

Defending Products Liability Suits Involving Off-Label Use: Does the Learned Intermediary Doctrine Apply?

Marisa A. Trasatti*
Lindsey N. Lanzendorfer‡

I. INTRODUCTION

Following state and federal government filings of *qui tam* actions, which alleged drug manufacturers engaged in unauthorized off-label promotion of drugs and medical devices in violation of the Food Drug and Cosmetic Act, several drug manufacturers paid staggering claims in settlement. For example, Pfizer paid \$430 million in 2004 to settle a claim that it encouraged physicians to prescribe the drug Neurontin, FDA approved for epilepsy, to treat bipolar disorder.¹ In 2010, Elan Pharmaceuticals settled a claim of unauthorized promotion for \$214.5 Million.² There, the company was alleged to have promoted Zonegran—another drug FDA approved to treat epilepsy—for bipolar disorder, migraine headaches, chronic daily headaches, eating disorders, and obesity.³ For a final example, AstraZeneca agreed to pay \$68.5 million in a 2011 settlement.⁴ In this multi-state claim, AstraZeneca was alleged to have pushed doctors to

* Ms. Trasatti is a principal at Semmes, Bowen, and Semmes in Baltimore, Maryland whose practice focuses on drug and medical device litigation.

‡ Ms. Lanzendorfer is a rising third year law student at the University of Maryland School of Law and Summer Associate at Semmes, Bowen, and Semmes in Baltimore, Maryland.

¹ Gardiner Harris, *Shamed Drug Firm Pays up \$636m*, THE AGE (May 15, 2004), <http://www.theage.com.au/articles/2004/05/14/1084289882827.html>.

² Steven Meyerowitz, *Elan Missing As Pharmaceutical Companies Pay \$214.5 Million to Settle FCA and Other Claims*, FINANCIAL FRAUD LAW (Dec. 16, 2010, 12:53 PM), <http://www.financialfraudlaw.com/lawblog/elan-missing-pharmaceutical-companies-pay-2145-million-settle-fca-and-other-claims/1813>.

³ *Id.*

⁴ Matthew Perrone, *AstraZeneca Paying \$68.5M in Seroquel Settlement*, WASH. POST (Mar. 10, 2011), <http://www.washingtonpost.com/wp-dyn/content/article/2011/03/10/AR2011031003328.html>.

prescribe its drug Seroquel for insomnia and Alzheimer’s although the FDA only approved the drug as an anti-psychotic.

Litigators now may be wondering if these large settlements for promotion of off-label use will translate into larger financial outcomes in private personal injury lawsuits. This depends, in part, on whether the “learned intermediary doctrine” is an affirmative defense for manufacturers in lawsuits involving off-label use.

The learned intermediary doctrine serves as a shield for manufacturers against consumer claims arising from allegations of failure to warn of a drug’s risks. Essentially, manufacturers are protected from liability if they warn physicians of the risks associated with a drug or device. Physicians commonly engage in off-label use, however, and it is impossible for manufacturers to warn physicians of every risk of any and all uses of a drug. Unfortunately, court decisions that address whether the learned intermediary doctrine insulated manufacturers from claims based on off-label use vary widely across circuits. Still, analysis of these decisions offers some guidance for defense attorneys in approaching these lawsuits.

II. OFF-LABEL USE OF PRESCRIPTION DRUGS AND MEDICAL DEVICES

By way of background, the Food and Drug Administration (FDA) regulates manufacturers’ marketing and distribution of medical devices and prescription drugs. To market drugs and devices, the manufacturer must first obtain FDA approval for the drug or device. The FDA will only approve a prescription drug or device for the uses that the manufacturer shows it is safe and effective.⁵ Once approved for a particular use, the FDA historically has prohibited manufacturers from promoting their products for any other uses, with limited exceptions.⁶

Physicians, however, often prescribe drugs or use medical devices in an off-label way.⁷ As the FDA does not regulate individual physicians, physicians are free to take these actions in the exercise of good medical judgment. In fact, the Supreme Court of the United States called off-label prescription “an accepted and necessary corollary of the FDA’s mission to regulate in this area without directly interfering with the practice of medicine.”⁸ The federal government has made clear that its regulations do not restrict a physician’s ability to prescribe drugs for off-label uses.⁹

Physicians prescribe off-label for many reasons. One reason is that sometimes no drug exists to treat a particular condition. For instance, Rituximab is FDA-approved for treatment of non-Hodgkin’s lymphoma, but one neurologist said that the only known treatment for “progressive encephalomyelitis with rigidity and myoclonus” (“PERM”) is Rituximab.¹⁰ If physicians did not prescribe Rituximab to treat this condition, it essentially would go untreated and the patient could die.

⁵ 21 U.S.C. § 355 (2006).

⁶ See *infra* text accompanying notes 15–19, for further description on what information the FDA permits drug manufacturers to provide to physicians.

⁷ Richard C. Ausness, “*There’s Danger Here, Cherie!*”: *Liability for the Promotion and Marketing of Drugs and Medical Devices for Off-Label Uses*, 73 BROOK. L. REV. 1253, 1253 (2008).

⁸ *Buckman Co. v. Plaintiff’s Legal Comm.*, 531 U.S. 341, 350 (2001).

⁹ Ausness, *supra* note 7, at 1259.

¹⁰ Tom Valeo, *A Catch 22: Neurologists Can Prescribe Off-Label, But Risk Health Insurers’ Denials for Reimbursement*, NEUROLOGY TODAY, Apr. 7, 2011, at 28–30.

