1985)).

²⁶⁴ 21 C.F.R. § 314.70(c)(6)(iii) (2009).

such a change would “add strengthen a contraindication, warning, precaution or adverse reaction.”²⁶⁵ According to the plaintiffs, since the regulation allowed drug manufacturers to strengthen or augment their warnings, FDA’s labeling requirements must be regarded as minimum standards.²⁶⁶ Consequently, tort liability would complement FDA’s labeling regulations, not conflict with them, if drug manufacturers changed their labeling in order to avoid such liability.²⁶⁷ However, the defendants pointed out that because FDA could order drug manufacturers to discontinue labeling changes adopted pursuant to § 314.70(c), drug labeling ultimately reflected the FDA’s judgment, not the manufacturer’s, about the information that should be included.²⁶⁸

The court considered three situations where a conflict might arise. The first was where neither FDA nor the manufacturer had addressed the particular risk. This was arguably the situation in *Wyeth* and one where a court was least likely to find that an actual conflict existed. The court in *Colacicco* made it clear that it would not rule on whether mere approval of particular labeling by FDA would be sufficient to preempt state tort claims based on a drug company’s failure to strengthen its warning.²⁶⁹ At the other end of the spectrum was the situation where the manufacturer sought to change a drug’s labeling and FDA refused to approve the proposed change. This would almost certainly give rise to an actual conflict. Even the plaintiffs conceded this by arguing that their failure to warn claims should not be preempted unless FDA explicitly rejected a drug manufacturer’s request to modify its product labeling.²⁷⁰ The court then concluded that the third situation applied, namely that the manufacturer had not formally sought to strengthen the labeling but that FDA had publically indicated that it was satisfied with the existing labeling.

In this case, the court observed, FDA had not ordered the defendants to remove language added to existing labeling under § 314.70(c), nor had the defendants attempted to change the labeling.²⁷¹ However, the court declared that deliberate inaction by a federal agency might be sufficient to preempt a state tort claim.²⁷² Furthermore, the court pointed out that FDA had actively monitored the possible association between SSRIs and suicide for nearly 20 years and had ultimately concluded that the warnings proposed by the plaintiffs were without scientific basis and, therefore, could be deemed false and misleading.²⁷³ Thus, if the defendants had added a warning about adult suicidality to their labeling, FDA would probably have withdrawn its approval of the drug until the new labeling was removed.²⁷⁴ This reasoning led the court to conclude that “a state law obligation to include a warning asserting the existence of an association between SSRIs and suicidality directly conflicts with FDA’s oft-repeated conclusion that the evidence did not support such an association.”²⁷⁵ Consequently, the court in *Colacicco* concluded that, under the circumstances, the plaintiffs’ failure to warn claims were preempted by FDA’s determination that there was no proven link between SSRIs and adult suicidality.²⁷⁶

²⁶⁵ *Id.*

²⁶⁶ *Colacicco*, 521 F.3d at 268.

²⁶⁷ *Id.*

²⁶⁸ *Id.* at 268-269.

²⁶⁹ *Id.* at 271-272.

²⁷⁰ *Id.* at 272.

²⁷¹ *Id.* at 269.

²⁷² *Id.*

²⁷³ *Id.* at 269-271.

²⁷⁴ *Id.* at 271.

²⁷⁵ *Id.*

²⁷⁶ *Id.*

At the present time, it remains to be seen whether the Court's reasoning in *Wyeth* will lead to a finding of no preemption when the circuit court reexamines its decision in *Colacicco*. First of all, the court will have to reconsider its holding in light of the fact that the Court in *Wyeth* indicated that a robust presumption against preemption applied to implied preemption cases. Second, the court will have to take into account the *Wyeth* Court's unwillingness to give much deference to FDA's Preamble on Preemption and its determination that manufacturers have the principal responsibility for drug safety. All this would seem to weaken the defendant's obstacle preemption argument. The court will also have to decide what effect a drug manufacturer's failure to seek modification of a drug's labeling by means of a CBE supplement has on a conflict preemption claim. The Court in *Wyeth* rejected the notion that FDA takes the lead in promoting drug safety while drug manufacturers play a passive role. Rather, the Court declared "that manufacturers, not the FDA, bear primary responsibility for their drug labeling at all times."²⁷⁷ In addition, the *Wyeth* Court refused to preempt the plaintiff's claims on the basis of impossibility because the defendant provided no evidence that FDA would have refused to allow it to strengthen the existing warnings.²⁷⁸ Indeed, the Court accepted the state trial court's finding that neither the manufacturer nor FDA "gave more than passing attention" to the question of whether IV-drip administration was preferable to IV-push administration.²⁷⁹ Furthermore, the manufacturer did not provide FDA with an evaluation or analysis about the dangers of IV-push administration of Phenergan.²⁸⁰ This led the Court in *Wyeth* to declare that it "cannot credit Wyeth's contention that the FDA would have prevented it from adding a stronger warning about the IV-push method of intravenous administration."²⁸¹ The Court concluded by stating that "[t]he CBE regulation permitted Wyeth to unilaterally strengthen its warning, and the mere fact that the FDA approved Phenergan's label does not establish that it would have prohibited such a change."²⁸² However, in *Colacicco*, the court pointed out that FDA had actively monitored the risk of suicidality in adults for more than 20 years and concluded that decided not order Paxil's manufacturer to strengthen the drug's labeling because it concluded that the suicide warnings desired by the plaintiffs were without scientific basis and, therefore, would be false and misleading.²⁸³

2. *Mason v. SmithKline Beecham Corp*

*Mason v. SmithKline Beecham Corp.*²⁸⁴ involved the antidepressant drug, Paxil.²⁸⁵ In that case, the plaintiffs' daughter committed suicide two days after being treated for depression with Paxil.²⁸⁶ Her parents brought suit against SmithKline Beecham, the drug's manufacturer, alleging that the company failed to disclose the fact that

²⁷⁷ *Wyeth*, 129 S. Ct. at 1202.

²⁷⁸ *Id.* at 1198.

²⁷⁹ *Id.* at 1198-1199.

²⁸⁰ *Id.* at 1199.

²⁸¹ *Id.*

²⁸² *Id.*

²⁸³ *Colacicco*, 521 F.3d at 269, *see also* Douglas G. Smith, Preemption After *Wyeth v. Levine*, 70 OHIO ST. L.J. 1435, 1466-67 (2009) (concluding that *Wyeth* supports the notion that the preemption doctrine should apply when the defendant demonstrates that FDA actually considered the risks at issue and did not require a stronger warning).

²⁸⁴ 596 F.3d 387 (7th Cir. 2010).

²⁸⁵ *Id.* at 389.

