



The Voice of the Defense Bar

# *Preparing for Plaintiffs' Recent Theories in Drug and Device Litigation*

**Tuesday, April 10, 2007**

3:00 PM – 4:30 PM Eastern

2:00 PM – 3:30 PM Central

1:00 PM – 2:30 PM Mountain

12:00 PM – 1:30 PM Pacific

Presented By:

Joseph K. Hetrick

[joseph.hetrick@dechert.com](mailto:joseph.hetrick@dechert.com)

Mary Nold Larimore

[Larimore@icemiller.com](mailto:Larimore@icemiller.com)

Jeffrey Pilkington

[jeff.pilkington@dgsllaw.com](mailto:jeff.pilkington@dgsllaw.com)

## DEFENDING AGAINST NOVEL FAILURE TO WARN CLAIMS

BY

JEFFREY R. PILKINGTON AND JORDAN LIPP, DAVIS GRAHAM & STUBBS LLP

FOR THE DRI TELECONFERENCE OF APRIL 10, 2007

”PREPARING FOR PLAINTIFFS’ RECENT THEORIES IN DRUG AND DEVICE LITIGATION”

Jeffrey R. Pilkington is a partner of Davis Graham & Stubbs LLP, in Denver, Colorado. His practice focuses on pharmaceutical, medical device, products liability, civil rights and commercial litigation. He has served as national regional and local counsel for manufacturers of numerous products, including a wide variety of pharmaceuticals and dietary supplements. A very active portion of his practice involves the “generic only” cases discussed in this paper. He is active in DRI and other bar associations. Mr. Pilkington may be contacted as follows: Davis Graham & Stubbs LLP, 1550 Seventeenth Street, Suite 500, Denver, Colorado 80202; telephone or facsimile – 303.892.7513 (office) or 303.893.1379 (facsimile); or email – jeff.pilkington@dgsllaw.com.

Jordan Lipp is an associate in the product liability group of Davis Graham & Stubbs LLP. His practice focuses on pharmaceutical, medical device, products liability and commercial litigation. Mr. Lipp may be contacted as follows: Davis Graham & Stubbs LLP, 1550 Seventeenth Street, Suite 500, Denver, Colorado 80202; telephone or facsimile – 303.892.7471 (office) or 303.893.1379 (facsimile); or email – jordan.lipp@dgsllaw.com.

## TABLE OF CONTENTS

	Page
INTRODUCTION .....	1
DISCUSSION .....	2
I. LIABILITY FOR THE LABEL IN GENERIC ONLY CASES .....	2
A. Relevant FDA Regulations .....	2
1. Regulations Concerning Initial Approval of the Label .....	2
2. Regulations Concerning Post-Approval Revisions to the Label .....	3
3. Regulations Concerning Pharmacovigilance .....	3
B. The Innovator Has No Liability in Generic Only Cases .....	4
1. Foster and Its Progeny .....	4
2. Plaintiff Did Not Ingest and Was Not Injured by the Innovator’s Drug .....	5
3. The Innovator Does Not Owe a Duty .....	6
C. The Generic Manufacturer is Liable for Its Label in Generic Only Cases .....	8
D. Conclusion .....	9

**TABLE OF CONTENTS**  
(continued)

	<b>Page</b>
II. THE RESURGENCE OF CONFLICT PREEMPTION .....	9
A. The Preamble .....	10
B. The “Broad Preemption” Defense.....	11
1. Background and the Spectrum of Broad Preemption.....	11
2. “Approval Only” .....	11
3. “Approval Plus Rejection of Plaintiff’s Theories”.....	12
4. “Approval Plus” – Somewhere Between the Extremes .....	14
C. The “Generic Preemption” Defense.....	14
1. Arguments For and Against Generic Preemption, and the FDA’s Position .....	14
2. Court Rulings on Generic Preemption .....	16
a. Rulings in Favor of Generic Preemption .....	16
b. Rulings Against Generic Preemption.....	17
D. Use of the Preamble in Defending Failure to Warn Claims.....	17
E. Conclusion .....	18
III. THE CAUSATION DEFENSE TO FAILURE TO WARN CLAIMS .....	18
A. Brief Overview of Causation .....	18
B. Practice Implications.....	19
CONCLUSION .....	20

## **DEFENDING AGAINST NOVEL FAILURE TO WARN CLAIMS**

BY

JEFFREY R. PILKINGTON AND JORDAN LIPP, DAVIS GRAHAM & STUBBS LLP

FOR THE DRI TELECONFERENCE OF APRIL 10, 2007

”PREPARING FOR PLAINTIFFS’ RECENT THEORIES IN DRUG AND DEVICE LITIGATION”

### **INTRODUCTION**

This paper addresses three concepts with regards to successfully defending innovator and generic drug manufacturers against recent and novel failure to warn claims.

The first defense arises in “generic only cases” – cases in which the injured plaintiffs ingested only the generic drug, but not the innovator drug. In growing numbers, plaintiffs are asserting claims against both the innovator and generic manufacturer in such cases. Although plaintiffs still argue that the generic manufacturer is liable for its generic drug under traditional product liability doctrines, they also assert claims against the innovator. Plaintiffs argue that the innovator is liable for harm caused by the misrepresentations made in the label of its drug, which is virtually identical to the label of the generic drug. In some cases, the generic manufacturer has attempted to disclaim responsibility for the label and shift some or all responsibility to the innovator. As discussed below, the innovator has successfully defended these failure to warn claims by arguing that its product did not cause the harm and that it owed no duty to the plaintiff who consumed the generic drug.

The second defense is conflict preemption. The recent FDA Preemption Preamble and FDA amicus briefs have renewed the defenses of “broad preemption” for both innovators and generic manufacturers and “generic preemption” for generic manufacturers. *See, e.g.,* Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922, 3933-3936 (Jan. 24, 2006) (hereinafter “Preamble”). Although there continues to be great uncertainty about preemption, it seems that manufacturers will have greatest success where the FDA has considered and rejected the plaintiffs’ labeling theories. The generic manufacturer has an additional preemption defense – “generic preemption.” Under this doctrine, any failure to warn claims asserted against the generic manufacturer are preempted because it cannot revise its label without prior FDA approval. This narrower type of preemption has had mixed success in the courts. Finally, general attributes of preemption – the involvement of the FDA in the labeling process – could and should be used to defend the label.

The final defense is the element of causation for a failure to warn claim. As a general rule, the manufacturer should not be liable where the prescriber did not review the label and/or would not have changed her prescribing decision based on plaintiff’s labeling theories. Although there are variations in these legal principles from jurisdiction to jurisdiction, manufacturers should carefully consider causation throughout discovery and at trial. Section III briefly highlights some of the nuances and uses of the causation defense.

## DISCUSSION

### **I. LIABILITY FOR THE LABEL IN GENERIC ONLY CASES**

Plaintiffs' fundamental assertion in generic only cases is that both the innovator and generic manufacturer failed to adequately warn about the use of or risks associated with the drug. Accordingly, plaintiffs argue that the fault for the warning inadequacies should be allocated among both manufacturers. This assertion is premised on the undeniable reality that, for all intents and purposes, both drugs and both labels are identical. This section begins by explaining the relevant FDA regulations at issue in this debate and concludes by analyzing the liability of both manufacturers.

#### **A. Relevant FDA Regulations**

To better understand the liability in generic only cases, one must understand several basic regulations applicable to innovator and generic manufacturers. These regulations cover: (1) the initial approval of the label; (2) post-approval revisions to the label; and (3) post-approval pharmacovigilance.

##### **1. Regulations Concerning Initial Approval of the Label**

Pursuant to the Federal Food, Drug and Cosmetic Act ("FDCA"), the FDA regulates the manufacture, sale and labeling of prescription drug products. Among other responsibilities, the FDA ensures that drugs are safe and effective, 21 U.S.C. § 355(d) and § 393(b)(2)(B), and that they are properly labeled, *i.e.*, not "misbranded." *Id.* §§ 331(a), (b), and (k), 352 and 321(n).

Before marketing a prescription drug, a pharmaceutical manufacturer must obtain regulatory approval. For the innovator drug, the innovator must submit a New Drug Application ("NDA"). *Id.* § 355(a)-(i). The innovator must prove both safety and efficacy of the drug through extensive laboratory and clinical trials. *Id.* § 355(b)(1)(A). The innovator also must submit the proposed labeling that will accompany the drug. *Id.* § 355(b)(1)(F). The FDA will deny the NDA if the innovator does not provide, among other things, "adequate tests ... to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling." *Id.* § 355(d)(1).