Additionally, people respond to prescription drugs differently. These varying responses also cause physicians to prescribe drugs for off-label uses. Cynthia Harden, M.D., chief of the Division of Epilepsy and Electroencephalography at Long Island Jewish Hospital, commented that drugs are not targeted for specific types of epilepsy.¹¹ While some seizures start in the frontal lobe, others originate in the temporal lobe.¹² As such, treating epilepsy can require doctors to prescribe the drug differently than described on the drug's label depending on the locus of the seizure activity.

Physicians also often prescribe off-label when treating children. This occurs because children do not take part in clinical tests or trials. As such, only twenty to thirty percent of FDA approved drugs are labeled for use in children.¹³ If physicians were not permitted to prescribe off-label, many childhood diseases would go untreated.

Although physicians typically prescribe off-label, manufacturers do not rush to have the FDA approve drugs for additional uses. If a drug manufacturer wishes to have an already marketed drug approved for a new use, the manufacturer must go through a lengthy and expensive process to obtain FDA approval for a drug. But, because physicians can prescribe off-label without FDA approval, manufacturers have little incentive to obtain new approval once a drug goes to market. It is easier and less costly to allow physicians to deviate from the label instructions and prescribe the approved drugs for new uses.

While physicians can engage in off-label prescribing, drug manufacturers are only permitted to disseminate peer-reviewed scientific information to physicians regarding off-label uses. The FDA permits this dissemination for several reasons. For instance, if an off-label prescription is common enough to be the standard of care, a physician may commit medical malpractice if he does not prescribe the drug for that off-label use. Additionally, ensuring physicians know about these off-label uses can advance public health, since physicians will then properly treat patients.¹⁴

Although manufacturers can provide some information to physicians, the FDA provides strict guidance on the type of information that can be distributed to physicians and how the information can be distributed. The guidelines have changed slightly over the years, but are currently found under the "Good Reprint Practices of Medical Journal Articles and Medical Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices."¹⁵ The guidelines suggest, among other things, that any reprints or articles that drug companies provide to physicians be scientific or medical journals that are peer-reviewed and not funded by the drug manufacturer.¹⁶ They must recognize the risks associated with the off-label use.¹⁷ They also suggest that the information be in the form of an unabridged reprint, not marked or highlighted by the manufacturer, and be distributed separate from promotional material.¹⁸ Finally, the guidelines encourage drug manufacturers to include a

¹¹ *Id.*

¹² *Id.*

¹³ *Should Your Child be in a Clinical Trial?*, U.S. FOOD AND DRUG ADMINISTRATION, [HTTP://www.fda.gov/ForConsumers/ConsumerUpdates/ucm048699.htm](http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm048699.htm) (last visited May 28, 2011).

¹⁴ FDA GOOD REPRINT PRACTICES OF MEDICAL JOURNAL ARTICLES AND MEDICAL SCIENTIFIC REFERENCE PUBLICATIONS ON UNAPPROVED NEW USES OF APPROVED DRUGS AND APPROVED OR CLEARED MEDICAL DEVICES (2009).

¹⁵ *Id.*

¹⁶ *Id.*

¹⁷ *Id.*

¹⁸ *Id.*

statement disclosing that the uses described have not been approved by the FDA and identifying the manufacturer's financial interest in the drug or device.¹⁹

If manufacturers provide more information than the FDA guidelines permit, they are considered to have engaged in unauthorized promotion. This is against the law and is referred to as misbranding.²⁰ In recent *qui tam* actions, at least six (6) manufacturers settled charges pertaining to off-label marketing in 2010.²¹ Following is a chart outlining these six (6) settlements. It includes the name of the drug manufacturer, the related drug, the approved use of the drug, a non-exhaustive list of the off-label use the company was alleged to have illegally promoted, and the settlement amount.

Company Name	Drug	Approved Use(s)	Off-label Use(s) Allegedly Promoted	Settlement Amount
AstraZeneca	Quetiapine (Seroquel)	Schizophrenia and manic episodes in bipolar disorder	Alzheimer's disease, anger management, anxiety, attention deficit hyperactivity disorder, dementia, depression, and post-traumatic stress disorder	\$520 million
Ortho-McNeil-Janssen	Topiramate (Topamax)	Epilepsy and prevention of migraines	Alcohol dependence and weight loss	\$81 million
Novartis	Tobramycin (TOBI)	Cystic Fibrosis in adults	Cystic Fibrosis in patients under the age of six	\$72.5 million
Forest	Citalopram (Celexal) and Escitalopram (Lexapro)	Antidepressant for adults	Antidepressant for children and adolescents	\$313 million
Allegan	OnabotulinumtoxinA (Botox)	Blepharospasm (spasm of the eyelids), Cervical Dystonia (severe neck muscle spasms), and severe Primary Axillary Hyperhidrosis (excess sweating)	Headache, pain, and juvenile cerebral palsy.	\$600 million
Novartis	Oxcarbazepine (Trileptal)	Epilepsy	Bipolar disorder and neuropathic pain	\$422.5 million

¹⁹ *Id.*

²⁰ See 21 U.S.C § 331(b), 352(f), 333 (2006).

²¹ Molly Cohen, *Study: Whistleblower Cases Involving Off-Label Promotion Pervade Industry*, DRUG INDUS. DAILY, Apr. 11, 2011.