²⁸⁶ *Id.*

Paxil increased the risk of suicide among young adults.²⁸⁷ The lower court ruled that the plaintiffs' claims were preempted and granted summary judgment in favor of the manufacturer.²⁸⁸ However, this decision was reversed on appeal.²⁸⁹

The federal appeals court began by describing *Wyeth* as "a case that represents a sea change in the way courts are to consider issues of federal preemption."²⁹⁰ With that in mind, the court declared that it would review the plaintiffs' appeal in light of the *Wyeth* holding.²⁹¹ In so doing, the court gave considerable weight to the *Wyeth* opinion's statement that in order to argue successfully for federal preemption, a manufacturer must present "clear evidence" that FDA would have rejected the proposed change in the drug's label.²⁹² The court also relied on *Wyeth* to conclude that a drug manufacturer's ability to make labeling changes in accordance with the FDA's CBE regulation underscored the fact that "a manufacturer bears responsibility for the content of its label at all times."²⁹³

In order to determine whether the defendant had satisfied the "clear evidence" standard prescribed by *Wyeth*, the court compared the regulatory histories of Phenergan and Paxil.²⁹⁴ After reviewing the *Wyeth* Court's account of the regulatory history of Phenergan, the court observed that the Supreme Court had concluded that the defendant failed to present clear evidence that FDA would have refused to approve a labeling change in that case even though the FDA had seriously considered and rejected a warning that was a similar to the one proposed by the plaintiff.²⁹⁵ In comparison with this experience, the court concluded that the evidence was even less compelling that FDA would have rejected an effort by SmithKline Beecham to add a warning to Paxil about the risk of suicide.²⁹⁶ Consequently, the court concluded that the plaintiffs' claims were not preempted.²⁹⁷

B. Generic Drug Cases

Since the *Wyeth* decision, a number of courts have considered whether the FDCA impliedly preempts failure to warn claims against manufacturers of generic drugs who have failed to strengthen the labeling on their products.²⁹⁸ Almost all of these courts have relied, at least in part, on *Wyeth* to support a finding of no preemption.²⁹⁹ The great majority of these cases have involved metoclopramide, a drug used

²⁸⁷ *Id.*

²⁸⁸ *Id.*

²⁸⁹ *Id.* at 396.

²⁹⁰ *Id.* at 391.

²⁹¹ *Id.*

²⁹² *Id.* at 391.

²⁹³ *Id.* at 392.

²⁹⁴ *Id.*

²⁹⁵ *Id.* at 393.

²⁹⁶ *Id.* at 393-95.

²⁹⁷ *Id.* at 397.

²⁹⁸ *See, e.g.,* Demahy v. Actavis, Inc., 593 F.3d 428 (5th Cir. 2010); Mensing v. Wyeth, Inc., 588 F.3d 603 (8th Cir. 2009); Bartlett v. Mutual Pharmaceutical Co., 659 F. Supp. 2d 279 (D.N.H. 2009); Schrock v. Wyeth, Inc., 601 F. Supp. 2d 1262 (W.D. Okla. 2009); Morris v. Wyeth, Inc., 642 F. Supp. 2d 677 (W.D. Ky. 2009).

²⁹⁹ *See, e.g.,* Mensing v. Wyeth, Inc., 588 F.3d 603 (8th Cir. 2009); Bartlett v. Mutual Pharmaceutical Co., 659 F. Supp. 2d 279 (D.N.H. 2009); Stacel v. TEVA Pharmaceuticals, USA, 620 F. Supp. 2d 899 (N.D. Ill. 2009); Schrock v. Wyeth, Inc., 601 F. Supp. 2d 1262 (W.D. Okla. 2009); Demahy v. Actavis, Inc., 586 F. Supp. 2d 642 (E.D. La. 2008), *aff'd*, 593 F.3d 428 (5th Cir. 2010); but *see* Morris v. Wyeth, Inc., 642 F. Supp. 2d 677 (W.D. Ky. 2009) (holding that failure to warn claims were preempted); Wilson v. PLIVA, Inc., 640 F. Supp. 2d 879 (W.D. Ky. 2009);

to treat gastric reflux disease and other gastrointestinal ailments. Unfortunately, metoclopramide allegedly caused tardive dyskinesia, a severe neurological movement disorder, when ingested over for long periods of time.³⁰⁰ Regal, the “listed” or name brand drug,³⁰¹ was approved by FDA pursuant to the new drug application (NDA) process. However, the generic versions were approved as abbreviated new drug applications (ANDA) under the terms of the Hatch-Waxman Amendments to FDCA.³⁰² The proposed labeling submitted for FDA approval by the generic drug manufacturer under an ANDA must be the same as the labeling of the listed drug for which it is the equivalent. The question is if state tort law can require generic drug manufacturers to change their labeling when new risks are discovered or whether they can wait until either FDA or the manufacturer of the listed drug takes action first.

1. *Conte v. Wyeth, Inc.*

A number of courts addressed this issue prior to the *Wyeth* decision.³⁰³ One of the first was *Conte v. Wyeth, Inc.*,³⁰⁴ an unreported California case decided in 2006. In that case, the plaintiff alleged that although FDA had approved Reglan and its various generic substitutes for only 12 weeks of use, the labeling of these products substantially understated the side effects of prolonged use.³⁰⁵ The plaintiff claimed that this defective labeling caused her physician to prescribe metoclopramide for more than four years, causing her to develop tardive dyskinesia. One of the generic manufacturers, Purepac, moved for summary judgment, arguing that the plaintiff’s claims were preempted by the FDCA and its implementing regulations.³⁰⁶ According to Purepac, requiring it to add additional warnings about the risks of long-term use of metoclopramide would conflict with federal law because FDA regulations prohibited a generic manufacturer from altering a brand name drug’s labeling.³⁰⁷

The court began its consideration of the defendant’s preemption argument by observing that FDA in its Preamble on Preemption had declared prescription drug labeling to be solely a federal responsibility and consequently “any State law ‘failure to warn’ claims are necessarily preempted to the extent that they conflict with federal regulatory law by requiring additional labeling, i.e., additional warnings.”³⁰⁸ The court also relied on the reasoning of a federal district court in *In re Bextra and Clebrex Marketing Sales Practices and Products Liability Litigation*.³⁰⁹ That case held that state law failure to warn claims “were preempted by FDA regulations

³⁰⁰ See *Morris v. Wyeth, Inc.*, 642 F. Supp. 2d 677, 679 (W.D. Ky. 2009).

³⁰¹ 21 U.S.C. § 355(j)(7)(A)(i)(I)(2000) declared that a listed drug is one that has been approved for safety and effectiveness by FDA pursuant to 21 U.S.C. § 355(c) (2000).

³⁰² Now codified at 21 U.S.C. § 355(j) (2000).

³⁰³ Cf. *Wilson v. PLIVA, Inc.*, 640 F. Supp. 2d 879 (W.D. Ky. 2009); *Morris v. Wyeth, Inc.*, 613 F. Supp. 2d 861 (W.D. Ky. 2008) (holding failure to warn claims were preempted); *Mason v. SmithKline Beecham Corp.*, 546 F. Supp. 2d 618 (C.D. Ill. 2008) (same) with *Kellogg v. Wyeth*, 612 F. Supp. 2d 421 (D. Vt. 2008) (holding that failure to warn claims were not preempted); *Demahy v. Wyeth, Inc.*, 586 F. Supp. 2d 642 (E.D. La. 2008), aff’d, 612 F.3d 511 (5th Cir. 2010) (same); *McKenney v. Purepas Pharm. Co.*, 83 Cal. Rptr. 3d 810 (Ct. App. 2008) (same).

³⁰⁴ 2006 WL 2692469 (Cal. Super. Ct. 2006); aff’d in part and rev’d in part on other grounds, 85 Cal. Rptr. 3d 299 (Ct. App. 2008) [hereinafter cited as “slip opinion”].

³⁰⁵ *Conte v. Wyeth, Inc.*, 85 Cal. Rptr. 299, 305 (Ct. App. 2008).

³⁰⁶ *Id.* at 306.

³⁰⁷ *Conte*, slip opinion at *1.

³⁰⁸ *Id.* at *4.

