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Memorandum

To: **Senate Judiciary I Subcommittee on Pharmaceutical Liability**
From: **Bill Patterson, Subcommittee Counsel**
Date: **April 24, 2012**
Re: **Comparison of FDA Compliance Provisions in Bill Draft 2011-TG-14A and Current Law of North Carolina, Michigan and New Jersey**

This memorandum summarizes and compares Bill Draft 2011-TG-14A and existing North Carolina, New Jersey and Michigan statutes with regard to of the effect on a defendant's product liability under each law if there is a finding that the drug alleged to have caused the injury giving rise to the action was in compliance with FDA regulations at the time it left the control of the manufacturer or seller. Copies of all cited authorities are enclosed.

I. SUMMARY OF REGULATORY COMPLIANCE PROVISIONS

A. Current North Carolina Law

In determining whether a manufacturer is liable for inadequate design or formulation of a product, G.S. 99B-6(b) requires consideration of the following factors, among others:

1) the extent to which the design or formulation conformed to any applicable government standard that was in effect when the product left the control of its manufacturer; and

2) the extent to which the labeling for a prescription or nonprescription drug approved by the United States Food and Drug Administration conformed to any applicable government or private standard that was in effect when the product left the control of its manufacturer.

Under current law, no presumption arises from a finding that the drug's design, formulation or labeling conformed to a government or private standard.

B. Bill Draft 2011-TG-14A (Proposed New G.S. 99B-12)

In a product liability action against a manufacturer or seller of a drug that was approved for safety and efficacy by the FDA, a finding that the drug and its labeling were in compliance with FDA approval at the time the drug left the control of the manufacturer or seller would give rise to a rebuttable presumption that the drug was safe and effective for its approved use, and the manufacturer or seller would not be liable. The proposed law would require clear and convincing evidence to rebut this presumption.

This defense would not apply if:

1. the claimant establishes any of the following by a preponderance of the evidence:

    a) the defendant sold the drug after the effective date of an FDA order recalling the drug or withdrawing its approval or substantially altering the terms of approval in a way that would have avoided the claimant's injury;

    b) the defendant Intentionally, and in violation of FDA regulations as determined final agency action, withheld or misrepresented to the FDA information material to drug approval and relevant to the harm caused to the plaintiff; or

    c) the defendant made an illegal payment to a government agency employee to secure drug approval;

2. the action was brought under the False Claims Act and is not based on allegations that the drug was not safe or effective or that the manufacturer failed to provide an adequate warning; or

3. the claimant establishes, by a preponderance of the evidence, all of the following:

    a) the manufacturer or seller recommended, promoted, or advertised the drug for an indication not approved by the United States Food and Drug Administration;

    b) the drug was used as recommended, promoted, or advertised; and

    c) the recommended, promoted, or advertised use of the drug was the proximate cause of the claimant's injury.

C. Michigan Law

In a product liability action against a manufacturer or seller of a drug that was approved for safety and efficacy by the FDA, the manufacturer and seller are not liable if the drug and its labeling were in compliance with the FDA's approval at the time it left the control of the manufacturer or seller. This defense is not available to the defendant if the drug was sold in the United States after the effective date of an FDA order recalling the drug or withdrawing its approval. M.C.L.A. 600.2946(5).

This statute's "fraud on the FDA" provision, under which the defense would not apply if FDA approval of the drug was procured by withholding material information from the FDA or through bribery, has been declared preempted under federal law to the extent that it requires a state court finding of fraud on the FDA. Garcia v. Wyeth –Ayerst Laboratories, 385 F.3d 961 (6th Cir. 2004).

D. New Jersey Law

In product liability claims based on inadequate product warning or instruction, a rebuttable presumption arises that the warning or instruction given in connection with a drug is adequate if it was approved or prescribed by the FDA. N.J.S.A. 2A:58C-4.

To overcome this presumption, the claimant must offer substantial evidence of deliberate concealment or nondisclosure of after-acquired knowledge of harmful effects by the manufacturer. Kendall v. Hoffman-La Roche, Inc., 209 N.J. 173, 195-196, 36 A.3d 541, 554-555 (N.J.,2012).

In product liability claims involving a drug, punitive damages shall not be awarded if the drug was approved or licensed by the FDA, or is generally recognized as safe and effective pursuant to conditions established by the FDA and applicable regulations, including packaging and labeling regulations. N.J.S.A. 2A:58C-5(c).

A statutory exception that would permit an award of punitive damages upon a finding of fraud on the FDA has been declared invalid as preempted by federal law. McDarby v. Merck & Co., Inc., 401 N.J. Super. 10, 949 A.2d 223 (A.D. 2008).

II. SUMMARY OF DIFFERENCES

Under current North Carolina law, compliance with FDA regulations is simply one factor that must be considered in determining liability for inadequate design or formulation, but it gives rise to no presumption.

In contrast to current North Carolina law, under the bill draft and under the current New Jersey and Michigan law, a finding of FDA compliance either would bar liability altogether, bar the imposition of punitive damages, or give rise to a presumption that the claimant must overcome before liability can be imposed.

Under Bill Draft 2011-TG-14A, FDA compliance would give rise to a rebuttable presumption that the drug was safe and effective for its approved use and would bar liability unless the presumption is rebutted by clear and convincing evidence. The defense would be unavailable:

1) if FDA approval resulted from bribery or intentional failure to disclose information to the FDA (assuming that this exception is not successfully challenged on grounds of federal preemption);
2) in False Claims Act claims that do not allege that the drug was not safe or effective or that the manufacturer failed to provide an adequate warning; and
3) in claims arising from the consumer's use of the drug in accordance with advertised uses not approved by the FDA ("off-label use").

Under Michigan law, regulatory compliance bars liability altogether unless the drug was sold after FDA recall or withdrawal of approval.

Under New Jersey law, regulatory compliance bars punitive damages in all claims, and in claims based on inadequate warning, establishes a rebuttable presumption of no liability that can be overcome only by substantial evidence of deliberate concealment or nondisclosure of harmful effects by the manufacturer.

Cited Authorities

North Carolina

N.C.G.S. 99B-6

Michigan

M.C.L.A. 600.2946
Garcia v. Wyeth –Ayerst Laboratories, 385 F.3d 961 (6th Cir. 2004)

New Jersey

N.J.S.A. 2A:58C-4
N.J.S.A. 2A:58C-5
Kendall v. Hoffman-La Roche, Inc., 209 N.J. 173, 195-196, 36 A.3d 541, 554-555 (N.J.,2012)
McDarby v. Merck & Co., Inc., 401 N.J. Super. 10, 949 A.2d 223 (A.D. 2008)

West's North Carolina General Statutes Annotated Currentness
Chapter 99B. Products Liability (Refs & Annos)

➞➞ § 99B-6. Claims based on inadequate design or formulation

(a) No manufacturer of a product shall be held liable in any product liability action for the inadequate design or formulation of the product unless the claimant proves that at the time of its manufacture the manufacturer acted unreasonably in designing or formulating the product, that this conduct was a proximate cause of the harm for which damages are sought, and also proves one of the following:

(1) At the time the product left the control of the manufacturer, the manufacturer unreasonably failed to adopt a safer, practical, feasible, and otherwise reasonable alternative design or formulation that could then have been reasonably adopted and that would have prevented or substantially reduced the risk of harm without substantially impairing the usefulness, practicality, or desirability of the product.

(2) At the time the product left the control of the manufacturer, the design or formulation of the product was so unreasonable that a reasonable person, aware of the relevant facts, would not use or consume a product of this design.

(b) In determining whether the manufacturer acted unreasonably under subsection (a) of this section, the factors to be considered shall include, but are not limited to, the following:

(1) The nature and magnitude of the risks of harm associated with the design or formulation in light of the intended and reasonably foreseeable uses, modifications, or alterations of the product.

(2) The likely awareness of product users, whether based on warnings, general knowledge, or otherwise, of those risks of harm.

(3) The extent to which the design or formulation conformed to any applicable government standard that was in effect when the product left the control of its manufacturer.

(4) The extent to which the labeling for a prescription or nonprescription drug approved by the United States Food and Drug Administration conformed to any applicable government or private standard that was in effect when the product left the control of its manufacturer.

(5) The utility of the product, including the performance, safety, and other advantages associated with that design or formulation.

(6) The technical, economic, and practical feasibility of using an alternative design or formulation at the time of manufacture.

(7) The nature and magnitude of any foreseeable risks associated with the alternative design or formulation.

(c) No manufacturer of a product shall be held liable in any product liability action for a claim under this section to the extent that it is based upon an inherent characteristic of the product that cannot be eliminated without substantially compromising the product's usefulness or desirability and that is recognized by the ordinary person with the ordinary knowledge common to the community.

(d) No manufacturer of a prescription drug shall be liable in a product liability action on account of some aspect of the prescription drug that is unavoidably unsafe, if an adequate warning and instruction has been provided pursuant to G.S. 99B-5(c). As used in this subsection, “unavoidably unsafe” means that, in the state of technical, scientific, and medical knowledge generally prevailing at the time the product left the control of its manufacturer, an aspect of that product that caused the claimant's harm was not reasonably capable of being made safe.

(e) Nothing in this section precludes an action against a manufacturer in accordance with the provisions of G.S. 99B-5.

CREDIT(S)

Added by Laws 1995, c. 522, § 1, eff. Jan. 1, 1996.

The statutes and Constitution are current through S.L. 2012-1 of the 2011 Regular Session of the General Assembly.

➡➡ 600.2946. Product liability actions; admissibility of evidence; liability, burden of proof; presumption; drugs

Sec. 2946. (1) It shall be admissible as evidence in a product liability action that the production of the product was in accordance with the generally recognized and prevailing nongovernmental standards in existence at the time the specific unit of the product was sold or delivered by the defendant to the initial purchaser or user.

(2) In a product liability action brought against a manufacturer or seller for harm allegedly caused by a production defect, the manufacturer or seller is not liable unless the plaintiff establishes that the product was not reasonably safe at the time the specific unit of the product left the control of the manufacturer or seller and that, according to generally accepted production practices at the time the specific unit of the product left the control of the manufacturer or seller, a practical and technically feasible alternative production practice was available that would have prevented the harm without significantly impairing the usefulness or desirability of the product to users and without creating equal or greater risk of harm to others. An alternative production practice is practical and feasible only if the technical, medical, or scientific knowledge relating to production of the product, at the time the specific unit of the product left the control of the manufacturer or seller, was developed, available, and capable of use in the production of the product and was economically feasible for use by the manufacturer. Technical, medical, or scientific knowledge is not economically feasible for use by the manufacturer if use of that knowledge in production of the product would significantly compromise the product's usefulness or desirability.

(3) With regard to the production of a product that is the subject of a product liability action, evidence of a philosophy, theory, knowledge, technique, or procedure that is learned, placed in use, or discontinued after the event resulting in the death of the person or injury to the person or property, which if learned, placed in use, or discontinued before the event would have made the event less likely to occur, is admissible only for the purpose of proving the feasibility of precautions, if controverted, or for impeachment.

(4) In a product liability action brought against a manufacturer or seller for harm allegedly caused by a product, there is a rebuttable presumption that the manufacturer or seller is not liable if, at the time the specific unit of the product was sold or delivered to the initial purchaser or user, the aspect of the product that allegedly caused the harm was in compliance with standards relevant to the event causing the death or injury set forth in a federal or state statute or was approved by, or was in compliance with regulations or standards relevant to the event causing the death or injury promulgated by, a federal or state agency responsible for reviewing the safety of the product. Noncompliance with a standard relevant to the event causing the death or injury set forth in a federal or state statute or lack of approval by, or noncompliance with regulations or standards relevant to the event causing the death or injury promulgated by, a federal or state agency does not raise a presumption of negligence on the part of a manufacturer or seller. Evidence of compliance or noncompliance with a regulation or standard not relevant to the event causing the death or injury is not admissible.

(5) In a product liability action against a manufacturer or seller, a product that is a drug is not defective or unreasonably dangerous, and the manufacturer or seller is not liable, if the drug was approved for safety and efficacy by the United States food and drug administration, and the drug and its labeling were in compliance with the United States food and drug administration's approval at the time the drug left the control of the manufacturer or seller. However, this subsection does not apply to a drug that is sold in the United States after the effective date of an order of the United States food and drug administration to remove the drug from the market or to withdraw its approval. This subsection does not apply if the defendant at any time before the event that allegedly caused the injury does any of the following:

(a) Intentionally withholds from or misrepresents to the United States food and drug administration information concerning the drug that is required to be submitted under the federal food, drug, and cosmetic act, chapter 675, 52 Stat. 1040, 21 U.S.C. 301 to 321, 331 to 343-2, 344 to 346a, 347, 348 to 353, 355 to 360, 360b to 376, and 378 to 395, and the drug would not have been approved, or the United States food and drug administration would have withdrawn approval for the drug if the information were accurately submitted.