III. THE LEARNED INTERMEDIARY DOCTRINE

While the above chart refers to actions alleging misbranding in violation of the Federal Drug and Cosmetic Act, off-label use may also affect drug manufacturers' civil liability for consumer injuries allegedly sustained as a result of off-label use. When a patient claims an injury from a prescription drug or medical device, he or she usually sues both the physician and the drug or device manufacturer. In such products liability lawsuits, plaintiffs' claims include those for negligence and/or strict liability against the product manufacturers for failure to warn of the potential risks of a particular drug or device.²²

In most cases, however, the learned intermediary doctrine protects manufacturers from liability as it has been found to apply in negligence and strict liability claims, including design defect, misbranding, and breach of implied warranty claims.²³ Before discussing whether the learned intermediary doctrine applies in cases involving off-label use, it will be helpful to give a general overview of the learned intermediary doctrine.

The doctrine recognizes that if a treating physician received adequate notice of possible risks, the manufacturer has no duty to warn the end consumer.²⁴ This doctrine exists because physicians, as learned intermediaries, are in the best position to weigh the risks and benefits based on patient selection, needs, and conditions.²⁵ Essentially, a manufacturer's duty to warn extends only to the prescribing physician, who then assumes responsibility for advising patients of the risks associated with the drug or device.

For the doctrine to apply, however, the physician must be aware of the risks associated with each drug or device.²⁶ This awareness does not have to come from the manufacturer. Indeed, even if a manufacturer's warning is inadequate, the doctrine will still apply if the physician has been sufficiently warned from other sources.²⁷ In essence, the learned intermediary doctrine encompasses the physician's entire field of knowledge.²⁸

Every State in the country has some precedent concerning the learned intermediary defense.²⁹ In thirty-five states and the District of Columbia, the jurisdiction's highest court or the legislature by statute has adopted the learned intermediary doctrine. These include Alabama,³⁰ Alaska,³¹ Arkansas,³² California,³³ Connecticut,³⁴ Delaware,³⁵ the District of

²² RESTATEMENT (THIRD) OF TORTS §, cmt. d (1998).

²³ See, e.g., *Fellows v. USV Pharm. Corp.*, 502 F. Supp. 297 (D. Md. 1980).

²⁴ Richard B. Goetz & Karen R. Growden, *A Defense of the Learned Intermediary Doctrine*, 63 FOOD & DRUG L.J. 421, 421 (2008).

²⁵ *Lee v. Baxter Healthcare Corp.*, 721 F. Supp. 89, 94–95 (D. Md. 1989), *aff'd*, 898 F.2d 146 (4th Cir. 1990).

²⁶ *Chambers v. G.D. Searle & Co.*, 441 F. Supp. 377, 377 (D. Md. 1975)

²⁷ See, e.g., *Dean v. Eli Lilly & Co.*, 387 F.App'x 28, 30 (2d Cir. 2010) (finding learned intermediary doctrine applied where plaintiff alleged manufacturer failed to warn because doctor had actual knowledge of the alleged warning); *Sita v. Danek Medical, Inc.*, 43 F. Supp. 2d 245 (E.D.N.Y. 1999) (finding learned intermediary doctrine applied where plaintiff claimed manufacturer failed to warn physician of risks because physician was aware of risks notwithstanding).

²⁸ *Ames v. Apothecon, Inc.*, 431 F. Supp. 2d 566, 572 (D. Md. 2006).

²⁹ See *The Closing of the Learned Intermediary Frontier*, DRUG AND DEVICE LAW (June 2, 2011), <http://druganddevicelaw.blogspot.com/2011/06/closing-of-learned-intermediary.html>, for an extensive list of the relevant case law.

³⁰ See *Stone v. Smith, Kline & French Lab.*, 447 So. 2d 1301, 1305 (Ala. 1984).

³¹ See *Shanks v. Upjohn Co.*, 835 P.2d 1189, 1200 & n.17 (Alaska 1992).

Columbia,³⁶ Florida,³⁷ Georgia,³⁸ Hawaii,³⁹ Idaho,⁴⁰ Illinois,⁴¹ Kansas,⁴² Kentucky,⁴³ Maryland,⁴⁴ Massachusetts,⁴⁵ Michigan,⁴⁶ Minnesota,⁴⁷ Mississippi,⁴⁸ Missouri,⁴⁹ Montana,⁵⁰ Nebraska,⁵¹ Nevada,⁵² New Jersey,⁵³ New York,⁵⁴ North Carolina,⁵⁵ Ohio,⁵⁶ Oklahoma,⁵⁷ Oregon,⁵⁸ Pennsylvania,⁵⁹ South Carolina,⁶⁰ Tennessee,⁶¹ Texas,⁶² Utah,⁶³ Virginia,⁶⁴ Washington,⁶⁵ and Wyoming.⁶⁶

Five states' intermediate appellate authority has applied the rule. These are Arizona,⁶⁷ Colorado,⁶⁸ Indiana,⁶⁹ Louisiana,⁷⁰ and New Mexico.⁷¹ Federal Courts applying state law have assumed the state would adopt the doctrine in seven states. These include Iowa,⁷² Maine,⁷³ New Hampshire,⁷⁴ North Dakota,⁷⁵ Rhode Island,⁷⁶ South Dakota,⁷⁷ and Wisconsin.⁷⁸ Vermont only

³² See *West v. Searle & Co.*, 806 S.W.2d 608, 613 (Ark. 1991).