³⁰⁹ 2006 WL 2374742 (N.D. Cal. Aug. 16, 2006).

because FDA's interpretation of the preemptive effects of its regulations set forth in the January 24, 2006 Preamble, is entitled to deference.³¹⁰ The court also noted that the *Bextra* court acknowledged that FDA's position in the Preamble represented a shift in its former view on preemption, but declared that it should still accord deference to the Preamble.³¹¹ The court concluded by finding that the issues involved were similar to those of *Bextra* and *Colacicco* "insofar as their resolution turns on whether the recently promulgated FDA Preamble preempts State law 'failure to warn' claims" and since it found the reasoning of the two cases very persuasive, the court granted Purepac's motion for summary judgment.³¹²

The superior court subsequently granted a summary judgment in favor of Wyeth, the manufacturer of Reglan and all the manufacturers of the generic drug.³¹³ In dismissing the case against Wyeth, the court concluded that the plaintiff failed to show that her physician relied on the product labeling disseminated by Wyeth and that the manufacturer of a listed drug had no duty to patients who took only the generic version of the drug.³¹⁴ The court granted summary judgment in favor of the manufacturers of generic metoclopramide on grounds of federal preemption and because it found that plaintiff's physician had not relied on the product labeling.³¹⁵

On appeal, a California intermediate appellate court ruled that Wyeth owed a common law duty of due care that was not limited to those who prescribed or consumed Reglan, but extended to physicians who might foreseeably rely on the listed drug's labeling even though they prescribed the generic version of the drug.³¹⁶ For this reason, the court reversed the summary judgment in favor of Wyeth.³¹⁷ However, it affirmed the summary in favor of the manufacturers of generic metoclopramide because the plaintiff was unable to prove that she relied on any product safety information supplied by them.³¹⁸ The appeals court disposed of the preemption issue by declaring that "it is unnecessary for us to reach the generic defendants' further contention that federal law preempts state tort claims based upon allegedly inadequate drug labeling."³¹⁹

2. *Mensing v. Wyeth, Inc.*

Recently, two courts have appeal have ruled that the FDCA did not preempt failure to warn claims against manufacturers of generic drugs. One of these was *Mensing v. Wyeth, Inc.*³²⁰ In *Mensing*, the plaintiff brought suit against the manufacturers of Reglan and generic versions of metoclopramide, claiming that the drug caused her to develop tardive dyskinesia.³²¹ The plaintiff alleged that the drug's labeling failed to warn about the dangers of tardive dyskinesia associated

³¹⁰ Conte, slip opinion at *5.

³¹¹ *Id.* at *6.

³¹² *Id.*

³¹³ See Conte v. Wyeth, Inc., 85 Cal. Rptr. 3d 299, 304 (Ct. App. 2008).

³¹⁴ *Id.*

³¹⁵ *Id.*

³¹⁶ *Id.* at 304-305, but see Lars Noah, This Is Your Products Liability Restatement on Drugs, 74 BROOKLYN L. REV. 839, 911 (2009) (concluding that most courts have refused to hold brand-name manufacturers liable to consumers of generic versions of a drug)..

³¹⁷ *Id.* at 305.

³¹⁸ *Id.*

³¹⁹ *Id.*

³²⁰ 588 F.3d 603 (8th Cir. 2009).

³²¹ See *Mensing v. Wyeth, Inc.*, 562 F. Supp. 2d 1056 (D. Minn. 2008).

with long-term use.³²² The lower court ruled that failure to warn claims against the generic manufacturers were preempted and dismissed them.³²³

On appeal, the circuit court first considered the presumption against preemption.³²⁴ The court acknowledged that the *Wyeth* court had noted the historic coexistence of state tort law and federal regulation of prescription drugs.³²⁵ It also declared that after *Wyeth* it must treat with skepticism any assertion by the defendants that Congress intended to silently grant tort immunity to most prescription drug manufacturers.³²⁶ The defendants tried to distinguish *Wyeth* by claiming that it was solely concerned with the tort liability of brand name manufacturers, but the court in *Mensing* disagreed, pointing that virtually all post-*Wyeth* decisions had refused to preempt failure to warn claims against manufacturers of generic drugs.³²⁷

Turning to the question of whether it was “impossible” for drug manufacturers to modify existing product labeling because FDA regulations required generic drug labeling to be the same as the labeling of a listed drug, the court quoted *Wyeth’s* admonition that “[i]mpossibility pre-emption [was] a demanding defense.”³²⁸ The generic drug manufacturers pointed to a federal regulation that provided that FDA could withdraw its approval of a generic drug if its label was “no longer consistent” with the name brand label.³²⁹ This provision prohibited them from utilizing the CBE process to make a unilateral labeling change without first obtaining FDA approval.³³⁰ However, the court responded that even if the CBE process were not available, the defendants could have used the prior approval process.³³¹

In this case we need not decide whether generic manufacturers may unilaterally enhance a label warning through the CBE procedure because the generic defendants could have at least *proposed* a label change that the FDA could receive and impose uniformly on all metoclopramide manufacturers if approved (expended the majority of its discussion) is immaterial to the preemption analysis in light of this clear directive to generic manufacturers and the availability of the prior approval process.

Furthermore, the court declared that 21 C.F.R. § 201.57(e) imposed a duty on generic drug manufacturers to initiate labeling changes by whatever means was available when they became aware of new risks associated with the use of their product.³³² The court pointed out that this provision required that drug labeling “shall be revised as soon as there is reasonable evidence of an association of a serious hazard with a drug.”³³³ Citing *Wyeth*, the court concluded that this provision did not allow manufacturers of generic drugs “passively to accept the inadequacy of their drug’s label as they market and profit from it.”³³⁴ Instead, they must do more and initiate changes in labeling rather than waiting for the manufacturers of listed drugs to do so. This duty would require them to use the prior approval process if the CBE process were not available.³³⁵

³²² *Id.* at 1057.

³²³ *Id.* at 1064-1065.

³²⁴ See *Mensing v. Wyeth, Inc.*, 588 F.3d 603, 607-608 (8th Cir. 2010).

³²⁵ *Id.* at 607.

³²⁶ *Id.* at 607.

³²⁷ *Id.* at 607-608.

³²⁸ *Id.* at 608 (quoting from *Wyeth*, 129 S. Ct. at 1199).

³²⁹ *Id.* (citing 21 C.F.R. § 314.150(b)(10) (2009)).

³³⁰ *Id.*

³³¹ *Id.*

³³² *Id.* at 608-609.

³³³ *Id.* (quoting from 21 C.F.R. § 201.57(e) (2009)).

³³⁴ *Id.* at 609.

³³⁵ *Id.*

The availability of one particular procedure (the CBE process, on which the district court expended the majority of its discussion) is immaterial to the preemption analysis in light of this clear directive to generic manufacturers and the availability of the prior approval process.