(b) Makes an illegal payment to an official or employee of the United States food and drug administration for the purpose of securing or maintaining approval of the drug.

CREDIT(S)

Amended by P.A.1995, No. 249, § 1, Eff. March 28, 1996.
The statutes are current through P.A.2012, No. 71, of the 2012 Regular Session, 96th Legislature.

United States Court of Appeals,
Sixth Circuit.
Julia GARCIA, Plaintiff-Appellant,
v.
WYETH-AYERST LABORATORIES, Defendant-Appellee.

No. 03-1712.
Argued: Aug. 5, 2004.
Decided and Filed: Oct. 7, 2004.

Background: Patient allegedly injured by a non-steroidal, anti-inflammatory drug brought a products liability suit against the drug manufacturer. On a variety of motions, including cross-motions for summary judgment, the United States District Court for the Eastern District of Michigan, David M. Lawson, J., 265 F.Supp.2d 825, granted defendant's motion for summary judgment. Plaintiff appealed.

Holdings: The Court of Appeals, Kennedy, Circuit Judge, held that:
(1) a Michigan statute immunizing drug manufacturers from products liability if, inter alia, the drug was approved for safety and efficacy by the United States Food and Drug Administration (FDA) was not unconstitutional;
(2) patient failed to state a claim of denial of access to courts; and
(3) statute did not violate patient's substantive Due Process rights.

Affirmed.

West Headnotes

[1] Federal Courts 170B 387

170B Federal Courts
170BVI State Laws as Rules of Decision
170BVI(B) Decisions of State Courts as Authority
170Bk387 k. Federal Constitution and Laws. Most Cited Cases

A federal court evaluating a statute's validity under the federal constitution is not bound by a state court's evaluation of the same statute under the state constitution.

[2] Products Liability 313A 103

313A Products Liability
313AI In General
313Ak101 Constitutional and Statutory Provisions
313Ak103 k. Validity and Constitutionality. Most Cited Cases
(Formerly 313Ak2)

Products Liability 313A 225

313A Products Liability
313AIII Particular Products
313Ak223 Health Care and Medical Products
313Ak225 k. Drugs in General. Most Cited Cases
(Formerly 313Ak2)

States 360 18.65

360 States
360I Political Status and Relations
360I(B) Federal Supremacy; Preemption

360k18.65 k. Product Safety; Food and Drug Laws. Most Cited Cases

Michigan statute immunizing drug manufacturers from products liability if, inter alia, the drug was approved for safety and efficacy by the United States Food and Drug Administration (FDA) was not rendered unconstitutional by the fact that it created an immunity for drug manufacturers that could be upset only by a statutory exception, proof of fraud on the FDA, which federal law generally preempted; if the state had decided that the federal regulatory scheme furnished its citizens protection enough against potential injury from the unanticipated effects of a new medication, the state had the prerogative to withdraw the compensatory and remedial safeguards that the tort reparations system might otherwise have provided. U.S.C.A. Const. Art. 6, cl. 2; M.C.L.A. § 600.2946(5).

[3] States 360 18.3

360 States
360I Political Status and Relations
360I(B) Federal Supremacy; Preemption
360k18.3 k. Preemption in General. Most Cited Cases

A federal law may preempt a state law where a federal statute may expressly preempt the state law, a federal law may impliedly preempt a state law, or preemption results from an actual conflict between a federal and a state law. U.S.C.A. Const. Art. 6, cl. 2.

[4] States 360 18.7

360 States
360I Political Status and Relations
360I(B) Federal Supremacy; Preemption
360k18.7 k. Occupation of Field. Most Cited Cases

States 360 18.11

360 States
360I Political Status and Relations
360I(B) Federal Supremacy; Preemption
360k18.11 k. Congressional Intent. Most Cited Cases

Implied preemption occurs if a scheme of federal regulation is so pervasive as to make reasonable the inference that Congress left no room for the States to supplement it, if the Act of Congress touches a field in which the federal interest is so dominant that the federal system will be assumed to preclude enforcement of state laws on the same subject, or if the goals sought to be obtained and the obligation imposed reveal a purpose to preclude state authority. U.S.C.A. Const. Art. 6, cl. 2.

[5] States 360 18.3

360 States
360I Political Status and Relations
360I(B) Federal Supremacy; Preemption
360k18.3 k. Preemption in General. Most Cited Cases

In analyzing implied preemption, a court must begin with the assumption that a state law is valid and should be reluctant to resort to the Supremacy Clause. U.S.C.A. Const. Art. 6, cl. 2.

[6] Constitutional Law 92 994

92 Constitutional Law
92VI Enforcement of Constitutional Provisions
92VI(C) Determination of Constitutional Questions
92VI(C)3 Presumptions and Construction as to Constitutionality
92k994 k. Avoidance of Constitutional Questions. Most Cited Cases

(Formerly 92k48(1))

Where possible, the Supreme Court interprets congressional enactments to avoid raising serious constitutional questions.

[7] Constitutional Law 92 656

92 Constitutional Law
92V Construction and Operation of Constitutional Provisions
92V(F) Constitutionality of Statutory Provisions
92k656 k. Facial Invalidity. Most Cited Cases
(Formerly 92k38)

Under Michigan law, a legislative enactment can be held to be facially invalid only if there are no factual circumstances under which the provision could be constitutionally implemented.

[8] Statutes 361 64(1)

361 Statutes
361I Enactment, Requisites, and Validity in General
361k64 Effect of Partial Invalidity
361k64(1) k. In General. Most Cited Cases

The law remaining after an invalid portion of the law is severed will be enforced independently unless the invalid provisions are deemed so essential, and are so interwoven with others, that it cannot be presumed that the legislature intended the statute to operate otherwise than as a whole.

[9] Constitutional Law 92 2312

92 Constitutional Law
92XIX Rights to Open Courts, Remedies, and Justice
92k2312 k. Abrogation, Modification, or Recognition of Remedies. Most Cited Cases
(Formerly 92k328)

Products Liability 313A 103

313A Products Liability
313AI In General
313Ak101 Constitutional and Statutory Provisions
313Ak103 k. Validity and Constitutionality. Most Cited Cases
(Formerly 313Ak2)

Products Liability 313A 225

313A Products Liability
313AIII Particular Products
313Ak223 Health Care and Medical Products
313Ak225 k. Drugs in General. Most Cited Cases
(Formerly 313Ak2)

Patient allegedly injured by a non-steroidal, anti-inflammatory drug failed to state a claim of denial of access to courts, which she asserted was effected by a Michigan statute immunizing drug manufacturers from products liability if, inter alia, the drug was approved for safety and efficacy by the United States Food and Drug Administration (FDA); she did not allege that she was unable to gain access to court to litigate her claim, but rather, she claimed that the statute required too much, and that the immunity it granted to drug manufacturers was too broad. U.S.C.A. Const. Art. 4, § 2, cl. 1; U.S.C.A. Const.Amends. 1, 14; M.C.L.A. § 600.2946(5).

[10] Constitutional Law 92 4420

92 Constitutional Law
92XXVII Due Process
92XXVII(G) Particular Issues and Applications
92XXVII(G)19 Tort or Financial Liabilities
92k4418 Torts and Personal Injuries
92k4420 k. Immunity in General. Most Cited Cases
(Formerly 92k301(1))

Products Liability 313A 103

313A Products Liability
313AI In General
313Ak101 Constitutional and Statutory Provisions
313Ak103 k. Validity and Constitutionality. Most Cited Cases
(Formerly 313Ak2)

Products Liability 313A 225

313A Products Liability
313AIII Particular Products
313Ak223 Health Care and Medical Products
313Ak225 k. Drugs in General. Most Cited Cases
(Formerly 313Ak2)

Michigan statute immunizing drug manufacturers from products liability if, inter alia, the drug was approved for safety and efficacy by the United States Food and Drug Administration (FDA) did not violate patient's substantive Due Process rights, despite her claim that the statute effectively foreclosed an injured party's right to recover damages from manufacturers of defective drugs; it was not difficult to divine a rationale which may have been the basis of the State's preference of drug manufacturers over tort claimants that would comfortably fall within the wide boundaries of the rational basis test. U.S.C.A. Const.Amend. 14; M.C.L.A. § 600.2946(5).

West Codenotes
Limited on Preemption GroundsM.C.L.A. § 600.2946(5)(a, b) ***963** John J. Schutza (argued), Richard B. Worsham (briefed), Worsham & Victor, Southfield, MI, for Appellant.

Shana J. Long (argued and briefed), Michael L. Koon (briefed), Shook, Hardy & Bacon, Kansas City, MO, Scott L. Gorland (briefed), Pepper Hamilton, Detroit, MI, for Appellee.

Before: KENNEDY, SUTTON, and COOK, Circuit Judges.

KENNEDY, Circuit Judge.

Plaintiff Julia Garcia appeals the district court order granting summary judgment to Defendant Wyeth-Ayerst Laboratories in this drug product liability case on the basis of a statutory immunity provided in MICH. COMP. LAWS § 600.2946(5). Plaintiff argues that the district court erred in failing to declare the statute unconstitutional on the grounds that (1) it has been impliedly preempted by the federal Food, Drug and Cosmetic Act (FDCA), 21 U.S.C. § 301, *et seq.*, in violation of the Supremacy Clause, (2) it has interfered with her fundamental right of access to the courts and her Seventh Amendment right to a jury trial, and (3) it violated the Due Process Clause by depriving her of the right to use a traditional common law tort remedy as a means of seeking redress for her injuries. Finding no error in the district court's decision, we affirm.

BACKGROUND

In September of 1997, Plaintiff was treated for persistent pain in her neck and shoulders by her physician. To alleviate her pain, her physician gave her multiple prescriptions for Duract, a non-steroidal, anti-inflammatory prescription medication manufactured by Defendant. The medication had been approved for use earlier that year by the United States Food and Drug Administration ("FDA"). The medication, however, caused liver failure and Plaintiff was required to undergo a liver transplant in 1998 to save her life. Plaintiff

sued Defendant for making and selling an unsafe drug, and she seeks compensation for her injury, reimbursement for past medical expenses, and future medical expenses including a likely additional liver transplant. Defendant has since voluntarily withdrawn the drug from the market. The district court granted Defendant's motion for summary judgment and dismissed the case on the basis of Michigan's products liability statute that immunizes drug manufacturers from liability under certain conditions. The present appeal followed.

ANALYSIS

Michigan law governs this diversity action. *Westfield Ins. Co. v. Tech Dry, Inc.*, 336 F.3d 503, 506 (6th Cir.2003). The State of Michigan has adopted a drug products liability statute that immunizes drug manufacturers from liability from ***964** damages in suits contending that their drug was defective or unreasonably dangerous "if the drug was approved for safety and efficacy by [the FDA], and the drug and labeling were in compliance with [the FDA's] approval at the time the drug left the control of the manufacturer or seller." MICH. COMP. LAWS § 600.2946(5). The immunity is subject to two exceptions: (1) if the manufacturer intentionally withheld or misrepresented material information concerning the drug that it is required to be submitted under the Food and Drug Cosmetics Act and the drug would not have been approved, or the FDA would have withdrawn approval if the information was accurately submitted to the FDA, or if the manufacturer bribed an FDA official or employee to secure the drug's approval, MICH. COMP. LAWS § 600.2946(5)(a) & (b); and (2) if the offending drug was sold after the FDA withdrew approval or ordered the drug removed from the market, *id.*

[1] In prior unrelated litigation, the Michigan Court of Appeals had held that this statute was repugnant to the Michigan Constitution because it impermissibly delegated legislative authority to the FDA as the final arbiter of drug safety in Michigan. *Taylor v. Gate Pharms.*, 248 Mich.App. 472, 639 N.W.2d 45 (2001). The Michigan Supreme Court overturned that ruling holding that:

> MCL 600.2946(5) is a statute that refers to factual conclusions of independent significance, i.e., the FDA conclusion regarding the safety and efficacy of a drug, that once made causes, at the Michigan Legislature's direction, Michigan courts to find as a matter of law that the manufacturer or seller acted with due care.