Once the NDA is approved, the innovator has the exclusive right to market the drug for a certain period of time. Once that exclusivity period has expired, other drug manufacturers may market generic versions of the innovator drug if such approval has been obtained under the FDCA.

The approval procedure for generic drugs was relaxed and abbreviated by the Drug Price Competition and Patent Term Restoration Act of 1984 (commonly known as the "Hatch-Waxman Amendments"), Pub. L. No. 98-417, 98 Stat. 1584 (1984). Before 1984, a generic manufacturer was required to submit its own NDA, which required the same proof required for an innovator drug. Since the adoption of these amendments, a generic manufacturer is required to submit only an Abbreviated NDA, or "ANDA." The generic manufacturer no longer has to submit independent evidence of safety or efficacy. Instead, it must establish, among other things, that: (1) the generic drug generally has the same active ingredient as the brand name drug and is a "bio-equivalent" to the innovator drug, *id.* § 355(j)(2)(A)(ii), (iv); and (2) the proposed label of the generic drug is "the same as" that of the innovator drug. *Id.* § 355(j)(2)(A)(v).

To establish that the label is the same, the generic manufacturer must submit a side-by-side comparison of the previously approved innovator label and the proposed generic label. 21 C.F.R. § 314.94(a)(8)(iv). The only differences that are allowed are those that reflect a different manufacturer or a different “active ingredient” or “route of administration, dosage form, or strength” than the innovator drug. *Id.* § 314.93(b). Simply stated, the FDA will not approve an ANDA unless, with exceptions not relevant here, the applicant demonstrates that the “labeling proposed for the [generic] drug is the same as the labeling approved for the listed drug.” 21 U.S.C. § 355(j)(2)(A)(v). Thus, the generic manufacturer can provide no input to or diverge from the innovator’s label in any pertinent way at the time of approval.

## **2. Regulations Concerning Post-Approval Revisions to the Label**

Once the NDA is approved, an innovator may revise its labels in two ways. First, it may submit a proposed labeling change to the FDA for prior approval. In this situation, the innovator submits information and support for the proposed revision and awaits the FDA’s approval. This is by far the most common approach used by innovators to effect labeling changes. Second, the innovator may add or strengthen a warning statement in a label without prior FDA approval. 21 C.F.R. § 314.70(c)(6)(iii)(A). To do so, the manufacturer must make a supplemental submission to the FDA about the proposed change along with a full basis for the change. *Id.* § 314.70(c). If the FDA does not reject the submission within 30 days, the innovator may distribute the drug with the new labeling. The FDA, however, may choose to reject the proposed labeling change even after that date, and may order the manufacturer to cease distribution of the drug with the revised labeling. *Id.* § 314.70(c)(7). Innovators rarely use this latter method; instead, they usually seek prior FDA approval.

In contrast, a generic manufacturer has only one way to make post-approval labeling revisions. If a generic manufacturer believes that new safety information should be added to its label, the generic manufacturer must seek prior approval from the FDA and submit “adequate supporting information” for the proposed revision. Abbreviated New Drug Application Regulations, 57 Fed. Reg. 17,950, 17,961 (Apr. 28, 1992). As the FDA has explained, “[a]fter approval of an ANDA, if an ANDA holder believes that new safety information should be added, it should provide adequate supporting information to FDA, and FDA will determine whether the labeling for the generic and listed drugs should be revised.” *Id.* at 17,961. The FDA will consider this information to determine whether the labeling for both the generic and innovator drug should be revised. *Id.* This is similar to the prior-approval procedure followed by the innovator. Unlike the innovator, however, the generic manufacturer may not make a labeling change without prior FDA approval. If the generic manufacturer did so, it would be in violation of the regulations and subject to FDA withdrawal of its approved ANDA. *See* 21 C.F.R. § 314.150(b)(10); *see also* Abbreviated New Drug Application Regulations, 57 Fed. Reg. at 17,961.

## **3. Regulations Concerning Pharmacovigilance**

Following FDA approval to market a drug, both the innovator and generic manufacturer are subject to continuing obligations to monitor, analyze and report adverse effects associated with the drug. *See* 21 U.S.C. § 355(k); 21 C.F.R. §§ 314.80, 314.81, 314.98. They must keep records of and report adverse effects associated with the use of their drug regardless of whether they are “considered drug related.” 21 C.F.R. §§ 314.80(a), (c), 314.98(a). For “serious and unexpected” adverse events, manufacturers must submit a report within 15 days after learning of the adverse event and investigate these events. *Id.* § 314.809(c)(1). Manufacturers also must review the published literature relating to their drugs. *See id.*

§§ 314.80(b), (d), 314.81(b)(2). Published literature and other information must be reported to the FDA in annual and special reports. *See id.* § 314.80.

Many generic manufacturers, however, do not perform some of these tasks. Instead, they rely on the innovator to do so. Generic manufacturers often justify this conduct as the “custom and practice” of the generic industry.

## **B. The Innovator Has No Liability in Generic Only Cases**

Although some plaintiffs pursue traditional product liability claims against the innovator, most now limit their claims to fraud and misrepresentation only. In doing so, they plead the simple and basic common law elements of these claims, as set forth below. *See* Restatement (Second) of Torts § 311 (negligent misrepresentation involving risk of physical harm to another). First, the innovator owed a duty to the physician and/or the injured plaintiff to provide an accurate label. Second, the label contained false and/or misleading statements. Plaintiffs allege that the innovator provided false and misleading information to physicians and/or patients in its label and/or marketing materials for the innovator drug. Third, the prescribing physician and/or plaintiff relied on the misstatements in the label in prescribing and/or using the generic drug. Finally, such reliance was justified. Since the innovator and the generic drug are the same, such reliance is foreseeable and expected.

Plaintiffs’ approach often creates competing tensions between the innovator and generic manufacturer. The innovator disclaims liability because the plaintiff was not injured by its drug; whereas, the generic manufacturer disclaims liability because it was compelled by regulation to use the innovator’s label. As explained below, courts resolve these competing tensions by referring to both basic product liability principles and the public policy embodied by the FDA’s regulatory scheme. Thus far, courts have correctly and universally held that an innovator is not liable in a generic only case.

### **1. Foster and Its Progeny**

The first case to consider these arguments was *Foster v. American Home Products Corp.*, 29 F.3d 165 (4<sup>th</sup> Cir. 1994). In *Foster*, the parents of Brandy Foster sued Wyeth, the innovator of Phenergan, a drug used to treat colic in infants. Brandy Foster died after taking several doses of promethazine syrup plain, the generic equivalent of Phenergan. The Fosters argued that Wyeth was liable for Brandy’s death on a negligent misrepresentation theory. The district court accepted plaintiffs’ argument that this claim was distinct from a product liability claim, and thus did not require that the defendant be the manufacturer of the drug ingested. *Id.* at 168.

On appeal, the Fourth Circuit disagreed and held that “a name brand manufacturer cannot be held liable on a negligent misrepresentation theory for injuries resulting from use of another manufacturer’s product.” *Id.* at 167. In doing so, the court articulated two different bases for its holding – both of which have become the stated rationale in subsequent cases.

The first basis was that, in any case where a plaintiff alleges an injury caused by a product, regardless of the legal theory relied upon, the plaintiff must prove that the defendant was the manufacturer or seller of the product. *Id.* at 170-71. Thus, the court found that the Fosters had no claims for negligent misrepresentation and fraud against the innovator because it did not manufacture the drug their daughter actually ingested. *Id.*

The second basis was that as a matter of law, an innovator owes no duty to the consumer of the generic equivalent. *Id.* at 171. In assessing whether a duty existed, the court applied Maryland law and focused exclusively on whether the injury was foreseeable to the innovator. With minimal analysis, it concluded:

[t]o impose a duty in the circumstances of this case would be to stretch the concept of foreseeability too far. The duty required for the tort of negligent misrepresentation arises when there is “such a relation that one party has the right to rely for information upon the other, and the other giving the information owes a duty to give it with care.” There is no such relationship between the parties to this case, as Brandy Foster was injured by a product that Wyeth did not manufacture.