In response, the defendants argued that 21 C.F.R. § 314.70 limits the prior approval procedure to “major changes,” while changes to enhance warnings were solely within the purview of the CBE process.³³⁶ However, the court rejected this interpretation as “too restrictive.”³³⁷ It pointed out that while 21 C.F.R. § 314.70 established various methods of proposing changes to approved drugs, it repeatedly used the nonrestrictive phrase “[t]hese changes include, but are not limited to” in order to identify the types of changes manufacturers can propose through each kind of supplement.³³⁸ Thus, the court concluded that § 314.70 did not manifest an intent on the part of Congress or FDA to prohibit manufacturers of generic drugs from utilizing the prior approval process.³³⁹

The court then considered whether it was appropriate to impose liability for failing to propose a change in labeling when it was uncertain whether FDA would have approved the requested change.³⁴⁰ Quoting from *Wyeth*, the court declared “[a]bsent clear evidence that the FDA would not have approved a change to [the drug’s] label, we would not conclude that it was impossible for [the manufacturer] to comply with both federal and state requirements.”³⁴¹ However, the court pointed out that in this case, the record did not contain “clear evidence” that FDA would have rejected a proposed labeling change had one been made.³⁴² For these reasons, the court concluded that compliance with both state and federal requirements was not impossible.³⁴³

The court then addressed the generic manufacturers’ obstacle preemption argument. According to the defendants, proposing a label change as potentially required by state law, would require them to conduct expensive clinical studies, thereby frustrating the goal of the Hatch-Waxman Amendments to bring low cost generic drugs to market quickly.³⁴⁴ In response, the court observed that the scientific substantiation necessary to support a proposed change in labeling did not require the manufacturer to conduct new tests.³⁴⁵ In fact, as the *Wyeth* Court pointed out, multiple reports of adverse drug experiences might be sufficient to justify a manufacturer’s request for a labeling change.³⁴⁶ The court concluded by declaring that the state law duty to warn did not obstruct the purposes and objectives of the Hatch-Waxman Amendments.³⁴⁷ Rather, as *Wyeth* indicated, such actions reinforced “the FDCA’s premise that manufacturers, not the FDA, bear primary responsibility for their drug labeling at all times.”³⁴⁸

³³⁶ *Id.*

³³⁷ *Id.*

³³⁸ *Id.* at 609-610 (citing 21 C.F.R. ‘ 314.70(b)(2), (c) (2), (d)(2) (2009)).

³³⁹ *Id.* at 610.

³⁴⁰ *Id.*

³⁴¹ *Id.* (quoting *Wyeth*, 129 S. Ct. at 1198.

³⁴² *Id.* at 610-611.

³⁴³ *Id.* at 611.

³⁴⁴ *Id.*

³⁴⁵ *Id.* at 611-612.

³⁴⁶ *Id.* at 612.

³⁴⁷ *Id.*

³⁴⁸ *Id.* (quoting *Wyeth*, 129 S. Ct. at 1202.)

3. *Demahy v. Actavis, Inc.*

Recently, in *Demahy v. Actavis, Inc.*,³⁴⁹ another federal appeals court also ruled that state law failure to warn claims against generic drug manufacturers were not preempted by the FDCA. As in *Mensing*, the plaintiff came down with tardive dyskinesia after taking metoclopramide for four years to treat her acid reflux disease.³⁵⁰ The plaintiff brought suit based on the Louisiana Products Liability Act (LPLA) against Actavis (formerly Purepac), the manufacturer of the generic metoclopramide that she consumed.³⁵¹ The defendant argued that the lawsuit should be dismissed as a matter of federal conflict preemption because the label and package insert for its generic metoclopramide could not be altered from the labeling that had been approved for name brand metoclopramide.³⁵² The lower court, however, ruled that the plaintiff's claims were not preempted.³⁵³

On appeal, the court began by declaring that “[t]he Supreme Court ruled in [*Wyeth*] that the federal regulatory regime governing pharmaceuticals does not preempt a state-law failure to warn claim against the manufacturer of a name brand drug.”³⁵⁴ The defendant tried to distinguish *Wyeth* by claiming that manufacturers of generic drugs, unlike those of name brand drugs, could not change the labeling of their products unilaterally through the CBE process because generic drugs had to retain the same labeling as chemically similar brand name drugs.³⁵⁵ The court conceded that the *Wyeth* Court did rely on part on the availability of the CBE process to conclude that it was not impossible for a name brand manufacturer to comply with federal and state labeling requirements.³⁵⁶ Nevertheless, the court declared that the *Wyeth* case had some bearing of the defendant's situation as well.³⁵⁷

Citing *Wyeth*, the court stated that the presumption against preemption cautioned against a finding of federal preemption.³⁵⁸ Moreover, the court noted that five members of the *Wyeth* Court had held that the presumption applied “to conflict preemption cases at least where, as here, the question is whether federal regulation of prescription drugs preempts state-law failure to warn claims.”³⁵⁹ Furthermore, the court declared, “the bar to a finding of preemption [was] even higher because federal law provides no remedy for an injured consumer.”³⁶⁰ Finally, the court cited *Wyeth* for the proposition that the failure of Congress to expressly preempt failure to warn claims against drug manufacturers when it had done so against manufacturers of medical devices militated against finding of conflict preemption.³⁶¹

Turning to the impossibility argument, the court echoed *Wyeth*, concluding that “[r]equiring that the conflict be one of ‘physical impossibility’ readily suggests that this is a ‘demanding defense.’”³⁶² The court acknowledged that the Hatch-Waxman Amendments required that the labeling of the generic drug be identical to

³⁴⁹ 593 F.3d 428 (8th Cir. 2010).

³⁵⁰ See *Demahy v. Wyeth, Inc.*, 586 F. Supp. 2d 642, 643-64 (E.D. La. 2008).

³⁵¹ *Id.* at 644.

³⁵² *Id.*

³⁵³ *Id.* at 662.

³⁵⁴ *Demahy*, 393 F.3d at 433.

³⁵⁵ *Id.*

³⁵⁶ *Id.*

³⁵⁷ *Id.*

³⁵⁸ *Id.* at 434.

³⁵⁹ *Id.*

³⁶⁰ *Id.* at 435.

³⁶¹ *Id.*

³⁶² *Id.* at 436 (quoting *Wyeth*, 129 S. Ct. at 1199).

that of the name brand drug at the time that the manufacturer sought an ANDA approval.³⁶³ However, again referring to *Wyeth*, the court pointed out that “it has remained a central premise of federal drug regulation that the manufacturer bears responsibility for the content of the label at all times.”³⁶⁴ This means that the defendant had an obligation to inform FDA that long-term use of metoclopramide posed a serious hazard to consumers and to seek a change in the labeling.³⁶⁵ The defendant also argued that FDA might withdraw its approval for the drug if it concluded that the manufacturer lacked “substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended or suggested in the labeling thereof.”³⁶⁶ However, the court responded by observing that the Court in *Wyeth* had stated that it would find it “difficult to accept” that FDA would take punitive action against a manufacturer for strengthening a warning.³⁶⁷

The court then discussed the various methods a manufacturer could employ to change a drug’s labeling. The court first examined the CBE supplement procedure and concluded that it was the best suited to strengthen existing labeling to reflect “information not previously submitted to the [FDA].”³⁶⁸ After a detailed discussion of FDA statements and regulations, the court found that FDA had not expressly prohibited generic drug manufacturers from using the CBE process.³⁶⁹ Consequently, it declared that “[w]ithout explicit reference to the use of the CBE process by generic manufacturers, we decline to read in a bar to its use.”³⁷⁰ The court also determined that generic drug manufacturers could seek a change in labeling through the prior approval process.³⁷¹ Finally, the court concluded that while generic drug manufacturers could not warn healthcare professional about newly discovered risks by means of “Dear Doctor” letters without prior FDA approval, they could suggest that FDA send such letters on their behalf.³⁷²

Finally, the defendant argued that it would be unable to comply with state law duties and FDA requirements if FDA refused to approve changes in labeling that would satisfy the state law duty to warn.³⁷³ However, the court responded by pointed out that the *Wyeth* Court had indicated that “absent clear evidence that the FDA would not have approved a change to [the drug’s] label, we will not conclude that it was impossible for the [manufacturer] to comply with both federal and state requirements.”³⁷⁴ Thus, the court concluded that compliance with both state and federal requirements was not impossible.³⁷⁵

The *Demahy* court then considered whether state law failure to warn claims stood as an “‘obstacle to the accomplishment and execution of the full purposes and objectives of Congress’ as embodied in the Hatch-Waxman Amendments and

³⁶³ *Id.*

³⁶⁴ *Id.* at 437 (citing *Wyeth*, 129 S. Ct. at 1197-1198).