Taylor v. Smithkline Beecham Corp., 468 Mich. 1, 658 N.W.2d 127, 134 (2003). It concluded that the statute's linking of dangerousness to the FDA's complex and detailed approval process is nothing more than an incorporation of common standards, such as weights and measures or the time of day, which are also determined by federal agencies. According to the Michigan Supreme Court, therefore, the statute is valid under the Michigan Constitution. Plaintiff in this case, however, challenges the applicable statute under the *federal* constitution. As the district court properly noted, a federal court evaluating the statute's validity under the federal constitution is not bound by a state court's evaluation of the same statute under the state constitution. *Garcia v. Wyeth-Ayerst Labs.*, 265 F.Supp.2d 825, 2003 WL 21246424, slip op. at 3 (E.D.Mich. May 19, 2003) (citing *Barden Detroit Casino, L.L.C. v. City of Detroit*, 230 F.3d 848 (6th Cir.2000)). Before the district court, Plaintiff argued that the Michigan statute is unconstitutional because (1) it had been impliedly preempted by the FDCA and therefore runs afoul of the Supremacy Clause, (2) it interferes with Plaintiff's fundamental right of access to the courts and her Seventh Amendment right to a jury trial, and (3) it violates the Due Process Clause by depriving her of the right to use a traditional common law tort remedy as a means of seeking redress for her injuries.[FN1] For the reasons stated below, we agree with the district court that Plaintiff's arguments are without merit.

> FN1. On motion for summary judgment, the district court held that Plaintiff had submitted no evidence supporting its claims of bribery or misrepresentation to the FDA, nor any evidence that the withdrawal of Duract was precipitated by the FDA or based on any provable misconduct by Defendant. Plaintiff has not appealed that determination. Therefore, Plaintiff can only succeed in this action if we find that the two exceptions are unconstitutional and that the offending exceptions cannot be severed from the general immunity provision, thereby invalidating the general immunity provision and stripping Defendant of its statutory protection.

***965 A. Implied Preemption**

[2] Plaintiff argued before the district court that Section 600.2946(5) conflicts with and is impliedly preempted by federal law because it requires one to prove fraud on the FDA as part of her cause of action against Defendant. She cannot prove fraud on the FDA because such claims are preempted by federal law and, thus, cannot bring herself within the exceptions. The district court agreed with Plaintiff that the fraud-on-the-FDA exception to the general statutory immunity was preempted by federal law but held that it could sever the offending exception and uphold the general statutory immunity in light of an explicit severability provision in MICH. COMP. LAWS § 8.5.

[3][4][5] In general, a federal law may preempt a state law in any of the following three scenarios. First, a federal statute may expressly preempt the state law. *Gibson v. Am. Bankers Ins. Co.*, 289 F.3d 943, 948 (6th Cir.2002). Second, a federal law may impliedly preempt a state law. *Id.* at 948-49. Third, preemption results from an actual conflict between a federal and a state law. *Id.* at

949. Since neither express preemption nor an actual conflict is present in this case, we are concerned solely with the question of implied preemption. As this Court has explained:

> Implied preemption occurs if a scheme of federal regulation is so pervasive as to make reasonable the inference that Congress left no room for the States to supplement it, if the Act of Congress touches a field in which the federal interest is so dominant that the federal system will be assumed to preclude enforcement of state laws on the same subject, or if the goals sought to be obtained and the obligation imposed reveal a purpose to preclude state authority.

Id. (citations omitted). As the district court properly noted, in "analyzing implied preemption, a court must begin with the assumption that a state law is valid and should be reluctant to resort to the Supremacy Clause." *Garcia v. Wyeth-Ayerst Labs.*, 265 F.Supp.2d 825, 2003 WL 21246424, slip op. at 7 (E.D.Mich. May 19, 2003) (citations omitted).

The United States Supreme Court has expressly considered the question of a state common law fraud-on-the-FDA tort claim and found that it was impliedly preempted by the FDCA and the Medical Device Act ("MDA"), 21 U.S.C. §§ 360e(b)(1)(A) & (B). *Buckman Co. v. Pls.' Legal Comm.*, 531 U.S. 341, 350, 121 S.Ct. 1012, 148 L.Ed.2d 854 (2001) (explaining that "[s]tate-law fraud-on-the-FDA claims inevitably conflict with the FDA's responsibility to police fraud consistently with the Agency's judgment and objectives.") This case, however, presents a somewhat different legal regime from the one invalidated in *Buckman.* The Michigan legislature has provided a general immunity for drug manufacturers with a specific exception for circumstances involving, *inter alia*, fraud on the FDA [FN2] rather ***966** than a specific cause of action for fraud on the FDA. This difference, however, is immaterial in light of *Buckman.* As the district court properly found, "*Buckman* teaches that state tort remedies requiring proof of fraud committed against the FDA are foreclosed since federal law preempts such claims." *Garcia v. Wyeth-Ayerst Labs.*, 265 F.Supp.2d 825, 2003 WL 21246424, slip op. at 8 (E.D.Mich. May 19, 2003).

> FN2. The statute provides, in relevant part:
>
> > (5) In a product liability action against a manufacturer or a seller, a product that is a drug is not defective or unreasonably dangerous, and the manufacturer or seller is not liable, if the drug was approved for safety and efficacy by the United States food and drug administration, and the drug and its labeling were in compliance with the United States food and drug administration's approval at the time the drug left the control of the manufacturer or seller....This subsection does not apply if the defendant at any time before the event that allegedly caused the injury does any of the following:
> >
> > (a) Intentionally withholds from or misrepresents to the United States food and drug administration information concerning the drug that is required to be submitted under the federal food, drug, and cosmetic act ..., and the drug would have not been approved, or the United States food and drug administration would have withdrawn approval for the drug if the information were accurately submitted.
> >
> > (b) Makes an illegal payment to an official or employee of the United States food and drug administration for the purpose of securing or maintaining approval of the drug.
>
> MICH. COMP. LAWS § 600.2946(5).

Having concluded that M.C.L. § 600.2946(5)(a) and (b) were unconstitutional, the district court had to consider what effect that conclusion had on the rest of M.C.L. § 600.2946(5). It is unclear whether the district court concluded that the offending subsections can simply be severed from the rest of the section, giving drug manufacturers a full immunity from state-law lawsuits in the State of Michigan as long as they complied with the FDA's requirements and the drug had been approved by the FDA, or whether it concluded that in view of the preemption "the exceptions can only be triggered by a finding by the FDA that a drug manufacturer committed fraud or bribed an FDA official in order to obtain approval of a drug." Appellee's Br. at 18.

It is one thing, however, to say that *Buckman* applies to the exemptions contained in Michigan Compiled Laws § 600.2946(5); it is quite another to say that *Buckman* preempts these exemptions in all of their applications. Doubtless, *Buckman* prohibits a plaintiff from invoking the exceptions on the basis of *state court* findings of fraud on the FDA. Such a state court proceeding would raise the same inter-branch-meddling concerns that animated *Buckman.* But the same concerns do not arise when the *FDA itself* determines that a fraud has been committed on the agency during the regulatory-approval process. *Cf. Buckman*, 531 U.S. at 351, 121 S.Ct. 1012 ("[F]raud-on-the-FDA claims would also cause applicants to fear that their disclosures to the FDA, although deemed appropriate by the Administration, will later be judged insufficient in state court."). Thus, in this setting, it makes abundant sense to allow a State that chooses to incorporate a federal standard into its law of torts to allow that standard to apply when the federal agency itself determines that fraud marred the regulatory-approval process. In the final analysis, the exemptions are invalid as applied in some settings (*e.g.*,

when a plaintiff asks a state court to find bribery or fraud on the FDA) but not in others (*e.g.* claims based on federal findings of bribery or fraud on the FDA).

Having concluded that Michigan Compiled Laws § 600.2946(5)(a) & (b) are unconstitutional in some settings-including plaintiff's own suit (as she alleged bribery and fraud on the FDA but did not offer any federal findings)-we now face the issue urged upon us by the plaintiff: Does the preemption of these exemptions in some settings requires us to invalidate § 600.2946(5) in its entirety? We do not think so.

[6][7][8] The Michigan Legislature has provided a general severability clause that applies to all its enactments. The clause provides:

> In the construction of the statutes of this state the following rules shall be ***967** observed unless such construction would be inconsistent with the manifest intent of the legislature, that is to say: If any portion of an act or the application thereof to any person or circumstances shall be found to be invalid by a court, such invalidity shall not affect the remaining portions or applications of the act which can be given effect without the invalid portion or application ..., and to this end acts are declared to be severable.

Mich. Comp. Laws § 8.5. *See also Maki v. East Tawas*, 385 Mich. 151, 188 N.W.2d 593, 596 (1971) (upholding the remainder of the enacted law because it is "otherwise complete in itself and capable of being carried out without reference to the unconstitutional" section). The question, accordingly, is whether the Michigan Legislature would have preferred the situation where drug manufacturers would enjoy immunity in the absence of a federal finding of bribery or fraud on the FDA, or the situation urged by the Plaintiff where drug manufacturers would enjoy no immunity at all. As we explained on an earlier occasion, the law remaining after an invalid portion of the law is severed will be enforced independently "unless the invalid provisions are deemed so essential, and are so interwoven with others, that it cannot be presumed that the legislature intended the statute to operate otherwise than as a whole." *Moore v. Fowinkle*, 512 F.2d 629, 632 (6th Cir.1975).[FN3]

> FN3. Where possible, the Supreme Court "interprets congressional enactments to avoid raising serious constitutional questions," *Cheek v. United States*, 498 U.S. 192, 111 S.Ct. 604, 112 L.Ed.2d 617 (1991) (citations omitted). The Michigan courts adhere to a similar principle. "A legislative enactment can be held to be facially invalid only if there are no factual circumstances under which the provision could be constitutionally implemented." *Gora, Maxwell, et al., v. Ferndale* 456 Mich. 704, 576 N.W.2d 141 (1998) (citing *United States v. Salerno*, 481 U.S. 739, 107 S.Ct. 2095, 95 L.Ed.2d 697 (1987) n. 15, *Pigorsh v. Fahner*, 386 Mich. 508, 509, 194 N.W.2d 343 (1972) (we are bound, if possible, to construe statutes as to give them validity and a reasonable interpretation)).

We find that Plaintiff has failed to persuade us that the district court erred as a matter of law, and that given a choice between immunity absent a finding of bribery or fraud by the Federal Government and no immunity, the Michigan Legislature would prefer the former option. First, it appears that the Michigan legislature was concerned that unlimited liability for drug manufacturers would threaten the financial viability of many enterprises and could add substantially to the cost and unavailability of many drugs. *See generally* State Fiscal Agency, Revised Bill Analysis, S.B. 344 & H.B. 4508 (Mich.1996). Second, and most importantly, severing the preemption exemptions will not give license to drug manufacturers to use bribery or fraud as a means of obtaining FDA approval, then rely on that approval as a shield from products liability: it will merely place responsibility for prosecuting bribery or fraud on the FDA in the hands of the Federal Government rather than state courts.

B. Access to Courts and the Right to a Jury Trial

[9] Plaintiff also argues that her rights to have access to courts and a jury trial have been violated by her complete inability to obtain relief for her injury. We find it unnecessary to add anything to the thoughtful analysis provided by the district court on this question:

> Although a right-of-access case can be established when a person can prove that a state's judicial process does not provide an adequate procedure to remedy an alleged wrong, *see Glover v. Johnson*, 75 F.3d 264, 268 (6th Cir.1996) ***968** ("Access to the courts ... encompasses all the means a defendant ... might require to get a fair hearing from the judiciary on all charges brought against him or grievances alleged by him.") (citing *Gilmore v. Lynch*, 319 F.Supp. 105, 110 (N.D.Cal.1970), *aff'd sub nom. Younger v. Gilmore*, 404 U.S. 15, 92 S.Ct. 250, 30 L.Ed.2d 142 (1971)), such claims are generally recognized for civil litigants only in the context of spoliation of evidence or interference with filing a lawsuit. *See* [*Swekel v. City of River Rouge*, 119 F.3d 1259, 1263-64 (6th Cir.1997)]. A cognizable claim can be made out "only by showing that the defendants' actions foreclosed [a potential litigant] from filing suit in state court or rendered ineffective any state court remedy [the litigant] previously may have had." *Ibid.* The argument that a state statute stiffens the standard of proof of a common law claim does not implicate this right.

In this case, the plaintiff does not allege that she was unable to gain access to court to litigate her claim. Rather, she contends in essence that Section 600.2946(5) requires too much, and that the immunity it grants to drug manufacturers is too broad. These allegations do not constitute a claim of denial of access to the courts.