*Id.* (citations omitted). In reaching this conclusion, the court emphasized that fundamental fairness prohibited the innovator from being held liable for injuries caused by the generic drug. *Id.* at 169-70. It would be unfair for generic manufacturers to benefit from the research and development of the innovator while bearing no liability for their products. *Id.*

Numerous courts have addressed this same question, and all have followed or cited *Foster* with approval. *E.g.*, *Conte v. Wyeth, Inc.*, No. CGC-04-437832 (Cal. Sup. Ct. Jan. 29, 2007) (applying California law); *Goldych v. Eli Lilly & Co.*, No. 5:04-CV-1477, 2006 WL 2038436 (N.D.N.Y. July 19, 2006) (applying New York law); *Colacicco v. Apotex, Inc.*, 432 F. Supp. 2d 514 (E.D. Pa. 2006) (applying Pennsylvania law); *Tarver v. Wyeth, Inc.*, Civil Action No. 3-04-2036, 2005 WL 4052382 (W.D. La. June 7, 2005) (applying Louisiana law); *Block v. Wyeth, Inc.*, No. 3:02-CV-1077-N, 2003 U.S. Dist. LEXIS 1169 (N.D. Tex. Jan. 28, 2003) (applying Texas law); *DaCosta v. Novartis AG*, 01-cv-800, 2002 WL 31957424 (D. Or. Mar. 1, 2002) (applying Oregon law); *Sheeks v. Am. Home Prods. Corp.*, No. 02CV337, slip op. (Colo. Dist. Ct. Oct. 15, 2004) (applying Colorado law); *Sharp v. Leichus*, 2004-CA-0643, 2006 WL 515532 (Fla. Cir. Ct. Feb. 17, 2006), *aff’d* No. 1D06-1315, 2007 WL 135914 (Fla. App. Dist. Jan. 22, 2007) (applying Florida law); *Kelly v. Wyeth*, MICV 2003-03314-B, 2005 WL 4056740 (Super. Ct. Mass. May 6, 2005) (applying Massachusetts law); *Sloan v. Wyeth*, No. MRS-L-1183-04, slip op. (N.J. Sup. Ct. Oct. 13, 2004) (applying New Jersey law); *Beutella v. A.H. Robins Co.*, No. 980502372, slip op. (Utah Dist. Ct. Dec. 10, 2001) (applying Utah law). As discussed below, these courts have relied on either one or both of the arguments articulated in *Foster*, with many courts conflating the two.

## **2. Plaintiff Did Not Ingest and Was Not Injured by the Innovator’s Drug**

The innovator’s first and best argument in a generic only case is simply that it is a product liability case. Regardless of the name given to the claims, the plaintiff alleges injuries caused by a product – the generic drug. In a product liability case, the only cognizable claims are those against the manufacturer or seller of the generic drug; therefore, the plaintiff has no cognizable claim against the innovator. Two sources of authority for this argument are available – state statutes and common law.

Some states have statutes that provide a very strong basis for this argument. *See, e.g.*, Colo. Rev. Stat. § 13-21-401(2) (“‘Product liability action’ means any action brought against a manufacturer or seller of a product, regardless of the substantive legal theory or theories upon which the action is brought, for or on account of personal injury, death, or property damage caused by or resulting from the manufacture,

construction, design, formula, installation, preparation, assembly, testing, packaging, labeling, or sale of any product, or the failure to warn or protect against a danger or hazard in the use, misuse, or unintended use of any product, or the failure to provide proper instructions for the use of any product.”); La. Rev. Stat. § 9:2800.52 (“A claimant may not recover from a manufacturer for damage caused by a product on the basis of any theory of liability that is not set forth in this Chapter.”); N.J. Stat. Ann. § 2A:58C-1(b)(2) (“‘Product liability action’ means any claim or action brought by a claimant for harm caused by a product, irrespective of the theory underlying the claim . . .”). Courts have relied on these statutes to hold that plaintiffs may not bring claims of any kind against innovators for injuries caused by a drug manufactured by the generic manufacturer. *E.g.*, *Sheeks*, No. 02CV337, slip op. at 2 (citing Colorado statute); *Tarver*, 2005 WL 4052382, at \*2 (citing Louisiana statute); *Sloan*, No. MRS-L-1183-04, slip op. at 7 (citing New Jersey statute).

Other courts have relied on state common law rules for the same principle. *E.g.*, *Foster*, 29 F.3d at 168 (Maryland common law); *Goldych*, 2006 WL 2038436, at \*2 n.3 (New York common law); *Colacicco*, 432 F. Supp. 2d at 541 (Pennsylvania common law). Common law, however, generally supplies weaker support because few cases are actually on point. An infinite number of cases can be cited for the proposition that the defendant must be the manufacturer or seller of the product in a product liability action. Plaintiffs can persuasively argue, however, that this basic proposition begs the pivotal question of whether plaintiffs can sue a non-manufacturer on a non-product liability theory, such as fraud or misrepresentation.

To the extent state statutes or common law indicate that plaintiffs cannot bring a claim against an innovator that did not manufacture the drug ingested, this argument permits the cleanest analysis. The rule is clear and easy to apply. It constitutes an across-the-board determination that eliminates the need for each court to perform an ad hoc duty analysis. Moreover, as discussed below, it eliminates the uncertainty that innovators will face as long as individual courts are applying varying state laws to determine whether the innovator has a duty to generic consumers.

### **3. The Innovator Does Not Owe a Duty**

Even when they have concluded that no claim lies against the innovator, many courts go on to consider whether the innovator would be liable for fraud or misrepresentation. The key element under consideration is whether the innovator had a duty to the plaintiff (including her prescriber) as a consumer of the generic drug.

As the number of these cases has grown, the litigants’ arguments and the courts’ analyses of whether an innovator owes a duty to the consumer of a generic drug have become more sophisticated. While *Foster* focused only on foreseeability in assessing duty, the litigants have argued about, and courts have applied, a variety of factors, including: the relationship between the parties, the social utility of the actor’s conduct; the nature of risk imposed and foreseeability of the harm incurred; the consequences of imposing a duty upon the actor; and the overall public interest in the proposed solution.

Plaintiffs have used these factors to argue that an innovator does owe a duty to the consumer of a generic equivalent drug. They have argued that the innovator knows that generic manufacturers are obligated by law to copy its label and that physicians rely on the innovator’s label when writing prescriptions. Even when a physician prescribes the innovator drug, pharmacies may be permitted or required to fill the prescription with the generic equivalent. Plaintiffs further assert that most innovators publish their label in the Physicians’ Desk Reference, actively promote their products, and engage in

substantial advertising, including direct-to-consumer advertising. Finally, plaintiffs point to the public policy of the Hatch-Waxman Amendments – to provide cost-effective prescription drugs for Americans. They argue that the innovators can more easily bear the costs of liability, and that to solely impose liability on generic manufacturers would increase the cost of generic prescriptions.

To date, courts have universally rejected these arguments and have ruled that there is no duty. *See* cases cited in Section I.B.1., above. Regardless of how the court’s analysis is couched (*e.g.*, as issues of foreseeability, relationship between the parties, or public policy), its substance is usually the same. The court concludes that it is unfair for the innovator to be liable for injuries caused by a drug that it did not manufacture or sell, and from which it receives no economic benefit.

In *Foster*, for instance, the court focused on the fact that, for economic reasons, generic manufacturers choose to accept the label authored by the innovators “and simply copy verbatim the name brand drugs’ package circulars.” *Foster*, 29 F.3d at 169. The *Foster* Court reasoned that innovators “undertake the expense of developing pioneer drugs, performing the studies necessary to obtain premarketing approval, and formulating labeling information,” while “[g]eneric manufacturers avoid these expenses by duplicating successful pioneer drugs and their labels.” *Id.* at 170. The court thus concluded that no duty should lie with the innovator. *Id.*; *see also Colacicco*, 432 F. Supp. 2d at 541 (“[U]nfair consequences would result if we were to impose a duty upon [the innovator], when it obtained no benefit from the sale of [the] generic equivalent and had no control over the manufacturing or labeling of [the generic drug], yet it bore the expense of developing [the innovator drug] from which [the generic manufacturer] materially benefits.”); *Sharp*, 2006 WL 515532, at \*7 (“It would be manifestly unfair to hold a name brand manufacturer responsible for injuries that arise from a product that is beyond its control.”).