³⁶⁵ *Id.*

³⁶⁶ *Id.* at 438 (quoting 21 U.S.C. § 355(e)).

³⁶⁷ *Id.* at 439.

³⁶⁸ *Id.* (quoting Rules and Regulations, HHS, FDA, 21 CFR Parts 314, 601 and 814, Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics and Medical Devices, 73 Fed. Reg. 49,603, 49,604 (Aug. 22, 2008)).

³⁶⁹ *Id.* at 439-444.

³⁷⁰ *Id.* at 444.

³⁷¹ *Id.*

³⁷² *Id.* at 444-445.

³⁷³ *Id.* at 446.

³⁷⁴ *Id.* (quoting *Wyeth*, 129 S. Ct. at 1198).

³⁷⁵ *Id.*

the FDCA.³⁷⁶ According to the court, in order to for an obstacle preemption claim to prevail, it must impute to Congress an intent that manufacturers of name brand drugs bear the sole responsibility for responding to newly discovered risks even if they no longer manufacture the drug in question.³⁷⁷ In addition, the court declared that it would have to assume that Congress either intended for name brand drug manufacturers to be liable for all failure to warn claims, including those brought by consumers of generic drugs, or that such consumers would be left without a remedy.³⁷⁸ It was clear that the court was unwilling to make such an assumption.³⁷⁹

In response, the defendant argued that satisfying the state law duty to warn would require generic drug companies to perform duplicative studies, trials and other data gathering exercises in order to determine whether labeling changes were necessary.³⁸⁰ However, the court found that reasonable evidence of a serious hazard with a drug did not have to be based on tests performed by the generic drug company, but could be based on studies conducted by others.³⁸¹ Furthermore, the court observed that “nothing about the Hatch-Waxman Amendments, and their goal of cheaper drugs, obviates the concomitant prescription that all drugs, even cheaper ones, remain safe.”³⁸² Echoing *Wyeth*, the court declared that “failure to warn actions ... lend force to the FDCA’s premise that manufacturers, not the FDA, bear primary responsibility for their drug labeling at all times.”³⁸³

The court concluded by finding that the defendant had not provided sufficient evidence to overcome the presumption against preemption.³⁸⁴ According to the court, “[t]he presumption reflects the judiciary’s reluctance to find the intention of a coordinate federal branch to supplant state law.”³⁸⁵ Accordingly, the appeals court in *Demahy* affirmed the lower court’s decision in favor of the plaintiff.³⁸⁶

4. Other Lower Court Cases

Several other lower court cases have relied the reasoning of the *Wyeth* decision to conclude that failure to warn claims against the manufacturers of generic drugs were not preempted.³⁸⁷ In *Schrock v. Wyeth, Inc.*, the plaintiff alleged that she ingested metoclopramide from March, 2000 until June, 2006 and that this long-term use of the drug caused her to develop tardive dyskinesia.³⁸⁸ She argued that the defendants, distributors of Reglan, the name brand drug and generic metoclopramide, failed to warn about the risk of long-term use of the drug and failed to request a labeling revision to FDA.³⁸⁹ The defendants responded by moving to dismiss the plaintiff’s claims on the basis of federal preemption.³⁹⁰

³⁷⁶ *Id.* (quoting *Crosby v. Nat’l Foreign Trade Council*, 530 U.S. 363, 372-373 (2000)).

³⁷⁷ *Id.* at 447.

³⁷⁸ *Id.*

³⁷⁹ *Id.* at 449.

³⁸⁰ *Id.* at 447.

³⁸¹ *Id.*

³⁸² *Id.* at 448.

³⁸³ *Id.* (quoting *Wyeth*, 129 S. Ct. at 1202).

³⁸⁴ *Id.* at 449.

³⁸⁵ *Id.*

³⁸⁶ *Id.*

³⁸⁷ See *Bartlett v. Mutual Pharmaceutical Co.*, 659 F. Supp. 2d 279 (D.N.H. 2009); *Stacel v. Teva Pharmaceuticals, USA*, 620 F. Supp. 2d 899 (N.D. Ill. 2009); *Schrock v. Wyeth, Inc.*, 601 F. Supp. 2d 1262 (W.D. Okla. 2009).

³⁸⁸ *Schrock*, 601 F. Supp. 2d at 1263.

³⁸⁹ *Id.*

³⁹⁰ *Id.*

The court began by observing that the drug manufacturer made similar preemption arguments in *Wyeth*. In resolving these preemption arguments, the Court in *Wyeth* invoked the presumption against preemption.³⁹¹ In addition, the court pointed out, the *Wyeth* Court declared that Congress “adopted a rule of construction to make it clear that manufacturers remain responsible for updating their labels.”³⁹² Finally, quoting from *Wyeth*, the court declared that “[u]nless the prescription drug manufacturer makes a clear evidentiary showing that the FDA would not have approved a change in the label, a court may not conclude that it was impossible for the prescription drug manufacturer to comply with both federal and state requirements.”³⁹³ Based on these considerations, the court rejected the defendant’s impossibility argument.³⁹⁴

The court also considered the defendant’s claim that failure to warn claims stood as an obstacle to the purposes and objectives of the FDCA. Once again, the court relied heavily on the reasoning of *Wyeth*. First, it agreed with the *Wyeth* Court that the failure of Congress to expressly preempt state tort claims was “powerful evidence that Congress did not intend FDA oversight to be the exclusive means of ensuring drug safety and effectiveness.”³⁹⁵ Second, following the *Wyeth* Court’s lead, the court refused to rely on FDA’s Preamble on Preemption.³⁹⁶ The court concluded by declaring “[a]s in *Wyeth*, however, this Court finds that there is a longstanding coexistence of state and federal law in the regulatory history and background relevant to this case.”³⁹⁷ Accordingly, the court rejected the defendants’ obstacle preemption claim.³⁹⁸

Another federal district court reached a similar conclusion in *Stacel v. Teva Pharmaceuticals, USA*.³⁹⁹ The plaintiff in that case contended that she developed lupus as a result of consuming a generic version of minocycline manufactured by the defendant, Teva.⁴⁰⁰ The plaintiff alleged, *inter alia*, that Teva negligently failed to warn about the risk of drug-induced lupus.⁴⁰¹ Teva moved to dismiss, arguing that the plaintiff’s claims were preempted by the labeling requirements of the FDCA.⁴⁰² Citing *Wyeth*, the court began its analysis by invoking the presumption against preemption.⁴⁰³ After reviewing the various procedures by which manufacturers could change drug labeling, the court declared that while the Court’s analysis in *Wyeth* was not directly controlling, it concluded that “key parts of its analysis are applicable here.”⁴⁰⁴

First, the court noted that the *Wyeth* Court had found that when Congress amended the FDCA in 1982, it expressly declared that state-law claims should not be preempted unless there was a “direct and positive” conflict with the FDCA.⁴⁰⁵ The court also quoted the *Wyeth* opinion for the proposition that “the manufacturer

³⁹¹ *Id.* at 1264.