Garcia v. Wyeth-Ayerst Labs., 265 F.Supp.2d 825, 834, 2003 WL 21246424, *7 (E.D.Mich. May 19, 2003). Plaintiff has failed to set forth any legally binding precedent that would warrant a reversal of the district court's opinion in this respect.

C. Due Process

[10] Plaintiff finally challenges the district court's finding that the abolition of her cause of action does not violate the Due Process Clause. Plaintiff's argument is without merit. As this Court has previously stated,

> Legislatures do not violate federal due process rights by creating statutes of repose that prevent causes of action from accruing. A litigant has no vested property right in a cause of action until it accrues. The United States Supreme Court has held that due process does not prohibit the abolition of causes of action[. Those] cases have clearly established that a person has no property, no vested interest, in any rule of the common law [,and that t]he "Constitution does not forbid the creation of new rights, or the abolition of old ones recognized by the common law, to attain a permissible legislative object" despite the fact that otherwise settled expectations may be upset thereby.

Hartford Fire Ins. Co. v. Lawrence, Dykes, Goodenberger, Bower & Clancy, 740 F.2d 1362, 1367 (6th Cir.1984) (citations omitted). The only question for us to consider is whether Section 600.2946(5) rationally furthers a legitimate state objective. On that point, we agree with the district court's finding that "the Michigan legislature acted within its authority when it granted immunity from liability to drug sellers and manufacturers who market their products after obtaining approval from the FDA." *Garcia v. Wyeth-Ayerst Labs.*, 265 F.Supp.2d 825, 834, 2003 WL 21246424, *8 (E.D.Mich. May 19, 2003).

CONCLUSION

For the reasons stated above, we affirm the district court's order granting summary judgment in favor of Defendant.

C.A.6 (Mich.),2004.
Garcia v. Wyeth-Ayerst Laboratories
385 F.3d 961, Prod.Liab.Rep. (CCH) P 17,157, Prod.Liab.Rep. (CCH) P 17,092, 2004 Fed.App. 0346P

END OF DOCUMENT

New Jersey Statutes Annotated Currentness

Title 2A. Administration of Civil and Criminal Justice (Refs & Annos)

Subtitle 6. Specific Civil Actions

Chapter 58C. Products Liability (Refs & Annos)

➞➞ 2A:58C-4. Adequate product warning or instruction; rebuttable presumption of adequacy after approval

In any product liability action the manufacturer or seller shall not be liable for harm caused by a failure to warn if the product contains an adequate warning or instruction or, in the case of dangers a manufacturer or seller discovers or reasonably should discover after the product leaves its control, if the manufacturer or seller provides an adequate warning or instruction. An adequate product warning or instruction is one that a reasonably prudent person in the same or similar circumstances would have provided with respect to the danger and that communicates adequate information on the dangers and safe use of the product, taking into account the characteristics of, and the ordinary knowledge common to, the persons by whom the product is intended to be used, or in the case of prescription drugs, taking into account the characteristics of, and the ordinary knowledge common to, the prescribing physician. If the warning or instruction given in connection with a drug or device or food or food additive has been approved or prescribed by the federal Food and Drug Administration under the "Federal Food, Drug, and Cosmetic Act," 52 Stat. 1040, 21 U.S.C. § 301 et seq. or the "Public Health Service Act," 58 Stat. 682, 42 U.S.C. § 201 et seq., a rebuttable presumption shall arise that the warning or instruction is adequate. For purposes of this section, the terms "drug", "device", "food", and "food additive" have the meanings defined in the "Federal Food, Drug, and Cosmetic Act."

CREDIT(S)

L.1987, c. 197, § 4, eff. July 22, 1987.

Current with laws effective through L.2012, c. 2.

New Jersey Statutes Annotated Currentness
Title 2A. Administration of Civil and Criminal Justice (Refs & Annos)
Subtitle 6. Specific Civil Actions
Chapter 58C. Products Liability (Refs & Annos)
➡➡ 2A:58C-5. Punitive damages

a. (Deleted by amendment, P.L.1995, c. 142.)

b. (Deleted by amendment, P.L.1995, c. 142.)

c. Punitive damages shall not be awarded if a drug or device or food or food additive which caused the claimant's harm was subject to premarket approval or licensure by the federal Food and Drug Administration under the "Federal Food, Drug, and Cosmetic Act," 52 Stat. 1040, 21 U.S.C. § 301 et seq. or the "Public Health Service Act," 58 Stat. 682, 42 U.S.C. § 201 et seq. and was approved or licensed; or is generally recognized as safe and effective pursuant to conditions established by the federal Food and Drug Administration and applicable regulations, including packaging and labeling regulations. However, where the product manufacturer knowingly withheld or misrepresented information required to be submitted under the agency's regulations, which information was material and relevant to the harm in question, punitive damages may be awarded. For purposes of this subsection, the terms "drug", "device", "food", and "food additive" have the meanings defined in the "Federal Food, Drug, and Cosmetic Act."

d.

(Deleted by amendment, P.L.1995, c. 142.)

CREDIT(S)

L.1987, c. 197, § 5, eff. July 22, 1987. Amended by L.1995, c. 142, § 8.

Current with laws effective through L.2012, c. 2.

Supreme Court of New Jersey.
Kamie S. KENDALL, Plaintiff–Respondent,
v.
HOFFMAN–LA ROCHE, INC., Roche Laboratories, Inc., F. Hoffman–La Roche Ltd., and Roche Holding Ltd., Defendants–Appellants.

Argued Oct. 24, 2011.
Decided Feb. 27, 2012.

Background: Patient brought action against drug manufacturer after she developed inflammatory bowel disease (IBD) as an alleged result of her use of drug prescribed to her for treatment of recalcitrant nodular acne. The Superior Court entered judgment on jury verdict in favor of patient, awarding $10.5 million in compensatory damages and $78,500 in past medical expenses. Drug manufacturer appealed. The Superior Court, Appellate Division, 2010 WL 3034453, affirmed in part, and reversed and remanded in part. Manufacturer appealed.

Holdings: The Supreme Court, Long, J., held that:
(1) in determining accrual of cause of action for failure to warn, trial court may consider Product Liability Act (PLA) presumption that a Food and Drug Administration (FDA)-approved label is adequate to inform a reasonable person of the dangers of a product, and
(2) patient could not have reasonably known that drug caused or exacerbated her condition, and thus claim was not barred by two-year statute of limitations, notwithstanding PLA presumption of adequacy.

Affirmed.

Wefing, Judge (temporarily assigned), dissented and filed opinion.

West Headnotes

[1] Limitation of Actions 241 1

241 Limitation of Actions
241I Statutes of Limitation
241I(A) Nature, Validity, and Construction in General
241k1 k. Nature of statutory limitation. Most Cited Cases

Statutes of limitation are intended to penalize dilatoriness and serve as measures of repose.

[2] Limitation of Actions 241 95(2)

241 Limitation of Actions
241II Computation of Period of Limitation
241II(F) Ignorance, Mistake, Trust, Fraud, and Concealment or Discovery of Cause of Action
241k95 Ignorance of Cause of Action
241k95(2) k. Want of diligence by one entitled to sue. Most Cited Cases

When a plaintiff knows or has reason to know that he has a cause of action against an identifiable defendant and voluntarily sleeps on his rights so long as to permit the customary period of limitations to expire, the pertinent considerations of individual justice as well as the broader considerations of repose, coincide to bar his action; where, however, the plaintiff does not know or have reason to know that he has a cause of action against an identifiable defendant until after the normal period of limitations has expired, the considerations of individual justice and the considerations of repose are in conflict and other factors may fairly be brought into play.

[3] Limitation of Actions 241 95(1)

241 Limitation of Actions
241II Computation of Period of Limitation
241II(F) Ignorance, Mistake, Trust, Fraud, and Concealment or Discovery of Cause of Action

241k95 Ignorance of Cause of Action
241k95(1) k. In general; what constitutes discovery. Most Cited Cases

The "discovery rule" postpones the accrual of a cause of action so long as a party reasonably is unaware either that he has been injured, or that the injury is due to the fault or neglect of an identifiable individual or entity; once a person knows or has reason to know of this information, his or her claim has accrued since, at that point, he or she is actually or constructively aware of that state of facts which may equate in law with a cause of action.

[4] Limitation of Actions 241 95(1)

241 Limitation of Actions
241II Computation of Period of Limitation
241II(F) Ignorance, Mistake, Trust, Fraud, and Concealment or Discovery of Cause of Action
241k95 Ignorance of Cause of Action
241k95(1) k. In general; what constitutes discovery. Most Cited Cases

At the heart of every discovery rule case is the issue of whether the facts presented would alert a reasonable person exercising ordinary diligence that he or she was injured due to the fault of another.

[5] Limitation of Actions 241 95(1)

241 Limitation of Actions
241II Computation of Period of Limitation
241II(F) Ignorance, Mistake, Trust, Fraud, and Concealment or Discovery of Cause of Action
241k95 Ignorance of Cause of Action
241k95(1) k. In general; what constitutes discovery. Most Cited Cases

Critical to the running of the statute of limitations is the injured party's awareness of the injury and the fault of another.

[6] Limitation of Actions 241 95(1)

241 Limitation of Actions
241II Computation of Period of Limitation
241II(F) Ignorance, Mistake, Trust, Fraud, and Concealment or Discovery of Cause of Action
241k95 Ignorance of Cause of Action
241k95(1) k. In general; what constitutes discovery. Most Cited Cases

The discovery rule prevents the statute of limitations from running when injured parties reasonably are unaware that they have been injured, or, although aware of an injury, do not know that the injury is attributable to the fault of another.

[7] Limitation of Actions 241 95(1)

241 Limitation of Actions
241II Computation of Period of Limitation
241II(F) Ignorance, Mistake, Trust, Fraud, and Concealment or Discovery of Cause of Action
241k95 Ignorance of Cause of Action
241k95(1) k. In general; what constitutes discovery. Most Cited Cases

For limitations purposes, where the relationship between plaintiff's injury and defendant's fault is not self-evident, it must be shown that a reasonable person, in plaintiff's circumstances, would have been aware of such fault in order to bar her from invoking the discovery rule.

[8] Limitation of Actions 241 95(1)

241 Limitation of Actions

241II Computation of Period of Limitation
241II(F) Ignorance, Mistake, Trust, Fraud, and Concealment or Discovery of Cause of Action
241k95 Ignorance of Cause of Action
241k95(1) k. In general; what constitutes discovery. Most Cited Cases

The discovery rule balances the need to protect injured persons unaware that they have a cause of action against the injustice of compelling a defendant to defend against a stale claim.

[9] Limitation of Actions 241 95(1)

241 Limitation of Actions
241II Computation of Period of Limitation
241II(F) Ignorance, Mistake, Trust, Fraud, and Concealment or Discovery of Cause of Action
241k95 Ignorance of Cause of Action
241k95(1) k. In general; what constitutes discovery. Most Cited Cases

Limitation of Actions 241 95(4.1)

241 Limitation of Actions
241II Computation of Period of Limitation
241II(F) Ignorance, Mistake, Trust, Fraud, and Concealment or Discovery of Cause of Action
241k95 Ignorance of Cause of Action
241k95(4) Injuries to the Person
241k95(4.1) k. In general. Most Cited Cases

Legal and medical certainty regarding injury and fault are not required for a claim to accrue, for limitation purposes.

[10] Limitation of Actions 241 95(1)

241 Limitation of Actions
241II Computation of Period of Limitation
241II(F) Ignorance, Mistake, Trust, Fraud, and Concealment or Discovery of Cause of Action
241k95 Ignorance of Cause of Action
241k95(1) k. In general; what constitutes discovery. Most Cited Cases

In order for a claim to accrue for statute of limitations purposes, a plaintiff need not be informed by an attorney that a viable cause of action exists.

[11] Limitation of Actions 241 95(1)

241 Limitation of Actions
241II Computation of Period of Limitation
241II(F) Ignorance, Mistake, Trust, Fraud, and Concealment or Discovery of Cause of Action
241k95 Ignorance of Cause of Action
241k95(1) k. In general; what constitutes discovery. Most Cited Cases

In order for a claim to accrue for statute of limitations purposes, a plaintiff does not need to understand the legal significance of the facts.

[12] Limitation of Actions 241 95(1)

241 Limitation of Actions
241II Computation of Period of Limitation
241II(F) Ignorance, Mistake, Trust, Fraud, and Concealment or Discovery of Cause of Action
241k95 Ignorance of Cause of Action
241k95(1) k. In general; what constitutes discovery. Most Cited Cases

A plaintiff's delaying his filing until he obtains an expert to support his cause of action does not delay accrual of action for limitations purposes.