In finding for the innovator, courts also invoke public policy and the wisdom of the FDA. They recite the “importance of new and effective prescription drugs” and “the need not to unduly burden the pharmaceutical industry with unfettered liability” in support of a determination that no duty lies with the innovator. *Colacicco*, 432 F. Supp. 2d at 542; *see also Kelly*, 2005 WL 4056740, at \*4-5 (focusing on the costs of research and development born by the innovators and evidence of Congress’s intent to encourage innovators to invest in new drugs). The courts have reasoned that such liability would be contrary to the FDCA. The purpose behind both the NDA and the ANDA process is to encourage innovators to invest in new drugs while at the same time enable generic competitors to bring cheaper generic drugs to the market. To impose liability on the innovator would not advance either purpose. Innovator liability would make innovators less likely to develop new products and would not advance the affordability of prescription drugs. *Sloan*, No. MRS-L-1183-04, slip op. at 9; *see also Kelly*, 2005 WL 4056740, at \*4-5. Indeed, one court has found that the plaintiff’s theory would mean that “name brand manufacturers could be held responsible for every injury caused by every product that was made by every competing generic manufacturer. . . . [S]uch a result would have a substantial and extraordinary impact on the pharmaceutical industry.” *Sharp*, 2006 WL 515532, at \*7 (footnote omitted).

Courts have also relied on the absence of any relationship between the innovator and the plaintiff – the innovator did not provide information about the generic product to the plaintiff. *Kelly*, 2005 WL 4056740, at \*4; *Conte*, CGC-04-437382, at \*4. Instead, the innovator supplied information for its product only. Moreover, the injured plaintiff rarely relies on the information included in the innovator label.

Finally, the courts also emphasize that the injured plaintiff has a viable claim against the generic manufacturer. *Sloan*, No. MRS-L-1183-04, slip op. at 10; *Sharp*, 2006 WL 515532, at \*7. This finding, however, may be weakened by successful preemption rulings obtained by generic manufacturers. See Section II.C.2., below.

### C. The Generic Manufacturer is Liable for Its Label in Generic Only Cases

Some generic manufacturers have asserted a defense that they have no duty to warn about their drugs. The generic manufacturer points to FDA regulations that require the innovator to investigate the safety and efficacy of the drug and to draft the initial label. To obtain approval for its generic drug, the generic manufacturer must establish only that its generic version is the bioequivalent of the innovator drug and that its label is identical to that of the innovator drug. Further, the generic manufacturer argues that, unlike the innovator, it cannot modify the label without prior FDA approval. The generic manufacturer argues that it is against public policy to require the generic manufacturer to (1) acquire the scientific information that supported the original NDA and then (2) assess whether a different or stronger warning is required. The imposition of the duty implicitly withheld by the Hatch-Waxman Amendments would defeat the purposes of the Act by delaying the emergence of generic equivalents and increasing generic cost to the consumer.

Plaintiffs oppose this argument by citing basic product liability law. Any manufacturer must be responsible for the label that accompanies its product. Although the generic manufacturer has to use the innovator label, it has the obligation to approach the FDA about labeling revisions when new safety information is discovered through the exercise of its pharmacovigilance obligations.

The leading case to consider and reject these arguments by a generic manufacturer is *Colacicco*. In *Colacicco*, the court concluded that the generic manufacturer's duty was proper and foreseeable because "basic tort concepts always hold a manufacturer liable for its products," and the Hatch-Waxman Amendments did not render it unforeseeable that the generic manufacturer would "be held liable for inadequacies in *its own* labels." *Colacicco*, 432 F. Supp. 2d at 544 (emphasis in original). The court disagreed that the generic manufacturer was just an intermediary that passes along the information provided by the innovator. Further, the court considered the social utility of the generic manufacturer's conduct and the public policy interests at stake. In doing so, the court explained that, "while one could argue that there is social utility in making less-expensive, generic substitutes available to the public, this Court is mindful of the fact that [the generic manufacturer] is still a business, manufacturing drugs . . . not for some altruistic reason, but to realize a profit." *Id.*

Although *Colacicco* is the only published decision in which the generic manufacturer has asserted that it has no duty, other cases have considered this same argument when raised by plaintiffs seeking to establish the liability of the innovator. For instance, in *Foster*, the plaintiffs sought to establish that the duty rested with the innovator rather than the generic, where the generic had already settled. Like *Colacicco*, the *Foster* court rejected the proposition that generics had no duty to the plaintiffs with respect to the information in the label. In support of its conclusion, the court noted that "[w]hen a generic manufacturer adopts a name brand manufacturer's warnings and representations without independent investigation, it does so at the risk that such warnings and representations may be flawed. . . . [A]s an expert, a manufacturer of generic products is responsible for the accuracy of labels placed on its products." *Foster*, 29 F.3d at 169-70. Finally, the court noted that generic manufacturers are permitted to add or strengthen warnings and delete misleading statements on labels. *Id.* "Manufacturers of generic drugs, like all other manufacturers, are

responsible for the representations they make regarding their products.” *Id.* at 170; *see also Sloan*, No. MRS-L-1183-04, slip op. at 10.

#### **D. Conclusion**

Based on the unanimous authority in its favor, the innovator has a very strong defense in the generic only case. The innovator must move to dismiss all claims based on the unanimous authority in its favor. Every court that has considered the issue has held that the innovator cannot be liable for the injuries caused by the generic drug regardless of the theories of liability. This authority appropriately places liability on the generic manufacturer for the injuries caused by its drug. To the extent courts insulate generic manufacturers from liability for their warnings, courts are more likely to do so because such liability is preempted by federal regulations, not because the generic manufacturers owe no duty to the consumers of their products.

## **II. THE RESURGENCE OF CONFLICT PREEMPTION**

Under the doctrine of “conflict preemption,” both the innovator and generic manufacturers argue that plaintiffs’ state law failure to warn claims are preempted by the FDCA and the regulations promulgated thereunder. Although the preemption defense historically has had limited success in pharmaceutical litigation, recent FDA statements and amicus briefs have renewed interest and resulted in some success for preemption. This section examines four topics relating to that defense.

The first section focuses on the Preemption Preamble. Some of the statutes and regulations relevant to the preemption defense are discussed in Section I.A., above.

The second section addresses the first of two types of the preemption defense asserted in generic only cases – “*broad preemption*.” It is best understood and analyzed by placing the FDA’s action along a spectrum. At one end of the spectrum is the “approval only” case – the FDA simply approves the label (as it does with every label) with little or no further action. At the other end of the spectrum is the “approval plus rejection of plaintiff’s theories” case – the FDA considers and rejects the substance of plaintiff’s labeling theories. Somewhere between the two extremes is the “approval plus” case – the FDA approves the label and takes some action relevant to the labeling issue in the case. As explained below, the closer the factual predicate for preemption is to the far right end of the spectrum – the FDA considered and rejected plaintiff’s labeling theories – the greater the likelihood for success for broad preemption.

The third section discusses the second type of preemption that is available only to the generic manufacturers – “*generic preemption*.” Generic preemption is premised on the FDA’s specific regulatory restrictions for generic manufacturers. Generic manufacturers assert that, unlike the innovator, they cannot change the label without prior FDA approval. Since the generic label cannot be changed, any state law failure to warn claims against the generic manufacturers conflict with the FDA’s regulatory framework, regardless of where the FDA’s oversight falls on the spectrum. Generic preemption also has had mixed success.

The final section underscores the use of basic preemption principles in defending failure to warn claims. Manufacturers can use concepts of preemption found in the Preamble to demonstrate the important role that FDA has in the labeling process. Since the FDA has not mandated a labeling change, manufacturers can persuasively argue to the trier of fact that the current labeling is reasonable and adequate.

## A. The Preamble

On January 24, 2006, the FDA issued its Preamble to the new labeling regulations. The most significant and relevant discussion of preemption is found in Comment 13 of the Preamble.