³³ See, e.g., *Carlin v. Superior Court*, 920 P.2d 1347, 1354 (Cal. 1996).

³⁴ See, e.g., *Hurley v. Heart Physicians, P.C.*, 3 A.3d 892, 899–900 (Conn. 2010).

³⁵ See *Lacy v. G.D. Searle & Co.*, 567 A.2d 398, 400–01 (Del. 1989).

³⁶ See, e.g., *Mampe v. Ayerst Lab.*, 548 A.2d 798, 801 & n.6 (D.C. 1988).

³⁷ See, e.g., *E.R. Squibb & Sons, Inc. v. Farnes*, 697 So. 2d 825, 827 (Fla. 1997).

³⁸ See, e.g., *McCombs v. Synthes (U.S.A.)*, 587 S.E.2d 594, 595 (Ga. 2003).

³⁹ See *Craft v. Peebles*, 893 P.2d 138, 155 (Haw. 1995).

⁴⁰ See *Silman v. Aluminum Company of America*, 731 P.2d 1267, 1270 (Idaho 1986).

⁴¹ See, e.g., *Happel v. Wal-Mart Stores, Inc.*, 766 N.E.2d 118, 1127 (Ill. 2002).

⁴² See, e.g., *Savina v. Sterling Drug, Inc.*, 795 P.2d 915, 928 (Kan. 1990).

⁴³ See, e.g., *Hyman & Armstrong, P.S.C. v. Gunderson*, 279 S.W.3d 93, 109–10, 112 (Ky. 2008).

⁴⁴ See, e.g., *Rite Aid Corp. v. Levy-Gray*, 894 A.2d 563, 577 (Md. 2006).

⁴⁵ See, e.g., *Coombes v. Florio*, 877 N.E.2d 567, 577 n.1 (Mass. 2007).

⁴⁶ See, e.g., *Smith v. E.R. Squibb & Sons, Inc.*, 273 N.W.2d 476, 479 (Mich. 1979),

⁴⁷ See, e.g., *Mulder v. Parke Davis & Co.*, 181 N.W.2d 882, 885 n.1 (Minn. 1970).

⁴⁸ See, e.g., *Janssen Pharm. Inc. v. Bailey*, 878 So. 2d 31, 57 (Miss. 2004).

⁴⁹ See, e.g., *Krug v. Sterling Drug, Inc.*, 416 S.W.2d 143, 146–47 (Mo. 1967).

⁵⁰ See, e.g., *Stevens v. Novartis Pharm. Corp.*, 247 P.3d 244, 257–60 (Mont. 2010).

⁵¹ See, e.g., *Freeman v. Hoffman-La Roche, Inc.*, 618 N.W.2d 827, 841–42 (Neb. 2000).

⁵² See, e.g., *Allison v. Merck & Co.*, 878 P.2d 948 (Nev. 1994).

⁵³ See, e.g., *Perez v. Wyeth Lab., Inc.*, 734 A.2d 1245, 1257 (N.J. 1999).

⁵⁴ See, e.g., *Spensieri v. Lasky*, 723 N.E.2d 544, 549 (N.Y. 1999);

⁵⁵ See, e.g., N.C. GEN. STAT. §99B-5(c) (1995).

⁵⁶ See, e.g., OHIO REV. CODE §2307.76(c) (West 2011).

⁵⁷ See, e.g., *McKee v. Moore*, 648 P.2d 21, 24 (Okla. 1982);

⁵⁸ See, e.g., *Oksenholt v. Lederle Lab.*, 656 P.2d 293, 296–97 (Or. 1982).

⁵⁹ See, e.g., *Baldino v. Castagna*, 478 A.2d 807, 812 (Pa. 1984);

⁶⁰ See, e.g., *Madison v. American Home Prod. Corp.*, 595 S.E.2d 493, 496 (S.C. 2004).

⁶¹ See, e.g., *Pittman v. Upjohn Co.*, 890 S.W.2d 425, 429 (Tenn. 1994).

⁶² See, e.g., *Humble Sand & Gravel, Inc. v. Gomez*, 146 S.W.3d 170, 190–91 (Tex. 2004).

⁶³ See, e.g., *Downing v. Hyland Pharmacy*, 194 P.3d 944, 946–47 (Utah 2008)

⁶⁴ See, e.g., *Pfizer, Inc. v. Jones*, 272 S.E.2d 43, 44 (Va. 1980).

⁶⁵ See, e.g., *Wash. State Physicians Ins. Exch. & Ass'n v. Fisons Corp.*, 858 P.2d 1054, 1061 (Wash. 1993).

⁶⁶ See, e.g., *Rohde v. Smiths Medical*, 165 P.3d 433, 438 (Wyo. 2007).

⁶⁷ See, e.g., *Piper v. Bear Med. Sys., Inc.*, 883 P.2d 407, 415 (Ariz. Ct. App. 1993).

⁶⁸ See, e.g., *Hamilton v. Hardy*, 549 P.2d 1099, 1110 (Colo. App. 1976).

⁶⁹ See, e.g., *Allberry v. Parkmor Drug, Inc.*, 834 N.E.2d 199, 202–03 (Ind. Ct. App. 2005)

⁷⁰ See, e.g., *Kampmann v. Mason*, 921 So. 2d 1093, 1094 (La. Ct. App. 2006);

⁷¹ See, e.g., *Serna v. Roche Lab., Div. of Hoffman-LaRoche, Inc.*, 684 P.2d 1187, 1189 (N.M. Ct. App. 1984);

⁷² See, e.g., *Petty v. United States*, 740 F.2d 1428, 1440 (8th Cir. 1984).