[13] Limitation of Actions 241 95(4.1)

241 Limitation of Actions
241II Computation of Period of Limitation
241II(F) Ignorance, Mistake, Trust, Fraud, and Concealment or Discovery of Cause of Action
241k95 Ignorance of Cause of Action
241k95(4) Injuries to the Person
241k95(4.1) k. In general. Most Cited Cases

In cases in which fault is not self-evident at the time of injury, a plaintiff need only have reasonable medical information that connects an injury with fault to be considered to have the requisite knowledge for the claim to accrue for limitations purposes.

[14] Limitation of Actions 241 95(5)

241 Limitation of Actions
241II Computation of Period of Limitation
241II(F) Ignorance, Mistake, Trust, Fraud, and Concealment or Discovery of Cause of Action
241k95 Ignorance of Cause of Action
241k95(4) Injuries to the Person
241k95(5) k. Diseases; drugs. Most Cited Cases

Temporal proximity of injury with exposure may be sufficient medical information for a claim to accrue for limitations purposes; however, it is not dispositive.

[15] Limitation of Actions 241 195(3)

241 Limitation of Actions
241V Pleading, Evidence, Trial, and Review
241k194 Evidence
241k195 Presumptions and Burden of Proof
241k195(3) k. Burden of proof in general. Most Cited Cases

The burden is on the plaintiff seeking application of the discovery rule to establish that a reasonable person in her circumstances would not have been aware within the prescribed statutory period that she was injured through the fault of another.

[16] Products Liability 313A 102

313A Products Liability
313AI In General
313Ak101 Constitutional and Statutory Provisions
313Ak102 k. In general. Most Cited Cases

Products Liability 313A 224

313A Products Liability
313AIII Particular Products
313Ak223 Health Care and Medical Products
313Ak224 k. In general. Most Cited Cases

Product Liability Act (PLA) was enacted as a remedial measure to limit the liability of manufacturers; in particular, the Legislature intended to reduce the burden on manufacturers of Food and Drug Administration (FDA)-approved products resulting

from products liability litigation. N.J.S.A. 2A:58C–1 et seq.

[17] Damages 115 94.9(1)

115 Damages
115V Exemplary Damages
115k94 Measure and Amount of Exemplary Damages
115k94.9 Statutory Provisions
115k94.9(1) k. In general. Most Cited Cases

Products Liability 313A 102

313A Products Liability
313AI In General
313Ak101 Constitutional and Statutory Provisions
313Ak102 k. In general. Most Cited Cases

Products Liability 313A 113

313A Products Liability
313AII Elements and Concepts
313Ak113 k. Strict liability. Most Cited Cases

Products Liability 313A 114

313A Products Liability
313AII Elements and Concepts
313Ak114 k. Negligence or fault. Most Cited Cases

Product Liability Act (PLA) was not intended to codify all issues relating to product liability, and basic common law principles of negligence and strict liability remain intact, except to the extent that the Act sets limits on liability and punitive damages. N.J.S.A. 2A:58C–1(a).

[18] Products Liability 313A 133

313A Products Liability
313AII Elements and Concepts
313Ak132 Warnings or Instructions
313Ak133 k. In general. Most Cited Cases

Under the common law, a product may be unsafe, and therefore defective, because of a failure to warn or an inadequate warning.

[19] Products Liability 313A 133

313A Products Liability
313AII Elements and Concepts
313Ak132 Warnings or Instructions
313Ak133 k. In general. Most Cited Cases

Products Liability 313A 151

313A Products Liability
313AII Elements and Concepts
313Ak151 k. Foreseeable or intended use. Most Cited Cases

An adequate warning, for products liability purposes, includes the directions, communications, and information essential to make the use of a product safe, and reveals the risks attendant on all foreseeable uses.

[20] Products Liability 313A 407

313A Products Liability
313AIV Actions
313AIV(D) Questions of Law or Fact
313Ak407 k. Warnings or instructions. Most Cited Cases

Generally, the adequacy of a warning, for products liability purposes, is a jury question.

[21] Products Liability 313A 133

313A Products Liability
313AII Elements and Concepts
313Ak132 Warnings or Instructions
313Ak133 k. In general. Most Cited Cases

Products Liability 313A 224

313A Products Liability
313AIII Particular Products
313Ak223 Health Care and Medical Products
313Ak224 k. In general. Most Cited Cases

Products Liability 313A 388

313A Products Liability
313AIV Actions
313AIV(C) Evidence
313AIV(C)4 Weight and Sufficiency of Evidence
313Ak388 k. Warnings or instructions. Most Cited Cases

Under the Product Liability Act (PLA), compliance with Food and Drug Administration (FDA) regulations provides compelling, although not absolute, evidence that a manufacturer satisfied its duty to warn about the dangers of its product. N.J.S.A. 2A:58C–4.

[22] Limitation of Actions 241 195(1)

241 Limitation of Actions
241V Pleading, Evidence, Trial, and Review
241k194 Evidence
241k195 Presumptions and Burden of Proof
241k195(1) k. Presumptions in general. Most Cited Cases

In determining, for statute of limitations purposes, accrual of cause of action for products liability against drug manufacturer based on a failure to warn, trial court may consider Product Liability Act (PLA) presumption that a Food and Drug Administration (FDA)-approved label is adequate to inform a reasonable person of the dangers of a product. N.J.S.A. 2A:58C–4.

[23] Limitation of Actions 241 195(1)

241 Limitation of Actions
241V Pleading, Evidence, Trial, and Review
241k194 Evidence
241k195 Presumptions and Burden of Proof

241k195(1) k. Presumptions in general. Most Cited Cases

In the context of determining accrual of cause of action for statute of limitations purposes, Product Liability Act (PLA) presumption that a Food and Drug Administration (FDA)-approved label is adequate to inform a reasonable person of the dangers of a product is capable of being overcome by evidence which tends to disprove the presumed fact, thereby raising a debatable question regarding the existence of the presumed fact; if, in the face of the evidence, reasonable people would differ regarding the presumed fact, the presumption will be overcome. N.J.S.A. 2A:58C–4; N.J.S.A. 2A:84A, App. A, Rules of Evid., N.J.R.E. 301.

[24] Limitation of Actions 241 95(5)

241 Limitation of Actions
241II Computation of Period of Limitation
241II(F) Ignorance, Mistake, Trust, Fraud, and Concealment or Discovery of Cause of Action
241k95 Ignorance of Cause of Action
241k95(4) Injuries to the Person
241k95(5) k. Diseases; drugs. Most Cited Cases

Patient could not have reasonably known that drug prescribed for treatment of her recalcitrant nodular acne caused or exacerbated her inflammatory bowel disease (IBD), and thus, under discovery rule, patient's failure-to-warn products liability action against drug manufacturer was not barred by two-year statute of limitations, notwithstanding application of Product Liability Act (PLA) presumption that a Food and Drug Administration (FDA)-approved label is adequate to inform a reasonable person of the dangers of a product; patient did not experience gastrointestinal effects through her first four courses of the drug, patient's doctors never advised patient not to take the drug or of the risks of IBD, drug warning did not mention IBD or ulcerative colitis, and warning would not have reasonably caused patient to doubt her physicians or to disregard the advice and information that had been imparted to her by them for the prior six years. N.J.S.A. 2A:58C–4.

****543** Paul W. Schmidt, a member of the District of Columbia bar, argued the cause for appellants (Gibbons, Dughi & Hewit, and Covington & Burling, attorneys; Mr. Schmidt, Michelle M. Bufano, Russell L. Hewit, Cranford, and Michael X. Imbroscio, a member of the District of Columbia bar, of counsel; Mr. Schmidt, Ms. Bufano, ****544** Mr. Hewit, Mr. Imbroscio and Natalie H. Mantell, Newark, on the briefs).

David R. Buchanan argued the cause for respondent (Seeger Weiss and Hook & Bolton, attorneys; Mr. Buchanan and Michael D. Hook, a member of the Florida bar, on the briefs).

John Zen Jackson, Morristown, submitted a brief on behalf of amicus curiae The Medical Society of New Jersey (McElroy, Deutsch, Mulvaney & Carpenter, attorneys).

Michael A. Galpern, Cherry Hill, and Jonathan W. Miller submitted a brief on behalf of amicus curiae New Jersey Association for Justice (Locks Law Firm, attorneys).

Stephen C. Matthews submitted a brief on behalf of amici curiae The New Jersey Business and Industry Association, The New Jersey State Chamber of Commerce, and The Commerce and Industry Association of New Jersey (Porzio, Bromberg & Newman, attorneys; Mr. Matthews and Brian P. Sharkey, Morristown, on the brief).

Edward J. Fanning, Jr. submitted a brief on behalf of amici curiae The New Jersey Lawsuit Reform Alliance and The Healthcare Institute of New Jersey (McCarter & English, attorneys; Mr. Fanning and David R. Kott of counsel; Mr. Fanning, Mr. Kott and Maritza Braswell, Newark, on the brief).

Justice LONG delivered the opinion of the Court.

***179** On December 21, 2005, plaintiff Kamie Kendall filed suit against Hoffman–LaRoche, Inc., Roche Laboratories, Inc., F. Hoffman–LaRoche Ltd., and Roche Holding, Ltd. (defendants), for injuries that allegedly resulted from her use of Accutane, a drug produced and marketed by defendants. Defendants moved to dismiss the action as untimely. The trial judge conducted a *Lopez* hearing [FN1] and ruled that Kendall's claim was not time-barred; her delay was reasonable under the circumstances.

FN1. *Lopez v. Swyer*, 62 *N.J.* 267, 275–76, 300 *A.*2d 563 (1973) (holding trial court should determine applicability of discovery rule in pretrial hearing).

A subsequent jury trial resulted in a large award to Kendall. Defendants appealed, challenging a number of the evidential rulings at trial and again arguing that the suit was barred by the statute of limitations. The Appellate Division declared the action timely, but reversed the award on other grounds. On certification, the sole issue before us is whether Kendall's action is time-barred.

The case requires us to revisit our discovery rule jurisprudence and to assess the place, if any, of the Product Liability Act (PLA), *N.J.S.A.* 2A:58C–1 to –11, in determining whether to countenance a filing delay. In particular, we are asked to decide if the presumption of adequacy of a Food and Drug Administration (FDA)-approved warning, provided in *N.J.S.A.* 2A:58C–4, affects the application of the discovery rule.[FN2]

FN2. We note that that issue was not raised during the *Lopez* hearing, but was advanced by defendants and decided by the Appellate Division.

Although that presumption is not a perfect fit for a statute of limitations analysis, we have concluded, as did the Appellate Division, that it cannot be totally ignored where the question is ***180** what a reasonable person knew or should have known about the risks of a product for discovery rule purposes. However, in the discovery rule setting, the presumption is not dispositive but may be overcome by evidence that tends to disprove the presumed fact.

****545** With that consideration in place, we are satisfied, as were the trial judge and the Appellate Division, that Kendall reasonably did not appreciate by December 21, 2003, that Accutane had caused or exacerbated her condition and that, therefore, her filing on December 21, 2005, was timely.

I.

The relevant facts are basically uncontroverted.

A. Accutane

Accutane, the brand name for isotretinoin, is a prescription drug developed and marketed by defendants.[FN3] *Physicians' Desk Reference* 2848 (59th ed. 2005). The drug is a retinoid, derived from vitamin A, that is used to treat recalcitrant nodular acne that has not responded to other regimens. *Id.* at 2849. Nodular acne is a condition marked by an accumulation of sebum under the skin, which ultimately ruptures the follicle wall and forms an inflamed nodule. John S. Strauss & Diane M. Thiboutot, *Diseases of the Sebaceous Glands, in Fitzpatrick's Dermatology in General Medicine* 771–73 (Irwin M. Freedberg et al. eds., 5th ed. 1999). Although much remains unknown about how Accutane treats acne, the drug appears to reduce the production of oil and waxy material in the sebaceous glands. *Physicians' Desk Reference, supra,* at 2849.

FN3. Defendants discontinued the sale of Accutane in 2009.

Accutane has a number of known side effects, including dry lips, skin and eyes; conjunctivitis; decreased night vision; muscle and joint aches; elevated triglycerides; and a high risk of birth defects if a woman ingests the drug while pregnant. *Id.* at 2848–49. This case concerns the effect of Accutane on the digestive tract and, in ***181** particular, the alleged propensity of the drug to cause inflammatory bowel disease (IBD).