³⁹² *Id.* (quoting *Wyeth*, 129 S. Ct. at 1194).

³⁹³ *Id.* at 1264-1265 (quoting *Wyeth*, 129 S. Ct. at 1198-1199).

³⁹⁴ *Id.* at 1265.

³⁹⁵ *Id.* (citing *Wyeth*, 129 S. Ct. at 1199-1200).

³⁹⁶ *Id.* (citing *Wyeth*, 129 S. Ct. at 1200-1201).

³⁹⁷ *Id.*

³⁹⁸ *Id.*

³⁹⁹ 620 F. Supp. 2d 899 (N.D. Ill. 2009).

⁴⁰⁰ *Id.* at 901.

⁴⁰¹ *Id.*

⁴⁰² *Id.* at 902.

⁴⁰³ *Id.* at 903 (citing *Wyeth*, 129 S. Ct. at 1194).

⁴⁰⁴ *Id.* at 904.

⁴⁰⁵ *Id.* (citing *Wyeth*, 129 S. Ct. at 1195).

bears responsibility for the content of its label at all times.⁴⁰⁶ In addition, the court reiterated the *Wyeth* Court's skepticism about the defendant's claim that the FDA would treat a drug with altered labeling as "misbranded."⁴⁰⁷ Finally, the court agreed with *Wyeth* that congressional silence on preemption, coupled with its awareness of the existence of tort litigation, indicated that it "did not intend FDA oversight to be the exclusive means of ensuring drug safety and effectiveness."⁴⁰⁸

According to the *Stacel* court, the preemption argument hinged on whether manufacturers of generic drugs could utilize the CBE process to alter existing labeling.⁴⁰⁹ As the court declared, "[i]f generic manufacturers can utilize the CBE, then the logic of [*Wyeth*] is directly applicable."⁴¹⁰ Teva argued that FDA regulations prohibited manufacturers of generic drugs from utilizing the CBE procedure.⁴¹¹ Specifically, Teva pointed to language in a proposed rule which declared that "CBE changes are not available for generic drugs approved under an abbreviated new drug application under 21 U.S.C. 355(j). To the contrary, a generic drug manufacturer is required to conform to the approved labeling of the listed drug."⁴¹² In response, the court pointed out that the *Wyeth* Court had applied *Skidmore* deference to FDA's Preamble on Preemption and concluded that it did not deserve any deference because it contradicted every statement on the issue that came from Congress.⁴¹³ Taking its cue from *Wyeth*, the court in *Stacel* also declined to accept FDA's preemption argument.⁴¹⁴ Instead, the court concluded that manufacturers of generic drugs could change the labeling of their products without prior FDA approval by utilizing the CBE procedure.⁴¹⁵ The court also determined that failure to warn claims would not frustrate the congressional purpose behind the FDCA or the Hatch-Waxman Amendments.⁴¹⁶ Echoing *Wyeth*, the court declared that "[t]he underlying purpose of the FDCA is not making sure that that drugs can be quickly and cheaply brought to market, but rather to assure that the drugs are safe when they are brought to market."⁴¹⁷ Accordingly, the court refused to conclude that the plaintiff's claims were preempted by federal law.⁴¹⁸

A New Hampshire federal district court reached a similar conclusion recently in *Bartlett v. Mutual Pharmaceutical Co.*⁴¹⁹ The plaintiff in that case was diagnosed with Stevens-Johnson syndrome which progressed to toxic epidermal necrosis of the skin and mucous membranes as a result of consuming Sulindac, a generic drug manufactured by the defendant drug companies.⁴²⁰ The plaintiff brought a number of claims against the defendants, including failure to warn.⁴²¹ The defendants, in turn, moved for judgment on the pleadings, arguing that the plaintiff's claims were

⁴⁰⁶ *Id.* (quoting *Wyeth*, 129 S. Ct. at 1197).

⁴⁰⁷ *Id.* (citing *Wyeth*, 129 S. Ct. at 1197).

⁴⁰⁸ *Id.* (quoting *Wyeth*, 129 S. Ct. at 1200).

⁴⁰⁹ *Id.* at 905.

⁴¹⁰ *Id.*

⁴¹¹ *Id.* at 906.

⁴¹² *Id.* (quoting Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices, 73 Fed. Reg. 2848, 2849 n. 1 (Jan. 16, 2008)).

⁴¹³ *Id.* (citing *Wyeth*, 129 S. Ct. at 1200.)

⁴¹⁴ *Id.* at 907.

⁴¹⁵ *Id.*

⁴¹⁶ *Id.*

⁴¹⁷ *Id.* (Citing *Wyeth*, 129 S. Ct. at 1195-1198).

⁴¹⁸ *Id.*

⁴¹⁹ 659 F. Supp. 2d 279 (D.N.H. 2009).

⁴²⁰ *Id.* at 282.

⁴²¹ *Id.*

preempted Title I of the Drug Price Restoration Act of 1984, a part of the Hatch-Waxman Amendments to the FDCA.⁴²² However, the court denied the defendants' motion, concluding that "[t]he Supreme Court's recent decision on the preemptive effect of federal drug regulation on state tort law in *Wyeth v. Levine*" makes it clear that the plaintiff's claims are not preempted.⁴²³

The court began its analysis (after discussing FDA labeling regulations and the ANDA process) with a reference to *Wyeth* and the presumption against preemption. The court observed that the Supreme Court had affirmed in *Wyeth* that "[i]n all preemption cases, and particularly in those in which Congress has legislated ... in a field which the States have traditionally occupied, we start with the assumption that the historic police powers of the States were not be superseded by the Federal Act unless that was the clear and manifest purpose of Congress."⁴²⁴ The court went on to declare that *Wyeth* not only affirmed that the presumption against preemption applied to implied preemption claims, but it also made it clear that the presumption applied to failure to warn claims in light of "the historic presence of state law" in the area of drug regulation.⁴²⁵ Thus, the court concluded, it must evaluate the defendants' preemption claims in light of the assumption "that Congress does not cavalierly pre-empt state-law causes of action."⁴²⁶ Unfortunately for the defendants, the court ultimately determined that their preemption arguments did "not withstand that level of scrutiny."⁴²⁷

Turning to the defendants' impossibility preemption argument, the court began by pointing out that "[i]mpossibility pre-emption is a demanding defense."⁴²⁸ The court acknowledged that the Hatch-Waxman Amendments prohibited FDA approval of an ANDA for a generic drug unless the proposed labeling was the same as that of the listed drug.⁴²⁹ However, the court held that nothing in either the statutory scheme or FDA regulations made it impossible for the manufacturer to change the labeling of an ANDA-approved generic drug to comply with a state law requirement.⁴³⁰ In particular, the court relied on the reasoning of the *Wyeth* case to conclude that manufacturers of generic drugs could use the CBE process to effectuate labeling changes to their products.⁴³¹ Finally, the court rejected the defendants' argument that FDA would treat a drug as misbranded if the manufacturer unilaterally changed the approved labeling.⁴³² Echoing *Wyeth*, the court declared that "[t]he FDCA does not provide that a drug is misbranded simply because the manufacturer has altered an FDA-approved label; instead, the misbranding provision focuses on the substance of the label and, among other things, proscribes labels that fail to include 'adequate warnings.'"⁴³³ Consequently, the court concluded that the defendants had failed to satisfy the requirements of impossibility preemption.⁴³⁴

⁴²² *Id.* at 281.