⁷³ See, e.g., *Violette v. Smith & Nephew Dyonics, Inc.*, 62 F.3d 8, 13 (1st Cir. 1995).

⁷⁴ See, e.g., *Brochu v. Ortho Pharm. Corp.*, 642 F.2d 652, 656 (1st Cir. 1981).

⁷⁵ See, e.g., *Ehlis v. Shire Richwood, Inc.*, 367 F.3d 1013, 1017 (8th Cir. 2004).

has a trial Court case that applied the rule.⁷⁹ Finally, West Virginia’s highest court, the Supreme Court of Appeals, is the only court to have rejected the learned intermediary doctrine.⁸⁰

IV.
APPLYING THE LEARNED INTERMEDIARY DOCTRINE
TO CLAIMS INVOLVING OFF-LABEL USE

Drug and medical device lawsuits increasingly involve uses of products that deviate from manufacturers’ FDA approved uses. This situation creates a paradox for drug makers: the learned intermediary doctrine applies when physicians are aware of the risks associated with drug or device, but manufacturers are to warn physicians of risks associated with on-label uses and cannot know of all other possible uses of a drug and the risks associated with those other uses. In turn, this paradox has resulted in substantial differences among state court decisions regarding a manufacturer’s liability for failure to warn claims involving off-label use.

Following is a survey of case law addressing when the learned intermediary doctrine will and will not insulate manufacturers from liability for off-label use based on failure to warn claims. This survey is not exhaustive, but merely provides examples of how some jurisdiction have approached the issue. Additionally, this survey does not address the causation defense: that any failure to warn did not cause the plaintiff’s injuries. For instance, the failure to warn cannot cause a plaintiff’s injuries when the physician was aware of the off-label risks from a different source or the physician would have prescribed the drug even if he would have known of the risks—both of which turn on the facts of an individual case.⁸¹

A. *The Learned Intermediary Doctrine Always Insulates Manufacturers from Liability for Off-Label Use*

1. *Maryland*

A United States District Court for the District of Maryland, applying Maryland law, addressed the learned intermediary doctrine and off-label use in *Robak v. Abbott Laboratories*.⁸² There, the plaintiff argued that the manufacturer had a duty to warn physicians of the risks associated with Omniflox when used for sinusitis, an off-label use.⁸³ The Court rejected this argument, reasoning that the physician, as a learned intermediary, made the decision to prescribe the drug for that off-label use, not the manufacturer.⁸⁴ As such, the Court found that the learned

⁷⁶ See, e.g., *Hogan v. Novartis Pharm. Corp.*, 06 CV 260, Trial Tr. (5/23/11), at 387-88 (E.D.N.Y.).

⁷⁷ See, e.g., *McElhaney v. Eli Lilly & Co.*, 575 F. Supp. 228, 231 (D.S.D. 1983), aff’d, 739 F.2d 340 (8th Cir. 1984).

⁷⁸ See, e.g., *Menges v. Depuy Motech, Inc.*, 61 F. Supp. 2d 817, 830 (N.D. Ind. 1999).

⁷⁹ See *Estate of Baker v. Univ. of Vt.*, No. 233-10-03 Oscv., 2005 WL 6280644 (Vt. Super. May 4, 2005).

⁸⁰ See *Johnson & Johnson Corp. v. Karl*, 647 S.E.2d 899, 913–14 (W. Va. 2007).

⁸¹ See, e.g., *Alexander v. Smith & Nephew, P.L.C.*, 98 F. Supp. 2d 1310 (N.D. Okla. 2000) (“Dr. Hayes testified that he was fully informed as to the FDA status of the Rogozinski System, know of its risks, did not rely on Defendant’s informational materials, and exercised his independent judgment based on the standards of care and Ms. Dentis’ situation in recommending the surgery. Plaintiff has presented no evidence to the contrary, not has Plaintiff shown that the device caused her current physical ailments. Given these facts, Plaintiff can show no injury resulting from any failure to warn Dr. Hayes”).

⁸² 797 F. Supp. 475 (D. Md. 1992).

⁸³ *Id.* at 476.

⁸⁴ *Id.*

intermediary doctrine applies in every case where the patient suffered injuries resulting from an off-label use of a drug.⁸⁵

2. Louisiana

In *Bell v. Danek Med., Inc.*,⁸⁶ an unreported opinion, the plaintiff alleged that a Spinal System, implanted in her spine, caused her extreme lower back pain, numbness, charley horses, and cramps.⁸⁷ Her physician's placement of pedicle screws into her spine was an off-label use of the screws, given that they were approved for other bones, but not the spine.⁸⁸ Bell filed a lawsuit, naming the manufacturer as one of the defendants, contending that it failed to warn her physician adequately of the risks associated with this off-label use.⁸⁹ Specifically, she alleged that Danek actually promoted the off-label use and therefore had a duty to warn the physician of its risks.⁹⁰ The United States District Court for the Eastern District of Louisiana found that the learned intermediary doctrine was unaffected by the manufacturer's over promotion because the plaintiff failed to provide any case law from Louisiana for her contention that over promotion defeats the doctrine.⁹¹