B. IBD

IBD includes several chronic incurable diseases characterized by inflammation of the intestine. Mark Feldman, Lawrence S. Friedman, & Marvin H. Sleisenger, *Sleisenger & Fordtran's Gastrointestinal and Liver Disease* 2005 (7th ed. 2002). It traditionally manifests as one of two diseases: Crohn's disease or ulcerative colitis. *Ibid.* Ulcerative colitis, Kendall's diagnosed condition, involves a chronic condition characterized by ulceration of the colon and rectum. *Id.* at 2039. Individuals suffering from ulcerative colitis experience frequent and often bloody bowel movements. *Id.* at 2046–47. Accompanying those bowel movements are fatigue, dehydration, anemia, cramping, abdominal pain, and bloating. *Ibid.;* William S. Haubrich, Fenton Schaffner, and J. Edward Berk, *Bockus Gastroenterology* 1338 (5th ed. 1995). The symptoms often wax and wane, but the condition is regarded as permanent. *The Merck Manual* 307 (17th ed. 1999).

The causes of IBD are unclear. *Sleisenger & Fordtran's Gastrointestinal and Liver Disease, supra,* at 2039. The peak onset of IBD is young adulthood. *Id.* at 2040. Statistically, it has been linked with family history, prior infections, frequent use of antibiotics, and possibly to use of contraceptives and nonsteroidal anti-inflammatory drugs. *Id.* at 2009, 2040, 2041; *Bockus Gastroenterology, supra,* at 1355.

C. Accutane Labels [FN4]

FN4. We will not recount here the various studies that led to the original labeling and later relabeling of Accutane. Those studies are relevant to the merits of plaintiff's cause of action. This aspect of the case is only about what plaintiff knew and when she knew it.

By way of background, in 1982 the FDA approved the use of Accutane and did not ****546** require a label warning of possible gastrointestinal side effects. In 1983 and 1984, defendants revised the ***182** warnings on the Accutane label, provided to physicians, to indicate that "[t]he following reactions have been reported in less than 1% of patients and may bear no relationship to therapy ... inflammatory bowel disease (including regional ileitis), [and] mild gastrointestinal bleeding...."

In 1984, defendants issued a "Dear Doctor" letter to prescribing physicians, which explained that:

> Ten Accutane patients have experienced gastrointestinal disorders characteristic of inflammatory bowel disease (including 4 ileitis and 6 colitis). While these disorders have been *temporally* associated with Accutane administration, i.e., they occurred while patients were taking the drug, a precise cause and effect relationship has not been shown. [Defendants are] ... continuing to monitor adverse experiences in an effort to determine the relationship between Accutane ... and these disorders.
>
> [(Emphasis added).]

At that time, defendants also amended the warning section of the Accutane package insert provided to physicians. Specifically, the revised physician's insert included:

> Inflammatory Bowel Disease: Accutane has been *temporally* associated with inflammatory bowel disease (including regional ileitis) in patients without a prior history of intestinal disorders. Patients experiencing abdominal pain, rectal bleeding or severe diarrhea should *discontinue* Accutane immediately.
>
> [(Emphasis added).]

That warning remained in effect until 2000.

In 1994, defendants issued a patient brochure that warned, among other things, that "ACCUTANE MAY CAUSE SOME LESS COMMON, BUT MORE SERIOUS SIDE EFFECTS" and that patients should "BE ALERT FOR ... SEVERE STOMACH PAIN, DIARRHEA, [AND] RECTAL BLEEDING." Patients who experienced any of those symptoms were advised to "discontinue" Accutane and consult with a doctor. The brochure warned that those symptoms "MAY BE THE EARLY SIGNS OF MORE SERIOUS SIDE EFFECTS WHICH, IF LEFT UNTREATED, COULD POSSIBLY RESULT IN PERMANENT EFFECTS." That patient brochure remained in effect until 1999. The same warning was printed on the blister packaging, which contained the individual Accutane pills.

***183** Defendants issued another "Dear Doctor" letter in August 1998 to board-certified dermatologists warning that patients taking Accutane should be monitored for several serious adverse events, including IBD. In 2000, defendants amended the warnings provided to physicians to remove "temporally" from the 1984 warning and added that the symptoms of IBD "have been reported to persist after Accutane treatment has stopped."

In 2003, defendants again strengthened the warnings accompanying Accutane. The written materials provided to Kendall included a patient brochure presented as a binder entitled "Be Smart, Be Safe, Be Sure." The binder materials primarily focused on the dangers of becoming pregnant while taking Accutane. The binder also contained a warning about gastrointestinal side effects:

> You should be aware that certain SERIOUS SIDE EFFECTS have been reported in patients taking Accutane. ****547** Serious problems do not happen in most patients. If you experience any of the following side effects or any other unusual or severe problems, *stop taking Accutane* right away and call your prescriber because they may result in permanent effects.
>
> ....
>
> Abdomen (stomach area) problems. Certain symptoms may mean that your internal organs are being damaged. These organs include the liver, pancreas, bowel (intestines), and esophagus .... If your organs are damaged, they may not get better even after you stop taking Accutane. *Stop taking Accutane* and call your prescriber if you get severe stomach, chest or bowel pain; have trouble

swallowing or painful swallowing; get new or worsening heartburn, diarrhea, rectal bleeding, yellowing of your skin or eyes, or dark urine.

[(Emphasis added).]

A similar warning was included on the medication guide provided to Kendall by the pharmacy and on the blister pack.

In addition to those warnings, patients were required to sign a "Patient Information/Consent" form, which stated that the patient had read and understood the written patient information and watched a video about contraception. A second "Informed Consent/Patient Agreement Form" listed several side effects of Accutane, including birth defects and the risk of depression and suicide. None of the 2003 patient warnings mentioned IBD or ulcerative colitis by name. The 2003 warnings were in place when Kendall began her final course of Accutane.

***184** D. Plaintiff Kamie Kendall

1. Initial Accutane Treatments

Kendall was first prescribed Accutane in January 1997, by her dermatologist, Dr. Steven Thomson, when she was twelve years old. Prior to taking Accutane, she had suffered from acne for approximately two years and had received antibiotics therefor. After other treatments failed to control her acne, Dr. Thomson prescribed Accutane.

Before he prescribed Accutane in 1997, Dr. Thomson addressed its side effects with Kendall and her mother (e.g., dry eyes, dry skin, risk of sunburn). He did not discuss the risk of IBD with Kendall because, according to him, he was not aware of its relationship to Accutane. Kendall only recalled being warned not to become pregnant.

In addition to the warnings that Dr. Thomson discussed with Kendall and her mother, he provided Kendall with a copy of the Accutane patient brochure. As noted, the 1994 brochure, in effect in 1997, warned that patients should be alert for stomach pain, diarrhea, and rectal bleeding, and advised that patients "discontinue" Accutane and consult with a doctor if experiencing any of those symptoms. Kendall signed a consent form acknowledging that she had received and read the patient brochure.

During that first treatment period, which ran from January 1997 to May 1997, Kendall experienced dry lips, cracking at the corner of her mouth, bloody noses, dry eyes, and back and knee pain, but no gastrointestinal side effects. Kendall received three more courses of Accutane: July to September 1997, February to April 1998, and July to September 1998. During each of these courses the warnings on Accutane remained the same. She reported only similar symptoms to those she had experienced during her initial course of treatment. In other words, during four courses of Accutane, Kendall experienced no gastrointestinal symptoms.

****548 *185** 2. IBD Diagnosis

Seven months later, in April 1999, Kendall experienced a severe case of bloody diarrhea, abdominal pain, and cramping, for which she was hospitalized. On April 14, 1999, Kendall's pediatric gastroenterologist, Dr. Linda Book, diagnosed her with ulcerative colitis. Although Dr. Book did not identify a cause for Kendall's colitis, hospital records indicated that Kendall's grandmother also suffered from the disease. Dr. Book discussed the use of Accutane with Kendall and her mother. At the time, however, because Dr. Book did not know of a connection between Accutane and ulcerative colitis, she did not raise that issue with the Kendalls.

To treat her ulcerative colitis, Kendall testified to taking various medications. She indicated that the symptoms of IBD disappeared and reappeared frequently, as is often the course of the disease.

3. Additional Accutane Treatments

In October 2000, Kendall returned to Dr. Thomson for acne treatment. Dr. Thomson consulted with Dr. Book before prescribing Accutane again. During consultation, Dr. Book expressed no objection to Kendall restarting Accutane, provided that Dr. Thomson monitored her liver enzymes. On December 11, 2000, Kendall began her next course of Accutane. Kendall was given a copy of the patient brochure, which was the same as that provided in 1997. Again she experienced several side effects, but no diarrhea or other gastrointestinal side effects. Thus, by 2000, Kendall had taken five courses of Accutane, never experiencing any gastrointestinal symptoms while on the drug.[FN5]

FN5. Kendall was taking medication for her IBD when she started her fifth course of Accutane, and she did not report any diarrhea during this course of treatment.

Three years later, in August 2003, Kendall returned to Dr. Thomson for persistent acne. Before that final course of treatment,

Kendall received the 2003 warnings, including the "Be Smart, Be Safe, Be Sure" binder. She signed both consent forms ***186** agreeing that she read and understood the written patient information and that she watched a video accompanying the product about contraception. Kendall testified that she "skimmed over the book" because she had taken courses of the drug before. Thereafter, in September 2003, she began her sixth and final course of Accutane, which continued through January 2004. Kendall suffered many of the side effects she had earlier experienced while on the drug and some increased diarrhea.

In January 2004, Kendall saw an advertisement in a magazine that listed the risks associated with Accutane, including IBD. At that point, she "started to think" that Accutane may have caused her IBD. In April 2004, Kendall's grandmother told her that she had seen a lawyer's advertisement linking Accutane to IBD. At some point Kendall called the telephone number of an attorney's office listed in the advertisement.

E. Procedural History

Kendall filed suit on December 21, 2005. In the complaint she alleged that defendants were liable because the warnings on Accutane were inadequate in that they failed to disclose the risk of developing IBD. Prior to trial, defendants filed a motion to dismiss the action due to the expiration of the statute of limitations.

1.

The trial court scheduled a *Lopez* hearing to determine whether Kendall had filed her complaint within the statutory period. At the hearing, Kendall testified, and deposition****549** testimony of Drs. Thomson and Book was read into the record. Kendall's position was that a reasonable person, in her circumstances, would not have known that Accutane was the cause of her ulcerative colitis by December 2003 because none of the warnings provided to her mentioned ulcerative colitis, IBD, or Crohn's Disease, by name, and because her doctors did not know of the risk. Individually and in consultation with each other, they continued to prescribe Accutane after her diagnosis.

***187** Conversely, defense counsel argued that Kendall should have known of the connection between her ulcerative colitis and Accutane, at the latest by August 2003, as a result of the 2003 warnings given when she received her last Accutane prescription. In addition, defendants argued that Kendall realized that during her 2003 dosages of Accutane her diarrhea worsened. Therefore, they contended that a reasonable person would have known of a connection between Accutane and colitis, thus accruing the claim, at the latest, in August, September, or October 2003, any of which is more than two years before the filing of the suit.

The trial judge denied defendants' motion to dismiss. After outlining the basic legal principles, the judge turned to the facts presented during the *Lopez* hearing. She considered Kendall's age at the time she began taking Accutane; the timing of the diagnosis; and the fact that her doctor continued to prescribe Accutane after Kendall was diagnosed. Regarding the warnings provided in 2003, the judge found that the booklet focused primarily on preventing pregnancy and, as a secondary concern, on suicide. Indeed, the judge estimated that of the 3,000 words in the initial pages of the booklet, only 80 were devoted to gastrointestinal side effects and that the booklet did not mention ulcerative colitis and only mentioned the bowel in a list of all the other organs of the gastrointestinal tract. Likewise, the judge noted that the consent forms focused on pregnancy and suicide and did not mention gastrointestinal side effects, but only referred generally to the other warnings provided in the booklet.

Based on those facts, the judge concluded that by December 2003, Kendall did not know that her ulcerative colitis was caused by Accutane and that a reasonable person, in her circumstances, would not have known. The judge, therefore, concluded that the suit was not barred by the statute of limitations.

2. Jury Trial and Verdict

Kendall's case was tried in April 2008. She testified, along with her mother, Dr. Thomson, Dr. Book, her surgeon, and her husband. In addition, a proverbial battle of the experts ensued with ***188** Kendall's expert opining that Accutane "certainly was a cause" of her IBD and defendants' experts declaring that there is no "experimental evidence to support the biological plausibility for Accutane causing IBD."