In Comment 13, the FDA was asked to state whether its “approval of labeling, whether it be in the old or new format, preempts conflicting or contrary State law, regulations, or decisions of a court of law for purposes of product liability litigation.” *Id.* at 3933-34. The FDA answered that “under existing preemption principles, FDA approval of labeling . . . preempts conflicting or contrary State law.” *Id.* at 3934. In doing so, the FDA listed six different categories in which a plaintiff’s labeling claims should be preempted by its regulation of prescription drug labeling:

- Warnings claims for “failing to put in Highlights or otherwise emphasize any information the substance of which appears anywhere in the labeling.”
- Warnings claims for “failing to include in an advertisement any information the substance of which appears anywhere in the labeling where the manufacturer has used Highlights consistent with FDA guidances for direct-to-consumer advertising.”
- Warning claims for “breach[ing] an obligation to warn by failing to include contraindications or warnings that are not supported by evidence that meets the [FDA’s] standards.”
- Warning claims for “failing to include a statement in labeling or in advertising, the substance of which had been proposed to FDA for inclusion in labeling, if that statement was not required by FDA at the time plaintiff claims the sponsor had an obligation to warn (unless FDA has made a finding that the sponsor withheld material information relating to the proposed warning before plaintiff claims the sponsor had the obligation to warn).”
- Warnings claims for “failing to include in labeling or in advertising a statement the substance of which FDA has prohibited in labeling or advertising.”
- Warning claims for “making statements that FDA approved for inclusion in the drug’s label (unless FDA has made a finding that the sponsor withheld material information relating to the statement).”

*Id.* at 3935-96. In articulating these categories, the FDA noted that its regulation of drug labels would not preempt all state law actions. *Id.* at 3936. The FDA further explained that “[s]tate laws conflict with and stand as an obstacle to achievement of the full objectives and purposes of Federal law when they purport to compel a firm to include in labeling or advertising a statement that FDA has considered and found scientifically unsubstantiated.” *Id.* at 3935. Thus, the inclusion of such information would render the drug misbranded and out of compliance. *Id.* The FDA noted that lawsuits may “conflict with the agency’s own interpretations and frustrate the agency’s implementation to its statutory mandate.” *Id.*

The FDA also made several statements about its obligations and role in drug labeling. It proclaimed that the agency is the “expert” for evaluating the label. *Id.* It “controls” the label and continues to monitor the accuracy and the need for revisions. *Id.* The agency further explained that its labeling requirements do

not provide a “minimum” safety standard. *Id.* Instead, the statutes and regulations “establish both a ‘floor’ and a ‘ceiling.’” *Id.* Additional disclosure of risk information in the label, as plaintiffs often contend should have been in place, is “not necessarily more protective of patients.” *Id.* Rather, it may “erode and disrupt the careful and truthful representation of benefits and risks that prescribers need,” “discourage appropriate use of a beneficial drug,” and dilute the significance of meaningful risk information. *Id.* Thus, plaintiffs’ claims for additional warnings “can lead to labeling that does not accurately portray a product’s risks, thereby potentially discouraging safe and effective use of approved products or encouraging inappropriate use and undermining the objectives of the act.” *Id.* Similarly, the FDA also was concerned about encouraging “defensive labeling.” *Id.*

## **B. The “Broad Preemption” Defense**

This section will provide basic background about “broad preemption,” including the spectrum of preemption. The final three parts of this section outline recent court decisions along the spectrum of preemption – from “approval only” to “approval plus rejection of plaintiff’s theories.”

### **1. Background and the Spectrum of Broad Preemption**

Under the Supremacy Clause of the United States Constitution, any state law that conflicts with the exercise of federal power is preempted. U.S. Const., art. VI, cl. 2. Conflict preemption occurs when a state law claim directly conflicts with a federal statute or regulation or where it is impossible to comply with federal law without violating state law. This preemption is best understood by placing FDA action along a spectrum. The far left side of the spectrum is defined as “*approval only*” and the far right side is defined as “*approval plus rejection of plaintiff’s theories*.” Somewhere in-between the two extremes is simply “*approval plus*.” As explained below, the more FDA action with respect to the labeling issues in the case, the greater the likelihood of success.

Before turning to the spectrum, it is important to list some recent preemption decisions. Recent court decisions that have ruled in favor of broad preemption include: *Colacicco*, 432 F. Supp. 2d 514; *In re Bextra and Celebrex Marketing Sales Practices and Prod. Liab. Litig.*, MDL No. 1699, 2006 WL 2374742 (N.D. Cal. Aug. 16, 2006); *Ackermann v. Wyeth*, No. 4:05cv84, 2006 WL 2591078 (E.D. Tex. Sep. 8, 2006), Report and Recommendation Withdrawn by *Ackermann v. Wyeth*, No. 4:05cv84, 2006 WL 3780913 (E.D. Tex. Dec. 20, 2006) (withdrawing report and recommendation on preemption issue once district court granted summary judgment on other grounds); *Abramowitz v. Cephalon, Inc.*, No. BER-L-617-04, 2006 WL 560639 (N.J. Sup. Ct. March 3, 2006). Some recent court decisions that have rejected preemption include: *Desiano v. Warner-Lambert & Co.*, 467 F.3d 85 (2<sup>nd</sup> Cir. 2006); *Peters v. Astrazeneca, LP*, 417 F. Supp. 2d 1051 (W.D. Wis. 2006); *Jackson v. Pfizer, Inc.*, 432 F. Supp. 2d 964 (D. Neb. 2006); *Laisure-Radke v. Par Pharm., Inc.*, No. C03-365RSM, 2006 WL 901657 (W.D. Wash. Mar. 29, 2006); *McNellis v. Pfizer, Inc.*, No. Civ. 05-1286 (JBS), 2006 WL 2819046 (D.N.J. Sept. 29, 2006); *In re Prempro Prods. Liab. Litig.*, No. 4:03CV1507WRW, slip op. (MDL June 15, 2006); *Perry v. Novartis Pharma. Corp.*, 456 F. Supp. 2d 678 (E.D. Pa. 2006); *Levine v. Wyeth*, \_\_\_ A.2d \_\_\_, 2006 WL 3041078 (Vt. Oct. 27, 2006).

### **2. “Approval Only”**

At the “approval only” end of the spectrum, the preemption defense is premised solely on the FDA’s approval of the label. Manufacturers argue that the FDA approved the label, and they cannot change the

label without FDA approval. Although an innovator can revise its label without prior FDA approval, innovators argue that this is only a matter of timing, not substance. The innovator can strengthen the label only temporarily, and the FDA always retains the authority to reject it. If an innovator effects a change without prior FDA approval that is then disapproved by the FDA, the drug is misbranded and distribution must cease. Further, as a practical matter, innovators rarely invoke their authority to change a label without prior FDA approval. Manufacturers also argue that the FDA has set both the floor and the ceiling for the label. The Preamble has certainly strengthened some of these arguments.

Plaintiffs sharply disagree and argue that the innovator is explicitly permitted to unilaterally change its label without prior FDA approval. 21 C.F.R. § 314.70(c)(6)(iii). Plaintiffs also argue that even though the generic manufacturers cannot change their labels without prior approval, they have a regulatory obligation to recommend labeling changes upon the discovery of new or different safety information.

Historically, courts have viewed approval only preemption with skepticism. Given recent statements of the FDA, that judicial skepticism likely will continue. *See, e.g., Peters*, 417 F. Supp. 2d at 1057 (where the FDA had not explicitly rejected the additional warning that the plaintiff requested, there was no actual conflict between state and federal law, and thus no conflict preemption). Courts typically reject the argument that the innovator cannot make changes to its label without prior FDA approval based on the simple text of 21 C.F.R. § 314.70. Because of the “changes being effected” option, “prior FDA approval need not be obtained, nor will a product be deemed mislabeled, if the manufacturer voluntarily or even unilaterally strengthens the approved warnings, precautions or potential adverse reactions upon the label pursuant to 21 C.F.R. § 314.70(c)(6)(iii)(A).” *McNellis v. Pfizer, Inc.*, No. 05-1286, 2005 WL 3752269, at \*5 (D.N.J. Dec. 29, 2005). For this and other reasons, some courts reject the proposition that the FDA sets both the floor and the ceiling with regard to labeling. Instead, they conclude that the FDA sets only the floor and does not shield the manufacturer from state law tort liability. *Id.*; *Levine*, 2006 WL 3041078, ¶ 13; *Jackson*, 432 F. Supp. 2d at 967.