B. The Learned Intermediary Doctrine Only Insulates Manufacturers Who Warn of Off-Label Use Risks

1. Florida

In *Upjohn Co. MacMurdo*,⁹² the Florida Supreme Court held that Upjohn had a duty to warn physicians of the risks associated with the off-label use of Depo-Provera.⁹³ There, a physician prescribed Depo-Provera to MacMurdo for contraceptive purposes even though the drug was labeled for endometrial carcinoma.⁹⁴ MacMurdo ultimately required a hysterectomy to stop excessive and continuous menstrual bleeding.⁹⁵ The Court failed to truly address off-label use and merely assumed Upjohn had a duty to warn, stating "the more crucial question is whether the warnings were adequate to warn a physician of the possibility that Depo-Provera might be causing the condition experienced by MacMurdo."⁹⁶

C. The Learned Intermediary Doctrine's Does Not Insulate Manufacturers Who Have Knowledge of the Off-Label Use

1. New Jersey

The United States District Court for the Eastern District of Pennsylvania applied New Jersey law in *Knipe v. SmithKline Beecham*.⁹⁷ The Court found that a drug manufacturer has a

⁸⁵ *Id.*

⁸⁶ No. CIV. A. 96-1393, 1999 WL 335612 (E.D. La. May 24, 1999).

⁸⁷ *Id.* at *1.

⁸⁸ *Id.* at *4.

⁸⁹ *Id.* at *3

⁹⁰ *Id.* at *4

⁹¹ *Id.*

⁹² 562 So.2d 680, 683 (Fla. 1990)

⁹³ *Id.* at 683.

⁹⁴ *Id.* at 682.

⁹⁵ *Id.*

⁹⁶ *Id.* at 683.

⁹⁷ 583 F. Supp. 2d 602 (E.D. Pa 2008).

duty to warn of the risks associated with known drug uses as soon as reasonably feasible.⁹⁸ There, Knipe alleged that GlaxoSmithKline failed to warn physicians of the increased suicide risk in younger patients who take the drug Paxil.⁹⁹ The Court rejected GlaxoSmithKline's argument that it did not have a duty to warn of risks associated with off-label uses of a drug, finding its knowledge of the suicide risks rebutted any use of the learned intermediary defense.¹⁰⁰

2. Ohio

In *Krumpelbeck v. Breg*,¹⁰¹ the Federal District Court for the Southern District of Ohio applied Ohio law in finding that a manufacturer did not have a duty to warn until it knew or should have known of the risks associated with a particular off-label use.¹⁰² There, Krumpelbeck alleged that she developed chondrolysis from a prescribed and implanted catheter of a Breg Pain infusion pump.¹⁰³ On Krumpelbeck's negligence claims, the Court granted summary judgment in favor of the manufacturer because plaintiff did not show that the manufacturer knew or should have known of the off-label risks associated with the product.¹⁰⁴

3. Georgia

In *Medics. Pharm. Corp. v. Newman*,¹⁰⁵ the Georgia intermediate appellate Court similarly found that a manufacturer had a duty to warn of risks associated with known off-label uses.¹⁰⁶ There, a physician prescribed Diastyl for preventing a miscarriage.¹⁰⁷ The daughter of the woman prescribed Diastyl developed genital cancer later in life.¹⁰⁸ The daughter alleged her cancer was a risk inherent in the off-label use of Diastyl to prevent miscarriages and brought a lawsuit against the manufacturer for negligence.¹⁰⁹ The Court concluded that whether the manufacturer could have foreseen the use of Diastyl for the prevention of miscarriages was a question for the jury.¹¹⁰ Importantly, if the jury answers in the affirmative, then the manufacturer would also be charged with using reasonable care in determining whether the drug was safe for that use.¹¹¹

4. Indiana

⁹⁸ *Id.* at 628.

⁹⁹ *Id.* at 609.

¹⁰⁰ *Id.* at 628. *But see* *Davenport v. Medtronic, Inc.*, 302 F. Supp. 2d 419 (E.D. Pa 2004) (finding a manufacturer's knowledge of off-label use does not automatically subject the manufacturer to liability for failure to warn).

¹⁰¹ 759 F. Supp.2d 958 (S.D. Ohio 2010).

¹⁰² *Id.* at 960; *see also* *Monroe v. Zimmer US Inc.*, 566 F. Supp. 2d 1012, 1033 (E.D. Cal. 2011) ("Accordingly, plaintiff must provide evidence that demonstrates defendants failed to give adequate warning of a risks associated with their product that defendants know or should have known about at the time the product was distributed.").

¹⁰³ *Id.*

¹⁰⁴ *Id.* at 975.

¹⁰⁵ 378 S.E.2d 487 (Ga. Ct. App. 1989).

¹⁰⁶ *Id.* at 488–89; *see also* *Woodbury v. Janssen Pharm., Inc.*, No. 93 C 7118, 1997 WL 201571 (N.D. Ill. Apr. 10, 1997) (finding manufacturer who should reasonably know of dangers associated with an off-label use has a duty to warn physicians of those dangers under Illinois law).

¹⁰⁷ *Id.* at 488.

¹⁰⁸ *Id.*

¹⁰⁹ *Id.*

¹¹⁰ *Id.* at 488–89.