The jury found in favor of Kendall and awarded her $10.5 million in compensatory damages and $78,500 in past medical expenses. Through special interrogatories, the jury found that: (1) "the use of Accutane [is] a cause of inflammatory bowel disease in some people who take it"; (2) defendants failed "to provide adequate warning" to Kendall's "prescribing physician about the risks of [inflammatory bowel disease] from Accutane that [defendants] knew or should have known about prior to April 1999"; and (3) defendants' failure to warn was "a proximate cause of [plaintiff] developing [inflammatory bowel disease.]" Defendants moved to set aside the jury verdict on multiple grounds. The trial court rejected the motions in their entirety.

****550** 3. Appellate Division

Defendants appealed the verdict and the trial court's ruling at the *Lopez* hearing. The panel reversed and remanded the case for a new trial because of a separate evidentiary issue, but rejected defendants' challenge to the trial court's decision on the statute of limitations.

In ruling, the panel first considered the newly minted contention that the presumption of adequacy in the PLA should govern the limitations issue. Although recognizing that the presumption does not "stringently apply" in a discovery rule proceeding, the panel nevertheless concluded that if the warnings are presumed "sufficient to place an adult consumer on reasonable notice of a pharmaceutical drug's risks before ingesting it, those warnings also bear upon what that same consumer knew, or reasonably should have known, about the drug and its potential adverse side effects for the purposes of contemplating potential litigation against the drug manufacturers."

Accordingly, the panel determined that the trial court in the *Lopez* hearing should "make a preliminary finding that the public ***189** policies underlying the presumption of adequacy are outweighed by the particular facts and circumstances presented, and that plaintiff has supplied a reasonable basis for overcoming the presumption for purposes of extending the statute of limitations." According to the panel, it would be for the jury ultimately to determine whether the presumption was overcome.

The panel went on to hold that the trial court's decision to permit Kendall's case to go forward did not undermine the policies underlying the presumption of adequacy because Kendall's failure to act sooner was not unreasonable under all of the circumstances. In particular, the panel restated the findings of the trial court that the 2003 warning materials "alluded to abdominal and bowel problems in a far less conspicuous or pointed manner" than to the effects on a pregnancy; that plaintiff was not informed by doctors of the risks of IBD or abdominal problems; and that Kendall had been repeatedly prescribed Accutane by her doctors, despite her diagnosis of IBD. The panel did not identify exactly when Kendall's claim accrued, instead holding that it had not accrued more than two years before December 21, 2005, the date on which she filed suit. Relying on those facts, the panel affirmed the trial court's denial of defendants' motion to dismiss the complaint as time-barred.

Defendants filed a petition for certification, which we granted on the issue of the timeliness of plaintiff's complaint. *Kendall v. Hoffman–LaRoche, Inc.*, 205 *N.J.* 99, 13 *A.*3d 362 (2011). We also granted leave to a number of organizations to appear as amici curiae: (1) New Jersey Lawsuit Reform Alliance (NJLRA) and Healthcare Institute of New Jersey (HINJ); (2) New Jersey Business and Industry Association, New Jersey State Chamber of Commerce, and Commerce and Industry Association of New Jersey; (3) Medical Society of New Jersey; and (4) New Jersey Association for Justice.

II.

Defendants argue that the Appellate Division's decision eviscerates the presumption of adequacy in the PLA and eradicates the ***190** carefully-developed limits that have been placed on the discovery rule by omitting consideration of the effect of constructive notice on claim accrual.

Kendall counters that the presumption of adequacy does not apply at all in discovery rule proceedings; that there was, in any event, sufficient evidence to rebut the presumption; and, that the Appellate Division properly applied the discovery rule in ****551** determining that her action was not time-barred.

Amici, NJLRA and HINJ, argue that the decline in New Jersey's important pharmaceutical industry coincides with a rise in pharmaceutical tort litigation and that the presumption of adequacy should be dispositive, absent evidence of fraud.

Amici, the New Jersey Business and Industry Association, New Jersey State Chamber of Commerce, and Commerce Industry of America, contend that the Appellate Division's decision will have a negative impact on the State's business community, attract out-of-state plaintiffs, and foster a hostile legal environment for New Jersey businesses. Amicus, Medical Society of New Jersey, argues that Kendall's claim is barred by the statute of limitations and by classic discovery rule principles.

Amicus, New Jersey Association for Justice, contends that the PLA has no relevance to a statute of limitations analysis; that the presumption of adequacy need not be rebutted in such a proceeding; and that the touchstone of a *Lopez* hearing remains reasonableness.

III.

Although at common law there was no limit on the time in which a party could institute a legal action, *Rothman v. Silber*, 90 *N.J.Super.* 22, 28, 216 *A.*2d 18 (App.Div.) (citing *Uscienski v. National Sugar Refining Co.*, 19 *N.J. Misc.* 240, 242, 18 *A.*2d 611 (C.P.1941)), *certif. denied*, 46 *N.J.* 538, 218 *A.*2d 405 (1966), statutes of limitations have since been adopted regarding all causes of action. At issue in this case is *N.J.S.A.* 2A:14–2(a), ***191** which provides that an action for "an injury to the person caused by the

wrongful act, neglect or default of any person ... shall be commenced within two years next after the cause of any such action shall have accrued....”

[1][2] Statutes of limitation are intended to

> penalize dilatoriness and serve as measures of repose. When a plaintiff knows or has reason to know that he has a cause of action against an identifiable defendant and voluntarily sleeps on his rights so long as to permit the customary period of limitations to expire, the pertinent considerations of individual justice as well as the broader considerations of repose, coincide to bar his action. Where, however, the plaintiff does not know or have reason to know that he has a cause of action against an identifiable defendant until after the normal period of limitations has expired, the considerations of individual justice and the considerations of repose are in conflict and other factors may fairly be brought into play.

[*Farrell v. Votator Div. of Chemetron Corp.*, 62 *N.J.* 111, 115, 299 *A.*2d 394 (1973) (citations omitted); *Fernandi v. Strully*, 35 *N.J.* 434, 438, 173 *A.*2d 277 (1961).]

[3] Those considerations comprise the so-called “discovery rule,” the goal of which is to

> avoid [the] harsh results that otherwise would flow from mechanical application of a statute of limitations. Accordingly, the doctrine postpones the accrual of a cause of action so long as a party reasonably is unaware either that he has been injured, or that the injury is due to the fault or neglect of an identifiable individual or entity. Once a person knows or has reason to know of this information, his or her claim has accrued since, at that point, he or she is actually or constructively aware of that state of facts which may equate in law with a cause of action.

****552** [*Caravaggio v. D'Agostini*, 166 *N.J.* 237, 245, 765 *A.*2d 182 (2001) (citing *Abboud v. Viscomi*, 111 *N.J.* 56, 62–63, 543 *A.*2d 29 (1988) (citations and internal quotation marks omitted)).]

[4][5][6][7] At the heart of every discovery rule case is the issue of “whether the facts presented would alert a reasonable person exercising ordinary diligence that he or she was injured due to the fault of another[.]” *Hardwicke v. Am. Boychoir Sch.*, 188 *N.J.* 69, 110, 902 *A.*2d 900 (2006) (quoting *Martinez v. Cooper Hosp.–Univ. Med. Ctr.*, 163 *N.J.* 45, 52, 747 *A.*2d 266 (2000)).

> Critical to the running of the statute is the injured party's awareness of the injury and the fault of another. The discovery rule prevents the statute of limitations from running when injured parties reasonably are unaware that they have been injured, or, although aware of an injury, do not know that the injury is attributable to the fault of another.

***192** [*Baird v. Am. Med. Optics*, 155 *N.J.* 54, 66, 713 *A.*2d 1019 (1998) (citations omitted).]

Knowledge of fault and knowledge of injury may occur simultaneously:
Fault is apparent, for example, where the wrong tooth is extracted during surgery, *Tramutola v. Bortone*, 118 *N.J.Super.* 503, 512–13, 288 *A.*2d 863 (App.Div.1972), or a foreign object has been left within the body after an operation. *See Fernandi, supra*, 35 *N.J.* at 452, 173 *A.*2d 277 [(holding that period of limitations on a patient's negligence cause of action began to run when the patient knew or had reason to know about the foreign object left in her body)].

[*Martinez, supra*, 163 *N.J.* at 53, 747 *A.*2d 266.]

However, where the relationship between plaintiff's injury and defendant's fault is not self-evident, it must be shown that a reasonable person, in plaintiff's circumstances, would have been aware of such fault in order to bar her from invoking the discovery rule. *See Alfone v. Sarno*, 139 *N.J.Super.* 518, 523–24, 354 *A.*2d 654 (App.Div.), *certif. denied*, 71 *N.J.* 498, 366 *A.*2d 654 (1976).

Thus,

> [i]n *Lopez, supra*, 62 *N.J.* at 271, 300 *A.*2d 563, for example, the plaintiff suffered from severe burns, pain, and nausea after undergoing radiation therapy following a radical mastectomy for breast cancer. Plaintiff's husband had previously been told by a physician that “this was not malpractice. This sometimes happens.” *Lopez v. Swyer*, 115 *N.J.Super.* 237, 244, 279 *A.*2d 116 (App.Div.1971). While Ms. Lopez was being treated for her symptoms by another doctor, she overheard him say to colleagues, “[a]nd there you see, gentlemen, what happens when the radiologist puts a patient on the table and goes out and has a cup of coffee.” *Lopez, supra*, 62 *N.J.* at 271, 300 *A.*2d 563. The Appellate Division reversed the trial court's grant of summary judgment for

the radiologist, and this Court affirmed. Although Ms. Lopez knew that her burns were caused by the radiation therapy, the record did not reveal that she knew or should have known, prior to overhearing the "cup of coffee" statement, of the causal connection between her physician's negligent treatment and her injury. Thus her complaint, filed slightly over five years after her injury, but within two years of the "cup of coffee" statement, was ruled timely.

[*Caravaggio, supra*, 166 *N.J.* at 247, 765 *A.*2d 182.]

Similarly, in *Lynch v. Rubacky*, 85 *N.J.* 65, 67–68, 424 *A.*2d 1169 (1981),
****553** plaintiff injured her ankle and was operated on by defendant. When she did not improve and suffered great pain and disability, the defendant continually assured her that her condition was due to the original injury and the healing process. It was not until after the statute of limitations expired that another physician suggested that plaintiff's problem was due to defendant's negligence. ***193***Id.* at 69, 424 *A.*2d 1169. We held that "all of the factors militating against adequate knowledge of physician fault" were present in the case. *Id.* at 77, 424 *A.*2d 1169. Included were plaintiff's faith in defendant, his reassurances that the pain and swelling were part of the healing process, and the fact that a physician whom plaintiff later consulted did not suggest defendant's medical negligence until after the statute had run. We held her action to be timely.

[*Martinez, supra*, 163 *N.J.* at 53–54, 747 *A.*2d 266.]

Likewise, in *Caravaggio*, plaintiff's femur-stabilization rod snapped and her surgeon, in good faith, blamed it on a structural defect in the rod. Subsequent metallurgical tests showed the rod was not defective. Plaintiff then sued the surgeon who moved to dismiss the action as untimely. The motion was granted and the judgment affirmed. We reversed on the ground that plaintiff had no reason to doubt her doctor's assessment of the situation or his conclusion that there was a defect in the rod. *Caravaggio, supra*, 166 *N.J.* at 253, 765 *A.*2d 182; *see also* *Gallagher v. Burdette–Tomlin Mem'l Hosp.*, 163 *N.J.* 38, 747 *A.*2d 262 (2000) (allowing plaintiff to amend claim after expiration of statute to include after-care physicians belatedly inculpated in adversary's expert report).

[8][9][10][11][12][13][14] As those cases reveal, the discovery rule balances the need to protect injured persons unaware that they have a cause of action against the injustice of compelling a defendant to defend against a stale claim. *Lopez, supra*, 62 *N.J.* at 273–74, 300 *A.*2d 563. To be sure, legal and medical certainty are not required for a claim to accrue. *See* *Lapka v. Porter Hayden Co.*, 162 *N.J.* 545, 555–56, 745 *A.*2d 525 (2000). Thus, a plaintiff need not be informed by an attorney that a viable cause of action exists, *Burd v. New Jersey Telephone Company*, 76 *N.J.* 284, 291, 386 *A.*2d 1310 (1978), nor does a plaintiff need to understand the legal significance of the facts. *See* *Lynch, supra*, 85 *N.J.* at 73, 424 *A.*2d 1169. Likewise, a plaintiff may not delay his filing until he obtains an expert to support his cause of action. *Brizak v. Needle*, 239 *N.J.Super.* 415, 429, 571 *A.*2d 975 (App.Div.), *certif. denied*, 122 *N.J.* 164, 584 *A.*2d 230 (1990). In cases in which fault is not self-evident at the time of injury, a plaintiff need only have "reasonable medical information" that connects an injury with fault to be considered to have the requisite knowledge for the claim to accrue. ***194** *Vispisiano v. Ashland Chem. Co.*, 107 *N.J.* 416, 435, 527 *A.*2d 66 (1987). Temporal proximity of injury with exposure may be sufficient medical information; however, it is not dispositive. *Compare* *Burd, supra*, 76 *N.J.* at 292–93, 386 *A.*2d 1310 *with* *Vispisiano, supra*, 107 *N.J.* at 436, 527 *A.*2d 66.