⁴²³ *Id.*

⁴²⁴ *Id.* at 291 (quoting *Wyeth*, 129 S. Ct. at 1194-95).

⁴²⁵ *Id.*

⁴²⁶ *Id.* (quoting *Wyeth*, 129 S. Ct. at 1195 n.3).

⁴²⁷ *Id.*

⁴²⁸ *Id.* at 293 (quoting *Wyeth*, 129 S. Ct. at 1193).

⁴²⁹ *Id.*

⁴³⁰ *Id.* at 293-302.

⁴³¹ *Id.* at 295-302.

⁴³² *Id.* at 306-307.

⁴³³ *Id.* at 306 (quoting *Wyeth*, 129 S. Ct. at 1197).

⁴³⁴ *Id.* at 307 (citing *Wyeth*, 129 S. Ct. at 1197-1198).

The defendants also contended that the plaintiff's failure to warn claims would frustrate the accomplishment of the full purposes and objectives of the Hatch-Waxman Amendments.⁴³⁵ According to the defendants, they would have to conduct duplicative clinical trials in order to generate the information necessary to satisfy their duty to warn under state law.⁴³⁶ This obligation would increase the cost of generic drugs and thus frustrate the congressional goal of making available more low-cost generic drugs by streamlining the procedure for the approval of such drugs.⁴³⁷ However, the court rejected this argument, pointing out that FDA rules already required manufacturers of generic drugs to comply with potentially expensive reporting and monitoring requirements.⁴³⁸ This strongly suggested that similar requirements imposed by state law would not be sufficient to undermine Hatch-Waxman's cost-cutting objectives.⁴³⁹ Finally, the court found that preempting failure to warn claims would leave injured consumers without a remedy.⁴⁴⁰ In the court's view, if Congress wished to make such a tradeoff, "it surely would have expressed that intent more clearly."⁴⁴¹ Consequently, the court held that the plaintiff's failure to warn claims were not preempted.⁴⁴²

VI. CONCLUSION

In *Wyeth v. Levine*, the Supreme Court held that a failure to warn against the manufacturer of a listed or name brand prescription drug was not impliedly preempted when the manufacturer had not attempted to change the FDA-approved labeling and FDA had not indicated that there was insufficient scientific evidence to justify a label change. However, the *Wyeth* Court did not limit itself to the issues in the case itself; instead, it created a template for courts to follow when they decide other preemption cases. As the discussion in Part V indicates, the lower federal courts have not been slow to take advantage of the *Wyeth* Court's template. Briefly, there are three steps to the Court's preemption analysis in *Wyeth*: First, the Court invokes presumption against preemption, thereby placing the burden on the defendant to prove convincingly the existence of a conflict. Second, the Court raises the bar against any impossibility argument by assuming that manufacturers can change a drug's labeling either by seeking FDA approval or by using the CBE process. To avoid this, the manufacturer must present compelling evidence that FDA would reject the proposed labeling change. Third, the Court makes it very difficult for defendants to make an obstacle preemption argument because it rejects FDA's assertion of a conflict in its Preamble on Preemption and it instead concludes that Congress has consistently affirmed the role of state tort claims as an effective complement to FDA's regulatory program.

The first element of the *Wyeth* Court's preemption analysis is the presumption against preemption. In *Wyeth*, the Court declared that "[i]n all preemption cases, and particularly in those in which Congress has legislated ... in a field which the States have traditionally occupied," a court must begin its examination of congressional intent "with the assumption that the historic police powers of the States were not to

⁴³⁵ *Id.*

⁴³⁶ *Id.*

⁴³⁷ *Id.*

⁴³⁸ *Id.*

⁴³⁹ *Id.* at 308.

⁴⁴⁰ *Id.*

⁴⁴¹ *Id.* at 309 (quoting *Bates v. Dow Agrosciences LLC*, 544 U.S. 431, 449 (2005).)

⁴⁴² *Id.*

be superseded by the Federal Act unless that was the clear and manifest purpose of Congress.”⁴⁴³ The Court described the presumption against preemption as one of the “two cornerstones” of our “preemption jurisprudence.”⁴⁴⁴ It also rejected the notion that the presumption should not apply in areas, such as drug regulation, where there was a longstanding and significant pattern of federal regulatory activity.⁴⁴⁵ Instead, the Court observed that the presumption “accounts for the historic presence of state law but does not rely on the absence of federal regulation.”⁴⁴⁶ In addition, the Court emphasized the historic coexistence of state tort law and federal drug regulation⁴⁴⁷ and concluded that “Congress took care to preserve state law” when it amended the FDCA on several occasions.⁴⁴⁸ This endorsement of the presumption against preemption has not been lost on the lower federal courts.⁴⁴⁹

The second element of the Court’s analysis involved impossibility preemption. The Court set the bar high for defendants by observing that “[i]mpossibility preemption is a demanding defense.”⁴⁵⁰ The Court also dampened the prospects for a successful impossibility claim by concluding that manufacturers could use the CBE procedure to change a drug’s labeling cheaply and expeditiously.⁴⁵¹ First, the Court sidestepped the defendant’s claim that it could only use the CBE procedure to change a drug’s labeling “to reflect newly acquired information.”⁴⁵² Next, it rejected the contention that changing Phenergan’s labeling would cause FDA to characterize it as a new drug lacking NDA approval or that FDA would treat it as “misbranded.”⁴⁵³ More importantly, the Court flatly rejected the defendant’s argument that FDA, not the manufacturer, bore the primary responsibility for drug labeling. Using language that has been subsequently repeated by a number of lower federal courts,⁴⁵⁴ the *Wyeth* Court declared:⁴⁵⁵

Yet through many amendments to the FDCA and to FDA regulations, it has remained a central premise of federal drug regulation that the manufacturer bears responsibility for the content of its label at all times. It is charged both with crafting an adequate label and with ensuring that its warnings remain adequate as long as the drug is on the market.

Finally, while the Court acknowledged that FDA could refuse to approve a proposed labeling change, “absent clear evidence that the FDA would not have

⁴⁴³ *Id.* at 1194-1195.

⁴⁴⁴ *Wyeth*, 129 S. Ct. at 1194-1195.

⁴⁴⁵ *Id.* at 1195, n. 3

⁴⁴⁶ *Id.*

⁴⁴⁷ *Id.* at 1200.

⁴⁴⁸ *Id.* at 1195-1196.

⁴⁴⁹ *See, e.g.*, *Demahy v. Actavis, Inc.*, 593 F.3d 428, 434, *3 (5th Cir. 2010); *Mensing v. Wyeth, Inc.*, 588 F.3d 603, 607-608 (8th Cir. 2009); *Bartlett v. Mutual Pharmaceutical Co.*, 659 F. Supp. 2d 279, 291 (D.N.H. 2009); *Stacel v. Teva Pharmaceuticals, USA*, 620 F. Supp. 2d 899, 903 (N.D. Ill. 2009); *Schrock v. Wyeth, Inc.*, 601 F. Supp. 2d 1262, 1264(W.D. Okla. 2009).

⁴⁵⁰ *Wyeth*, 129 S. Ct. at 1199.