¹¹¹ *Id.*

In *Meharg v. I-Flow Corp.*,¹¹² the Court found, in an unreported opinion, that under Indiana law, if a manufacturer does not promote an off-label use, the manufacturer does not have a duty to warn of the risks unless it (1) knows that the off-label use is occurring, and (2) knows that the off-label use carries a risk of the harm at issue with it.¹¹³ In that case, Meharg developed chondrolysis after receiving bupivacaine through a pain pump.¹¹⁴ Bupivacaine was a pain reliever, but it was not approved to be used with pain pumps.¹¹⁵ Thus, Meharg’s physician prescribed the pain pump as an off-label use.¹¹⁶ Meharg alleged that the manufacturer had a duty to warn the physician of the risk of chondrolysis, but the Court dismissed the claim.¹¹⁷ The Court pointed out that the line between having and not having a duty to warn of a particular risk often is hard to draw.¹¹⁸ On the facts at hand, however, the Court found that it would not assume the manufacturer had knowledge of the risks merely because experts in the relevant field had such knowledge.¹¹⁹

5. Minnesota

In *Riley v. Cordis Corp.*,¹²⁰ a physician implanted a “Cypher stent” in a patient’s coronary artery. This was an off-label use of that stent, and the patient suffered a heart attack.¹²¹ The patient alleged that the manufacturer of the Cypher Stent had a duty to warn the physician of the risks resulting from an off-label use of this product, but did not, and was therefore liable for the patient’s injuries.¹²² The U.S. District Court for the District of Minnesota found that at the time of this incident, the FDA had permitted drug manufacturers to disseminate information about off-label uses of drugs without warning the physicians of the risks associated with those uses.¹²³ Thus, merely being aware of off-label uses could not require a manufacturer to warn physicians of the risks of such uses under the FDA standards.¹²⁴ As such, the learned intermediary doctrine would shield the drug manufacturer from liability even if the manufacturer was aware of off-label uses, as long as the manufacturer did not promote the drug to physicians beyond what the FDA permitted.¹²⁵

D. The Learned Intermediary Doctrine Does Not Shield Manufacturers Who Receive a Large Volume of Sales from Off-Label Use

1. California

¹¹² No. 1:08-cv-184-WTL-TAB, 2010 WL 711317 (S.D. Ind. Mar. 1, 2010).

¹¹³ *Id.* at *2.

¹¹⁴ *Id.* at *1.

¹¹⁵ *Id.*

¹¹⁶ *Id.*

¹¹⁷ *Id.* at *4.

¹¹⁸ *Id.* at *3.

¹¹⁹ *Id.*

¹²⁰ 625 F. Supp. 2d 769 (D. Minn. 2009).

¹²¹ *Id.* at 775.

¹²² *Id.* at 780–81.

¹²³ *Id.* at 781–82. The current guidelines require manufacturers that disseminate information about off-label uses to include the relevant risks. FDA GOOD REPRINT PRACTICES OF MEDICAL JOURNAL ARTICLES AND MEDICAL SCIENTIFIC REFERENCE PUBLICATIONS ON UNAPPROVED NEW USES OF APPROVED DRUGS AND APPROVED OR CLEARED MEDICAL DEVICES (2009).

¹²⁴ *Id.* at 782.

¹²⁵ *Id.* at 783.

In *Miles Laboratories, Inc. v. Superior Court*, a California intermediate appellate Court found that the manufacturer could be liable for failure to warn when it profited from the off-label use and therefore knew or should have known the drug was being used for an off-label use.¹²⁶ There, the plaintiff was harmed by a drug prescribed for miscarriages, DES. The plaintiff alleged that although Miles Laboratories did not sell DES as a miscarriage preventative, it was common knowledge that other manufacturers sold DES for that purpose and that pharmacists prescribed whatever brand of the drug they had on hand, including Miles Laboratories' brand.¹²⁷ The Court found that Miles Laboratories knew or should have known that its brand of DES was being used for an off-label use and it benefited from that use. Thus, it had a duty to warn physicians of the possible risks associated with that use.¹²⁸ Not providing a description of those risks prevented the physician from being a "learned intermediary," so the doctrine did not apply.

2. Texas

In *McNeil v. Wyeth*,¹²⁹ the Fifth Circuit Court of Appeals, applying Texas law, found that manufacturers who substantially profit from off-label use of their products must warn physicians of the risks associated with that off-label use.¹³⁰ There, McNeil allegedly developed Tardive Dyskinesia, a severe neurological disease, from taking the prescription Reglan.¹³¹ Reglan was approved to speed up the digestive system.¹³² Prescribing Reglan for longer than twelve weeks, however, was considered an off-label use.¹³³ The Court found that Wyeth had a duty to warn physicians of the risks associated with this prolonged use because Wyeth knew physicians were prescribing Reglan for longer than twelve (12) week cycles as a majority of its sales came from these extended prescriptions.¹³⁴

E. *The Learned Intermediary Doctrine's Does Not Shield Manufacturers Who Engage in Unauthorized Promotion of the Off-Label Use*

1. Illinois

In *Proctor v. Davis*,¹³⁵ an Illinois Court found the learned intermediary doctrine did not apply because the manufacturer openly promoted the off-label use. In that case, a physician injected a corticosteroid, Depo-Medro, into a patient's eye, disfiguring the eye.¹³⁶ The drug was not approved for eye injections.¹³⁷ The Court found that Depo-Medro's manufacturer was liable because it actively encouraged physicians to use the drug for eye injections.¹³⁸ Indeed, Upjohn

¹²⁶ 133 Cal. App. 3d 587, 595 (Cal. App. 4th Dist. 1982).

¹²⁷ *Id.* at 102.

¹²⁸ *Id.* at 103.

¹²⁹ 462 F.3d 364 (5th Cir. 2006).

¹³⁰ *Id.* at 371.

¹³¹ *Id.* at 367.