In the few instances where the courts have arguably found preemption in approval only cases, the courts have focused primarily on the manufacturer’s compliance with the broad statutory and regulatory framework. For instance, in *Abramowitz*, 2006 WL 560639, at \*4, the court found preemption with minimal discussion of whether the FDA had previously considered and rejected the plaintiff’s proposed warning. Instead, the court principally relied on a New Jersey common law presumption that a manufacturer’s “duty to warn physicians about prescription drug dangers is presumptively met by compliance with federal labeling and that compliance with FDA regulations serves as compelling evidence that a manufacturer satisfied its duty to warn the physician about potentially harmful side effects of its product.” *Id.* at \*3. *See also Ackermann*, 2006 WL 2591078, at \*7 (finding preemption without relying on FDA’s prior treatment of proposed warning).

### **3. “Approval Plus Rejection of Plaintiff’s Theories”**

The second basis for broad conflict preemption – “*approval plus rejection of plaintiff’s theories*” – requires a fact intensive analysis. It is premised on factual scenarios in which the FDA has considered and rejected the particular information that plaintiff contends should have been in the label. In this instance, manufacturers argue that it would be “false and misleading,” and in violation of the regulations for the manufacturer to use the label the plaintiff argues that it should have used.

A well-publicized example of this end of the preemption spectrum is found in the anti-depressant litigation. In that litigation, the plaintiffs who took prescription anti-depressants argued that the manufacturers should have strengthened warnings regarding the possibility of increased suicidality. *See, e.g., Colacicco*, 432 F. Supp. 2d 514; *Jackson*, 432 F. Supp. 2d 964; *Laisure-Radke*, 2006 WL 901657; *McNellis*, 2006 WL 2819046. The manufacturers assert preemption because the FDA had repeatedly studied this issue and had found no link between anti-depressants and suicide during the times when plaintiffs' injuries had occurred. The manufacturers have received support from the FDA. In amicus briefs, the FDA explained that “any [strengthened] warning, no matter how worded, that could reasonably have been read as describing or alluding to such a relation [between anti-depressants and increased suicidality] would have been false or misleading, and therefore in conflict with federal law because there was no (and still is not) scientific support for such a warning.” *McNellis*, 2005 WL 3752269, at \*8 (citing FDA amicus briefs; emphasis in original). Remarkably, courts cannot agree about preemption in this context.

In response to the manufacturers' assertions, plaintiffs typically argue that the FDCA merely establishes minimum standards and permits both innovators and generic manufacturers to strengthen labels. Further, plaintiffs often argue that the manufacturers withheld pertinent information from the FDA. Thus, the FDA's determination is not dispositive because it did not have complete information regarding the subject of the proposed warning. *See, e.g., In re Bextra*, 2006 WL 2374742, at \*10. They also challenge the FDA's positions about preemption and the deference to be afforded to such positions.

There is mixed judicial precedent for a finding of conflict preemption in these cases. Some courts find preemption because plaintiffs' failure-to-warn claims sought to require the manufacturer to include in its label a warning that the FDA considered but rejected. *See id.* at \*9-10 (failure to warn claims were preempted because they sought to require the manufacturer to include in its promotion “a warning which the FDA had considered and found to be scientifically unsubstantiated”); *Colacicco*, 432 F. Supp. 2d at 526-27 (failure to warn claims were preempted, in part, because FDA had repeatedly determined that there was inadequate evidence to support plaintiff's labeling theories). The preemption defense should be stronger where the manufacturers have submitted detailed citations of the FDA's consideration and rejection of the would-be strengthened warnings, *see, e.g., Colacicco, Inc.*, 432 F. Supp. 2d at 526-27 & n.10; *Ackermann*, 2006 WL 2591078, at \*3-4, and where the FDA has submitted amicus briefs that it would have considered the label false and misleading if the manufacturers had added the proposed warnings. *Colacicco*, 432 F. Supp. 2d at 526-27 & n.10.

On the other hand, some courts have denied preemption in this context. These cases rely primarily on the rationale that the FDA's label sets only the floor for a prescription drug's warnings; it does not also set the ceiling. For instance, in *McNellis*, the court concluded that the manufacturers failed to satisfy their burden because the “‘FDA regulations are generally minimum standards of conduct’ unless Congress has expressed clear intent to preempt state common law, which it has not done here.” *McNellis*, 2005 WL 3752269, at \*8 (citation omitted). The court reached this result despite the fact that the FDA “through its amicus brief, urged that the warning of a causal relation between Zolofit and suicide would have ‘misbranded’ the drug.” *Id.* at \*8; *see also Jackson*, 432 F. Supp. 2d at 968-69 (conducting analysis similar to *McNellis*).

#### **4. “Approval Plus” – Somewhere Between the Extremes**

In most instances, the preemption defense will fall somewhere between the two ends of the spectrum – “*approval plus*.” The question is the “plus” – what type of and how much FDA action is necessary?

Manufacturers often cite to ADEs, published literature, clinical trials and other analyses submitted to the FDA as the factual predicate for preemption. They also rely on FDA pronouncements about similar labeling issues. Such evidence is used to show that the FDA has been given and has considered the same information that plaintiffs use to support their failure to warn claims. Since the FDA did not require a labeling change, the argument goes, the claims should be preempted.

Plaintiffs, of course, argue that the FDA’s inaction does not rise to the level of rejection of their theories. Further, they often argue that the manufacturers withheld certain information or downplayed the drug’s risks to the FDA.

Like the cases at each end of the spectrum, it is difficult to draw any firm conclusions about these in-between cases. The most that can be said is that the closer the specific preemption facts come to FDA consideration and rejection of plaintiffs’ labeling theories, the stronger the preemption defense. *Perry* is a good example. In that case, the court explained that where “the FDA has made a conclusive determination, positive or negative, as to the existence of a link between the drug at issue and some adverse health consequence, state law cannot mandate that a manufacturer include additional warnings beyond those that the FDA has determined to be appropriate to the risk.” *Perry*, 456 F. Supp. 2d at 685-86. However, the court found that because “the FDA had made no finding regarding a link between use of [the drug at issue] and increased cancer risk in children . . . no statute or regulation prevented [the manufacturer] from adding the warning.” *Id.* at 687 (footnote omitted); *see also Levine*, 2006 WL 3041078, at \*21 (no preemption where the record lacked evidence that “the FDA was concerned that a stronger warning was not supported by the facts, that such a stronger warning would distract doctors from other provisions in the drug’s label, or that the warning might lead to less effective administration of the drug”).

#### **C. The “Generic Preemption” Defense**

Generic manufacturers may be entitled to an additional preemption defense that will bar all failure to warn claims. This emerging defense of “generic preemption” is premised upon the different labeling obligations for the innovator and generic manufacturers. This section will summarize the arguments made in favor of and against this issue, including the FDA’s position, and address the recent case law ruling in favor of and against generic preemption.

##### **1. Arguments For and Against Generic Preemption, and the FDA’s Position**

Relying on the doctrine of conflict preemption, generic manufacturers argue that they must use the innovators’ label word-for-word; otherwise, approval of their ANDAs will be denied. More importantly, the generic manufacturer must maintain its label in conformity with the innovator’s label following approval. The generic manufacturer cannot unilaterally change its label as can the innovator. Instead, it may only change its label upon the FDA’s express direction or prior approval. Accordingly, the plaintiff’s claim that seeks to modify the generic manufacturer’s label would be in conflict with these federal statutes and regulations. The generic manufacturers also argue that the purpose of the Hatch-Waxman Amendments was

to encourage lower prices for generic drugs by permitting them to avoid the research and development costs already incurred by the innovators. Any imposition of failure to warn claims would be contrary to that purpose.

Plaintiffs have vigorously opposed these generic preemption arguments by arguing that the generic manufacturers have an affirmative obligation to revise their labels upon the discovery of new or different safety information. Thus, whether a generic manufacturer is able to change its label without prior FDA approval is irrelevant. Moreover, plaintiffs argue that they will be left without any remedy against the generic manufacturer, and perhaps the innovator, if they only used the generic form of the drug. They also cite to the inconsistencies of positions taken by the FDA as evidence that the FDA's positions should be afforded little weight. Finally, to avoid the scope of preemption, plaintiffs have tried to expand their claims beyond the label to promotional and informational materials.