⁴⁵¹ *Id.*

⁴⁵² *Id.* at 1196-1197 (citing Rules and Regulations, HHS, FDA, 21 CFR Parts 314, 601 and 814, Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics and Medical Devices, 73 Fed. Reg. 49,603, 49,609 (Aug. 22, 2008).

⁴⁵³ *Id.* at 1197.

⁴⁵⁴ *See, e.g.*, *Demahy v. Actavis, Inc.*, 593 F.3d 428, 448, *4 (5th Cir. 2010); *Mensing v. Wyeth, Inc.*, 588 F.3d 603, 612 (8th Cir. 2009); *Stacel v. Teva Pharmaceuticals, USA*, 620 F. Supp. 2d 899, 904 (N.D. Ill. 2009).

⁴⁵⁵ *Wyeth*, 129 S. Ct. at 1197-1198.

approved a change to [the] label," it declined to find that FDA would reject the proposed change.⁴⁵⁶ All of this suggests that manufacturers who wish to invoke impossibility preemption as a defense will have to show, at a minimum, that they made some affirmative effort to change their product's labeling or persuade FDA to do so. It is even possible that the lower courts will interpret this language in *Wyeth* as a requirement that FDA explicitly reject a proposed label change in order to raise impossibility preemption as a defense.

The third element of the *Wyeth* Court's analysis was concerned with obstacle preemption. The Court firmly rejected the defendant's obstacle argument, declaring that it relied on "an untenable interpretation of congressional intent and an overbroad view of the agency's power to preempt state law."⁴⁵⁷ The principal source of this "overbroad view" of FDA's power to preempt state law was its 2006 Preamble on Preemption.⁴⁵⁸ Had the Court deferred the FDA's position on preemption, as reflected in the Preamble, the defendant might have prevailed on this issue. However, the Court declared in no uncertain terms that the Preamble was not entitled to deference.⁴⁵⁹ In the first place, the Court pointed out that the Preamble suffered from a number of procedural deficiencies.⁴⁶⁰ For example, when FDA published a notice of proposed rulemaking in December, 2000, it assured the public that the rule would "not contain policies that have federalism implications or that preempt State law."⁴⁶¹ Furthermore, when FDA issued the final rule containing the Preamble, it did not offer the states or other interested parties a chance to comment or object even though the Preamble would have a significant adverse effect on state interests.⁴⁶² Consequently, the Court concluded that FDA's views were "inherently suspect in light of this procedural failure."⁴⁶³

The Court also observed that the Preamble reversed FDA's longstanding position that state tort law was compatible with FDA regulation of prescription drugs without providing any sort of reasoned explanation for such a radical change in its former position.⁴⁶⁴ According to the Court, on numerous occasions before 2006, FDA characterized its labeling requirements as "a floor upon which States could build" and it consistently declined to preempt state law failure to warn claims.⁴⁶⁵ The Court also declared that in the past FDA had acknowledged

⁴⁵⁶ *Id.* at 1198.

⁴⁵⁷ *Id.* at 1199.

⁴⁵⁸ *Wyeth*, 129 S. Ct. at 1200.

⁴⁵⁹ *Id.*

⁴⁶⁰ *Id.*

⁴⁶¹ *Id.* (quoting from Proposed Rules, HHS, FDA, 21 CFR Part 201, Requirements on Content and format of Labeling for Human Prescription Drugs and Biologics; Requirements for Prescription Drug Product Labels, 65 Fed. Reg. 81, 082, 81,103 (Dec. 22, 2000)).

⁴⁶² *Id.*

⁴⁶³ *Id.*

⁴⁶⁴ *Id.*

⁴⁶⁵ *Id.* at 1201-1202. See, e.g., Prescription Drug Product Labeling: Medication guide Requirements, 63 Fed. Reg. 66,378, 66,384 (Dec. 1, 1998) (declaring that "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"); Protecting the Identities of Reporters of Adverse Events and Patients; Preemption of Disclosure Rules, 59 Fed. Reg. 3944, 3948 (Jan. 27, 1994) (observing that "FDA recognizes the sophistication and complexity of private tort litigation in the United States and the proposed preemption action is not intended to frustrate or impede tort litigation in this area"); Labeling and Prescription Drug Advertising; Content and format for Labeling for Human Prescription Drugs, 44 Fed. Reg. 37,434, 37,437 (June 26, 1979) (stating that "[i]t is not the intent of the FDA to influence the civil tort liability of the manufacturer . . ."); but see Requirements on Content and Format of Labeling for Human Prescription Drug and biological Products, 71 Fed. Reg. 3922, 3934 (Jan. 24, 2006) (describing the position taken in the Preamble as reflecting "the government's long standing views on preemption").

the limited nature of its resources and had treated common law tort suits as a complementary form of drug regulation.⁴⁶⁶ In the Court's view, FDA's "dramatic change in position" provided no persuasive explanation for why tort litigation had suddenly changed from being a useful supplement to FDA regulation to an obstacle to that agency's regulatory mission.⁴⁶⁷

Furthermore, the Court also refused to give any deference to the United States' *amicus* brief, which supported FDA's contention that failure to warn claims should be preemption on obstacle preemption grounds.⁴⁶⁸ In contrast to the Government's *amicus* brief in *Geier*, for example, which explained in detail the potential adverse effects of "no airbag" claims on DOT's policy of gradual introduction of airbags, the *Wyeth* Court maintained that the Government's brief failed to adequately explain the reason for the FDA's sudden shift in its policy on preemption.⁴⁶⁹

Finally, the Court observed that "FDA has traditionally regarded state law as a complimentary form of drug regulation."⁴⁷⁰ The Court pointed out that FDA had limited resources to monitor the 11,000 drugs currently on the market.⁴⁷¹ On the other hand, tort suits led to the discovery of previously unknown drug hazards and provided an economic incentive for drug manufacturers to disclose risks promptly to health professionals and the public.⁴⁷² Consequently, the Court concluded that failure to warn claims like the plaintiff's did not obstruct federal regulation of drug labeling.⁴⁷³ It should be emphasized that the Court's view of the relationship of federal regulation and state tort law was not limited to the specifics of the *Wyeth* case, but was fully applicable to other FDA preemption cases as well.⁴⁷⁴

To conclude, it remains to be seen whether legal scholars will consider *Wyeth* to be a landmark preemption case. However, by providing a template for deciding whether failure to warn claims against the manufacturers of prescription drugs are preempted on actual conflict grounds, the *Wyeth* case has already had a significant influence on several failure to warn cases and is likely to provide guidance to other courts in the future. For that reason, it is an important contribution to the Supreme Court's preemption jurisprudence.

⁴⁶⁶ *Id.* at 1202.

⁴⁶⁷ *Id.* at 1203.

⁴⁶⁸ The United States had filed *amicus* briefs on behalf of FDA in a number of cases, including *Colacicco v. Apotex Inc.*, 432 F. Supp. 2d 514 (E.D. Pa. 2006), 521 F.3d 253 (3d Cir. 2008).

⁴⁶⁹ *Wyeth*, 129 S. Ct. at 1203 n. 13.

⁴⁷⁰ *Id.* at 1202.

⁴⁷¹ *Id.*

⁴⁷² *Id.*

⁴⁷³ *Id.* at 1204.

⁴⁷⁴ *See, e.g., Demahy v. Actavis, Inc.*, 593 F.3d 448-49, *14 (5th Cir. 2010); *Schrock v. Wyeth, Inc.*, 601 F. Supp. 2d 1262, 1265 (W.D. Okla. 2009).