¹³² *Id.* at 366.

¹³³ *Id.* at 371.

¹³⁴ *Id.*; see also *O'Neal v. Smithkline Beecham Corp.*, No. CIV S-06-1063 FCD/DAD, 2008 WL 1721891 (E.D. Cal. Apr. 10, 2008) ("In *McNeil*, the court determined the drug's extensive off-label use created the duty to warn; here, there was simply no evidence proffered by plaintiffs that prescriptions of Paxil to pediatric patients made up the majority of Paxil sales. Thus, there would be no basis to invoke the *McNeil* court's duty to warn.").

¹³⁵ 682 N.E.2d 1203 (Ill. Ct. App. 1997).

¹³⁶ *Id.* at 1210–11.

¹³⁷ *Id.* at 1206.

¹³⁸ *Id.* at 1215.

had paid a physician to experiment with the drug and when the doctor reported that all of his animal experiments were “very unsatisfactory,” Upjohn did not include these findings in an article it sent to practicing physicians.¹³⁹ This, in turn, falsely promoted an off-label use and therefore, diminished any warning of risks associated with the drug’s off-label use.¹⁴⁰ Therefore, physicians could not properly weigh the risks and benefits of the drug. As such, the Court found Upjohn was not protected by the learned intermediary doctrine.¹⁴¹

2. North Carolina

In *Dellinger v. Pfizer, Inc.*,¹⁴² the United States District Court for the Western District of North Carolina found, in an unreported opinion, that according to North Carolina law, a manufacturer cannot be liable for a plaintiff’s resulting injuries unless the manufacturer acted unreasonably in failing to warn physicians of the risks of the use of the product that caused the injuries.¹⁴³ In that case, Dellinger’s physician prescribed him Neurontin as a pain reliever.¹⁴⁴ Dellinger subsequently became very ill and was hospitalized.¹⁴⁵ After reading that Pfizer was alleged to have illegally promoted Neurontin for an off-label use, Dellinger brought a claim against Pfizer for his injuries.¹⁴⁶ The Court found that it was unreasonable for Pfizer not to warn physicians of Neurontin’s off-label risks because Pfizer fraudulently promoted the off-label use of the drug.¹⁴⁷ Specifically, the learned intermediary doctrine did not bar Dellinger’s claims because the Pfizer was aware of the off-label use dangers, as it promoted the use, but did not warn physicians of the dangers of the off-label use.¹⁴⁸

3. Tennessee

In *Smith v. Pfizer, Inc.*,¹⁴⁹ another case involving Neurontin, a widow alleged that Neurontin caused her husband to commit suicide.¹⁵⁰ She brought a claim against Pfizer alleging that it failed to warn physicians of the risks related to using Neurontin as a pain reliever, an off-label use.¹⁵¹ She alleged that Pfizer’s unauthorized off-label promotion of Neurontin showed that Pfizer did not adequately test the drug as a pain reliever even though it knew physicians were prescribing the drug for that use.¹⁵² As such, plaintiff argued, Pfizer could not adequately warn physicians of the risks.¹⁵³ Pfizer argued that because plaintiff did not show that Smith’s doctor relied on any off-label promotion, it was irrelevant.¹⁵⁴ The Federal District Court applied Tennessee law and disagreed.¹⁵⁵ The Court determined that Pfizer’s unauthorized promotion of

¹³⁹ *Id.* at 1207.

¹⁴⁰ *Id.* at 1212–13.

¹⁴¹ *Id.*

¹⁴² No. 5:03CV95, 2006 WL 2057654 (W.D.N.C. July 19, 2006).

¹⁴³ *Id.* at *6.

¹⁴⁴ *Id.* at *1.

¹⁴⁵ *Id.*

¹⁴⁶ *Id.* at *3.

¹⁴⁷ *Id.* at *6.

¹⁴⁸ *Id.*

¹⁴⁹ 714 F. Supp. 2d 845 (M.D. Tenn. 2010).

¹⁵⁰ *Id.* at 848.

¹⁵¹ *Id.* The FDA approved Neurontin to treat Epilepsy. *Id.*

¹⁵² *Id.* at 854.

¹⁵³ *Id.*

¹⁵⁴ *Id.*

¹⁵⁵ *Id.*

Neurontin for off-label uses made it more likely that the use was foreseeable and therefore required Pfizer to adequately test and warn physicians of the risks associated with the use.¹⁵⁶

V. CONCLUSION

The law regarding the learned intermediary doctrine and off-label use is conflicting. This creates difficulty in determining the best way to defend drug manufacturers in cases involving off-label use. In some cases, courts base their decision on whether the learned intermediary doctrine applies the totality of the circumstances, including the manufacturers' knowledge, their promotion of the off-label use, and/or the foreseeability of the use. In other cases, courts have assumed the manufacturers always have a duty to warn and have not applied the doctrine in the absence of the warnings. Still other courts find that the learned intermediary doctrine applies in all cases since physicians use their entire knowledge base and training to determine what is best for the patient. Given these varied approaches, the foregoing survey of case law may help those who defend drug manufacturers determine the relevant evidence and the likelihood that the learned intermediary doctrine will protect manufacturers sued in the jurisdictions discussed.

¹⁵⁶ *Id.*; *see also* Ebel v. Eli Lilly and Co., 536 F. Supp. 2d 767 (S.D. Tex. 1999) (finding under Texas law, promotion of off-label use rebuts the presumption that warnings are adequate).