The FDA recently has submitted amicus briefs in favor of generic preemption. In *Colacicco*, the FDA distinguished the labeling regulations for innovator and generic manufacturers. After explaining why it believed preemption barred the plaintiff's claims against both the innovator and the generic manufacturer, the FDA explained its position on generic preemption.

The plaintiff's failure-to-warn claims against [the generic manufacturer] . . . are barred by federal preemption for an additional reason: under federal law, a generic drug manufacturer is prohibited from changing the label for its drug product without prior FDA approval.

By statute and regulation, generic drug labels are required to replicate the warnings contained in the approved labeling for the innovator, or name-brand, drug. Accordingly, a generic manufacturer may not modify the labeling for its drug product to add a new warning or caution. If a generic drug manufacturer "believes that new safety information" should be included on the product's labeling, the manufacturer must "provide adequate supporting information to FDA, and FDA will determine whether the labeling for the generic and [innovator] drugs should be revised." Without prior FDA approval, however, no such change can be made.

The plaintiff's claim against Apotex[, the generic manufacturer,] is premised on the theory that Apotex had an obligation to modify its label under 21 C.F.R. § 314.70(c) to add a new warning for suicide or suicidality. As we have explained, however, . . . that provision does not permit generic manufacturers to modify their drug labeling without FDA approval. Generic drug manufacturers are required both by statute and by regulation to use drug labeling that is the same in relevant respects "as the labeling approved for the listed drug."

Brief of the United States as Amicus Curiae in Support of Defendants-Appellees at 23-24, *Colacicco v. Apotex*, No. 06-3107 (3d Cir. Dec. 4, 2006) (citations omitted; second alteration in original). Accordingly, the FDA has seemingly supported the generic manufacturers' position.

## 2. Court Rulings on Generic Preemption

Courts have ruled for and against generic preemption. Following the publication of the Preamble and the FDA's filing of amicus briefs, some cases have ruled in favor of the generic manufacturers.

### a. Rulings in Favor of Generic Preemption

The most extensive review of the generic preemption arguments is found in *Colacicco*. In *Colacicco*, the court found that preemption (an "approval plus rejection of plaintiff's theories" case) barred claims against both the innovator and the generic manufacturer. *Colacicco*, 432 F. Supp. at 518. The court went on to explain that:

[W]e find compelling [the generic manufacturer's] argument that, pursuant to the relaxed generic approval process mandated by the Hatch-Waxman Amendments, it was *required* to use verbatim the language of [the innovator]'s warning label during the ANDA application and approval process. Thus, assigning a duty to include a warning different from [the innovator]'s approved label inherently conflicts with the FDCA. Additionally, although many courts have held that once the ANDA is approved, 21 C.F.R. § 314.70 explicitly permits unilateral strengthening of product warning labels, the FDA now says otherwise. In its *amicus* brief, the FDA explicitly asserts that "there is no statutory or regulatory provision permitting the manufacturer to make a labeling change to its generic drug without prior FDA approval." Presumably, this is to insure that the added language is substantiated by scientific data and if not-as would have been the case if [the generic manufacturer] tried to add a label linking paroxetine hydrochloride to suicidality in October 2003-it would have been deemed "misleading" and, thus, in violation of federal law.

*Id.* at 537 (citations omitted; emphasis in original). Based on the foregoing, the *Colacicco* court found that:

[S]tate tort law which would hold a generic drug manufacturer liable for failing to modify a label when, pursuant to the Hatch-Waxman Amendments to the FDCA, the ANDA approval process required that the labeling be the same as that approved for the innovator drug, and a when [sic] the FDA would have deemed any post-approval enhancements "false or misleading," would actually conflict with the FDCA.

*Id.* at 537-38. Although its language is ambiguous, litigants have argued that, based upon the former quoted passage, the *Colacicco* court found that state law failure to warn claims against generic manufacturers are preempted by generic preemption.

A California Superior Court reached a similar result, finding that all of the plaintiff's claims against the generic manufacturer were "pre-empted by federal law." *McKenney v. Wyeth, Inc.*, No. 343927, slip op. (Cal. Sup., County of Stanislaus, Jan. 12, 2007). In doing so, the *McKenney* Court explained that the FDA "has clearly pre-empted the field of labeling of generically manufactured prescription drugs. . . . Defendant . . . is a generic manufacturer of metoclopramide and, as such, must obtain approval by the FDA

before issuing any label metoclopramide which deviates from the labeling previously approved by the FDA.” *Id.* at 2.

Finally, another California Superior Court found that the plaintiff’s failure to warn claims against the generic manufacturer were preempted. *Conte v. Wyeth, Inc.*, No. CGC-04-437382, 2006 WL 2692469 (Cal. Sup., County of San Francisco, Sept. 14, 2006). Without any specific discussion of generic preemption in particular, the court found preemption. In doing so, it relied on *In re Bextra*, a case that dealt with plaintiffs’ claims that an innovator failed to warn on an issue which the FDA considered and found to be scientifically unsubstantiated. *Conte*, 2006 WL 2692469. Until the appeal is resolved, it is unclear whether court relied on the broad preemption concept of “approval only” or the more narrow doctrine of “generic preemption.” Nonetheless, *Conte* is an example of a case where generic manufacturers successfully argued that plaintiff’s claims were preempted.

**b. Rulings Against Generic Preemption**

At least two courts have reached different results and ruled against generic preemption. In Colorado, a state trial court determined that plaintiff’s claims against a generic manufacturer were not preempted. *Sheeks v. Am. Home Prods.*, Case No. 02CV337 (Colo. Dist. Ct., El Paso County, June 17, 2005). The *Sheeks* Court, although noting that the generic manufacturer “could not change the warnings on the package labeling without FDA approval,” explained that if the generic manufacturer “were truly aware of unwarned risks of using . . . [the drug at issue], it may have been negligent in failing to request that the FDA allow a change in the package label warning.” *Id.* at 1-2. Thus, the fact that the generic manufacturer could not change the label without FDA approval, according to the court, “has no bearing” on the issue. *Id.* at 2.

The United States District Court for the Western District of Washington also has rejected the generic manufacturer’s preemption defense. *Laisure-Radke*, 2006 WL 901657; *see also Laisure-Radke v. Par Pharmaceutical, Inc.*, 426 F. Supp. 2d 1163, 1169 (W.D. Wash. 2006) (discussing the Court’s previous unpublished March 29, 2006 decision). In *Laisure-Radke*, the court explained that “generic drug manufacturers, after having received an approved ANDA, have the ability to add or strengthen warnings without prior FDA approval, as long as certain conditions are met.” *Laisure-Radke*, 2006 WL 901657, at \*4. Based upon this different reading of the regulations, the *Laisure-Radke* Court concluded that “there is no conflict between the state law at issue . . . and the federal regulations.” *Id.* at \*6. The Court therefore rejected the generic manufacturer’s preemption argument. *Id.*

**D. Use of the Preamble in Defending Failure to Warn Claims**

Even if a preemption defense fails or is unavailable, manufacturers should use the Preamble in its defense of the label. As explained above, the Preamble contains very positive statements about the role, power and control of the FDA in drug labeling. It proclaims that the FDA is the expert who is uniquely qualified to assess the adequacy of labeling. It also describes the thorough review and consideration of the label by FDA.

The Preamble should be used to obtain valuable concessions from plaintiffs’ experts and to support the manufacturers’ experts. The Preamble provides very influential and important sound bites to support the argument that neither the FDA nor the manufacturers found any need to change the label. The only persons to argue inadequacy of the label are plaintiffs’ “hired guns.”

## **E. Conclusion**

The Preamble and FDA amicus briefs have advanced arguments for broad preemption for both innovators and generic manufacturers. Until appellate courts address cases along the spectrum, there will continue to be significant uncertainty in this area. Nevertheless, both innovator and generic manufacturers should always consider whether a dispositive motion based upon broad preemption is warranted under the facts of each case. Generic manufacturers stand a reasonable chance of prevailing on the more narrow concept of generic preemption. Generic manufacturers have had no success, however, arguing that they have no duty to warn. Beyond preemption, manufacturers should use the Preamble in its defense strategies to convince the jury that the FDA – the protector of public health – has found that the label is adequate.

## **III. THE CAUSATION DEFENSE TO FAILURE TO WARN CLAIMS**

Plaintiff must prove several elements in a failure to warn case. The two most critical elements are: (1) the inadequacy of the label; and (2) causation. Most manufacturers spend most of their resources defending the adequacy of the warnings – and appropriately so. Such a defense includes challenging the plaintiff’s labeling theories and experts, developing the company and FDA labeling story, and presenting strong expert testimony in support of the labeling. But manufacturers must not forget the causation element. Plaintiffs must prove that the inadequate warnings caused the harm at issue. It is a powerful defense that often is overlooked by all parties.

This section outlines the some of the basic legal principles relating to the element of causation and discusses some of the applications to recent failure to warn claims.

### **A. Brief Overview of Causation**

A plaintiff in a failure to warn case against a prescription drug manufacturer must prove that the manufacturer’s failure to warn *caused* her injury. Although a duty to warn typically runs from the manufacturer of the product to the consumer of the product, almost all jurisdictions have adopted the “learned intermediary doctrine” when the product at issue is a prescription drug. “The learned-intermediary doctrine provides that the manufacturer or supplier of a prescription drug has no legal duty to warn a *consumer* of the dangerous propensities of its drug, as long as adequate warnings are provided to the *prescribing physician*.” Diane Schamuder Kane, “Construction and Application of the Learned-Intermediary Doctrine,” 57 A.L.R.5th 1, § 1[a]; *Restatement (Third) of Torts: Products Liability* § 6(d)(1). The learned intermediary doctrine “is based upon the premise that, as a medical expert, a patient’s prescribing physician is in the best position to evaluate the often complex information provided by the manufacturer concerning the risks and benefits of its drug or product and to make an individualized medical judgment, based on the patient’s particular needs and susceptibilities, as to whether the patient should use the product.” *Id.* at § 2[a].

Thus, the causation element relies upon whether the alleged inadequacies in the label caused the physician to prescribe the drug. In most jurisdictions, if the prescribing physician unequivocally testifies that she would have still prescribed the drug to the plaintiff even with plaintiff’s proposed warning, plaintiff cannot show that the manufacturer’s failure to warn caused her injuries. Similarly, although it is not as strong of a position, if the prescribing physician testifies that she simply did not review or rely upon the label in making her prescribing decisions, the manufacturer can still maintain that there is no causal connection between its alleged failure to warn and the plaintiff’s injuries. On the other hand, in most jurisdictions, if the

prescribing physician unequivocally testifies that she would not have prescribed the drug to the plaintiff if the manufacturer had added the warning suggested by plaintiff, then the plaintiff will meet the causation element of her claim.

The more interesting issue arises when no evidence has been obtained from the prescribing physician on whether the plaintiff's proposed warnings would have changed her prescribing behavior. In this circumstance, the question that arises is whether, under the learned intermediary doctrine, the plaintiff bears the burden of proving that the warning would have changed the doctor's course of action, or whether that burden is shifted to the defendant. "Because it may be difficult for a plaintiff to prove that his or her physician would not have prescribed or administered the particular drug or device had adequate warnings been provided, the vast majority of jurisdictions have held that the plaintiff is entitled to a rebuttable presumption that the manufacturer's failure to adequately warn the learned intermediary of the risks associated with its drug or product was a proximate cause of the plaintiff's injury." Kane, *supra*, § 2[a] (footnotes omitted); *see, e.g., Eck v. Parke, Davis & Co.*, 256 F.3d 1013, 1018 (10th Cir. 2001); *Garside v. Osco Drug, Inc.*, 976 F.2d 77 (1st Cir. 1992). In other jurisdictions, however, the courts have refused to apply a rebuttable presumption of causation in favor of the plaintiff and have required that the plaintiff affirmatively establish that an adequate warning would have changed the learned intermediary's decision to prescribe or administer the drug. Kane, *supra*, § 2[a]; *Odom v. G.D. Searle & Co.*, 979 F.2d 1001 (4th Cir. 1992); *Thomas v. Hoffman-LaRoche, Inc.*, 949 F.2d 806 (5th Cir. 1992). This rebuttable presumption issue, as discussed below, has important practical implications.

## **B. Practice Implications**

Practitioners need to thoroughly understand the law on causation for the jurisdiction at issue. Once understood, it is prudent to meet and confer with the prescriber's counsel (if ethically permitted) to share some defense theories and strategies. At that meeting you may learn more about the prescriber's thoughts about the adequacy of the label. Where appropriate, you may share plaintiff's labeling theories for input from the prescriber. In some cases, the prescriber will agree that she was adequately informed and that she would have prescribed the drug despite plaintiff's labeling theories. If so, it is prudent to ask the "would you still have prescribed" questions at the deposition, especially in the rebuttable presumption jurisdictions.

Often the plaintiff fails to ask the prescribing physician at deposition whether her prescribing practices would have been changed had the label contained the allegedly adequate warning. In jurisdictions without the rebuttable presumption, the plaintiff will not have met her burden and it is prudent for the manufacturer to use the absence of evidence on causation to move for summary judgment under the learned intermediary doctrine. *See e.g., Motus v. Pfizer*, 358 F.3d 659 (9th Cir. 2004).

Another interesting issue regarding causation and the learned intermediary doctrine arises with generic manufacturers. In many cases, the physician will testify that she did not review the label of the generic drug or any information from the generic manufacturer. Indeed, the prescriber might testify that she read the innovator's label in the PDR and prescribed the innovator drug. In such a case, the question arises whether the generic manufacturer should move for summary judgment. The answer, of course, largely depends on the particular jurisdiction; but persuasive arguments can be made for and against granting summary judgment on the causation issue. Our research has not found any cases that have directly addressed this issue.

The generic manufacturer could argue that the prescriber did not review or rely on any information that it distributed. Rather, the prescriber relied on other information, including by way of example, the PDR, literature and personal experience. Accordingly, the plaintiff's labeling changes would not have changed the prescriber's decision to use the generic drug. The generic manufacturer would rely on analogous case law. *Id.* at 661 ("Because the doctor testified that he did not read the warning label . . . before prescribing the drug to Dr. Motus, the adequacy of Pfizer's warnings is irrelevant to the disposition of this case."); *Thom v. Bristol-Myers Squibb Co.*, 353 F.3d 848, 856 (10th Cir. 2003) ("The majority of courts that have examined the issue have held that *when a physician fails to read or rely on a drug manufacturer's warnings*, such failure constitutes the intervening, independent and sole and proximate cause of the plaintiff's injuries, *even where the drug manufacturer's warnings were inadequate.*") (internal quotations and citations omitted; third emphasis in original). On the other hand, plaintiff will argue that the prescriber relied on the innovator label, which is identical to the generic label. Since the two labels must be identical, plaintiff's labeling revisions would have altered the prescribing decision. Language of at least one recent case seemingly supports this argument. *Ames v. Apothecan*, 431 F. Supp. 2d 566 (D. Md. 2006) ("By law, the warnings for all Amoxicillin brands must be identical down to the last syllable. Quite literally, if a doctor has read one, he has read them all. [The prescriber] considers the Amoxicillin warnings to be adequate and duplicative of what he already knows") (footnote omitted). In any event, it is prudent for generic manufacturers to establish that the prescriber did not rely upon the generic manufacturer's label, and consider whether the lack of such reliance breaks the causal connection.

## CONCLUSION

With the continued growth of the generic drug market and the creativity of plaintiffs' counsel, the liability of innovators and generic manufacturers in generic only cases will continue to be a concern for both types of manufacturers. Innovators should continue to have an absolute defense in generic only cases. Unless relieved of liability because of generic preemption, the defense of the generic manufacturer will depend on the pharmacovigilance of both manufacturers and the involvement of the FDA.

The Preamble and FDA amicus briefs have given manufacturers additional authority for a preemption defense. Beyond the principles of broad preemption, a generic manufacturer has an additional argument of "generic preemption." If its preemption defense fails, it must defend its generic product and, perhaps, the lessened pharmacovigilance practices of the generic industry. Unfortunately, there continues to be great uncertainty regarding the strength of both the "broad preemption" and the "generic preemption" defenses. The Third Circuit, which will decide *Colacicco* later this year, may provide significant guidance on both areas.

Finally, manufacturers should not ignore the causation element of the failure to warn claim. Whether there is a rebuttable presumption or not, proper preparation and consideration may produce evidence that entitles the manufacturer to summary judgment or that is convincing evidence of no liability at trial.