[15] At a *Lopez* hearing, the burden is on the plaintiff seeking application of the discovery rule to establish that a reasonable person in her circumstances would not have been aware within the prescribed statutory period that she was injured through the fault of another. *See* *Henry v. N.J. Dept. of Human Servs.*, 204 *N.J.* 320, 339, 9 *A.*3d 882 (2010) (citing *Lopez, supra*, 62 *N.J.* at 274–76, 300 *A.*2d 563). That is the backdrop for our inquiry.

****554** IV.

[16] The PLA, *N.J.S.A.* 2A:58C–1 to –11, was enacted as a remedial measure to limit the liability of manufacturers by establishing "clear rules with respect to certain matters ... including certain principles under which liability is imposed and the standards and procedures for the award of punitive damages." *N.J.S.A.* 2A:58C–1(a). In particular, in enacting the PLA, the Legislature intended to reduce the burden on manufacturers of FDA-approved products resulting from products liability litigation. *Rowe v. Hoffman–La Roche, Inc.*, 189 *N.J.* 615, 626, 917 *A.*2d 767 (2007).

[17] The Act was not intended to codify all issues relating to product liability, *N.J.S.A.* 2A:58C–1(a), and basic common law principles of negligence and strict liability remain intact, except to the extent that the Act sets new limits on liability and punitive damages. *See* *N.J.S.A.* 2A:58C–8 to –11, and *N.J.S.A.* 2A:15–5.9 to –17.

[18][19][20] Under the common law, "[a] product may be unsafe, and therefore defective, because of a failure to warn or an inadequate warning." *Feldman v. Lederle Labs.*, 125 *N.J.* 117, 144, 592 *A.*2d 1176 (1991) (citation omitted); *see also* ***195***Campos v. Firestone*, 98 *N.J.* 198, 205, 485 *A.*2d 305 (1984) (recognizing that no warning, or an inadequate warning, renders a product

defective). An adequate warning "includes the directions, communications, and information essential to make the use of a product safe [,]" *Freund v. Cellofilm Properties, Inc.*, 87 *N.J.* 229, 243, 432 *A.*2d 925 (1981), and reveals "the risks attendant on all foreseeable uses." *Id.* at 244, 432 *A.*2d 925. Generally, the adequacy of a warning is a jury question. *Mathews v. Univ. Loft Co.*, 387 *N.J.Super.* 349, 357, 903 *A.*2d 1120 (App.Div.), *certif. denied*, 188 *N.J.* 577, 911 *A.*2d 69 (2006). In that connection, *N.J.S.A.* 2A:58C–4 provides:

> In any product liability action the manufacturer or seller shall not be liable for harm caused by a failure to warn if the product contains an adequate warning or instruction or, in the case of dangers a manufacturer or seller discovers or reasonably should discover after the product leaves its control, if the manufacturer or seller provides an adequate warning or instruction. An adequate product warning or instruction is one that a reasonably prudent person in the same or similar circumstances would have provided with respect to the danger and that communicates adequate information on the dangers and safe use of the product, taking into account the characteristics of, and the ordinary knowledge common to, the persons by whom the product is intended to be used, or in the case of prescription drugs, taking into account the characteristics of, and the ordinary knowledge common to, the prescribing physician. *If the warning or instruction given in connection with a drug or device or food or food additive has been approved or prescribed by the federal Food and Drug Administration under the "Federal Food, Drug, and Cosmetic Act," ... or the "Public Health Service Act," ... a rebuttable presumption shall arise that the warning or instruction is adequate.*
>
> [*N.J.S.A.* 2A:58C–4 (emphasis added).]

[21] Compliance with FDA regulations provides compelling, although not absolute, evidence that a manufacturer satisfied its duty to warn about the dangers of its product. *Perez v. Wyeth Labs. Inc.*, 161 *N.J.* 1, 24, 734 *A.*2d 1245 (1999). Indeed, in *Perez* we created what can be denominated as a super-presumption: "absent deliberate concealment or nondisclosure of after-acquired knowledge of harmful effects,****555** compliance with FDA standards should be virtually dispositive of such claims[ ]"; only in the "rare case [ ]" will damages be assessed against a manufacturer issuing FDA-approved warnings. *Id.* at 25, 734 *A.*2d 1245; *see also* ***196** William A. Dreier, *Liability for Drug Advertising, Warnings, and Frauds*, 58 *Rutgers L.Rev.* 615, 616 (2006).[FN6]

> FN6. In *Perez,* we also recognized that a case in which the presumption is overcome might only warrant compensatory and not punitive damages, *Perez, supra*, 161 *N.J.* at 25, 734 *A.*2d 1245, thereby suggesting that circumstances less egregious than deliberate concealment could overcome the presumption. *See McDarby v. Merck & Co., Inc.*, 401 *N.J.Super.* 10, 949 *A.*2d 223 (App.Div.2008) (holding defendant's economically-driven opposition to post-market regulatory process not "deliberate concealment or non-disclosure" but sufficient to overcome presumption of warning adequacy), *certif. granted*, 196 *N.J.* 597, 960 *A.*2d 393 (2008), *certif. dismissed as improvidently granted*, 200 *N.J.* 267, 979 *A.*2d 766 (2009). We need not resolve that issue here.

V.

At the heart of this appeal is the question of what, if any, role the PLA's presumption of adequacy plays in the judicial analysis of whether plaintiff acted reasonably in delaying the filing of her suit. Defendants urge us to apply the "virtually dispositive" presumption as described in *Perez.* Kendall counters that the presumption does not apply at all in discovery rule proceedings and is intended solely for the liability phase of the case.

Each of those arguments proves too much. On the one hand, nothing in the language of the PLA or its legislative history suggests, even obliquely, an intention on the part of the drafters to alter our long-standing discovery-rule jurisprudence. Indeed, in its original 1987 form, the PLA did not even mention statutes of limitations. Later, in 1995, a single reference to the subject was added providing tolling of "the applicable statute of limitations" against a product manufacturer once a strict liability action against a seller is instituted. That is the sum and substance of reference to limitations of actions in the PLA. Moreover, nothing in the legislative history of the PLA suggests that, despite its silence regarding its effect on a statute of limitations, it was intended to apply to a timeliness analysis.

Further, in "rebalancing" the law in favor of manufacturers, *N.J.S.A.* 2A:58C–4 establishes that a product manufacturer "shall ***197** not be *liable* " for failure to warn if an "adequate warning" is given. *Ibid.* (emphasis added). It is that provision that is the source of the presumption of adequacy. It would thus be fair to say that, by its choice of language, the Legislature signaled that the presumption was only intended to be part of the ultimate liability calculus.

On the other hand, as the Appellate Division aptly noted: "it can be argued that the legislative desire to lessen a drug manufacturer's potential liability for using an FDA-sanctioned warning also would extend to protecting that same manufacturer from an open-ended burden of defending belatedly-filed product liability lawsuits." Further, the gravamen of *N.J.S.A.* 2A:58C–4 is that an FDA-approved label is presumably adequate to inform a reasonable person of the dangers of a product. Thus, there is something awry about the notion of barring that evidence altogether at a discovery rule hearing at which the very issue is when, in light of the warnings

actually received by plaintiff, plaintiff knew or should have known of the dangers of the product.

[22][23] We are accordingly satisfied, as was the Appellate Division, that a middle-of-the-road****556** approach is justified. That approach permits the judge at a *Lopez* hearing to consider the presumption of adequacy. However, we see no warrant for viewing the presumption, in the *Lopez* setting, as a "virtually dispositive" super-presumption. *Perez, supra*, 161 *N.J.* at 25, 734 *A.*2d 1245. Rather, it should be treated, as would any presumption in the ordinary course, as capable of being overcome by evidence which " 'tends to' disprove the presumed fact, thereby raising a debatable question regarding the existence of the presumed fact." *Shim v. Rutgers*, 191 *N.J.* 374, 386, 924 *A.*2d 465 (2007) (citing *Ahn v. Kim*, 145 *N.J.* 423, 439, 678 *A.*2d 1073 (1996)). If, in the face of the evidence, reasonable people would differ regarding the presumed fact, the presumption will be overcome. *See N.J.R.E.* 301; *Harvey v. Craw*, 110 *N.J.Super.* 68, 73, 264 *A.*2d 448 (App.Div.), *certif. denied*, 56 *N.J.* 479, 267 *A.*2d 61 (1970). Ultimately, the burden remains on the plaintiff seeking application of the ***198** discovery rule to show that a reasonable person in her circumstances would not have been aware, within the prescribed statutory period, that she had been injured by defendants' product.

VI.

[24] When that approach is adopted in this difficult case, the result remains that reached by the trial judge and the Appellate Division—that Kendall's suit may proceed because the evidence not only overcame the presumption, but established that under all the circumstances, Kendall reasonably was unaware that defendants caused her injury until after December 21, 2003.

We reach that conclusion based on the facts, the most important of which are as follows: Kendall was originally prescribed Accutane, when she was twelve years old. At that time, her dermatologist did not warn her or her mother of the risk of IBD because he was not aware of its relationship to Accutane. She took four courses of the drug from 1997 through 1998, with no gastrointestinal symptoms whatsoever. When she later developed ulcerative colitis, a disease that waxes and wanes, her pediatric gastroenterologist did not know of a connection between Accutane and ulcerative colitis. In 2000, when Kendall returned to her dermatologist, he consulted with the gastroenterologist and together they agreed that she could be prescribed Accutane despite her prior bout with colitis. Again, she did not experience gastrointestinal effects while on the drug.

In September 2003, Kendall returned to the dermatologist, who prescribed Accutane again. While on that sixth course of the drug, from September 2003 to January 2004, Kendall experienced the same side effects she had previously experienced and some increased diarrhea.

Kendall, who the trial judge found to be credible, said her doctors never advised her not to take Accutane or of the risks of IBD and that she would not have taken or continued the drug had they done so. The 2003 warning, which was focused on pregnancy and suicide, indicated that a patient should "*stop* taking Accutane" ***199** (emphasis added) if certain symptoms occurred, but did not mention IBD or colitis. Nor did the consent form Kendall signed. Indeed, she never received a warning which specifically mentioned IBD or ulcerative colitis.

Although we can conceive of circumstances in which the 2003 warning might have been sufficient to alert a plaintiff of the connection between Accutane and her disease, it was certainly not sufficient, in these circumstances, to cause Kendall to doubt her physicians or to disregard the advice and information that had been imparted to her by them for the prior six years. That is particularly so in light of ****557** the lack of a discernable link between Kendall's symptoms and the ingestion of the drug.

We take no position on whether the January and April 2004 lawyer's advertisements should have spurred Kendall to action. If they had, the December 2005 filing would be timely. Our conclusion is, like that of the Appellate Division—that a reasonable person in Kendall's circumstances would not have known by December 2003 of the relationship between Accutane and her condition. As such, her December 2005 filing was timely.

VII.

The judgment of the Appellate Division is affirmed.

Judge WEFING (temporarily assigned), dissenting.

In New Jersey, actions for personal injuries must be commenced within two years of accrual of the cause of action. *N.J.S.A.* 2A:14–2. If the individual who wishes to commence such an action was a minor at the time the cause of action accrued, the period of limitations is extended until two years after the date the individual attains majority. *N.J.S.A.* 2A:14–21; *Green v. Auerbach Chevrolet Corp.*, 127 *N.J.* 591, 592–93, 606 *A.*2d 1093 (1992) (noting that although the Legislature did not amend *N.J.S.A.* 2A:14–21 at the time it reduced the age of majority from twenty-one to eighteen, the period of limitations within which to commence***200** suit for injuries received as a minor is computed from the individual's eighteenth birthday).

Plaintiff Kamie Kendall was born on January 28, 1984. Her eighteenth birthday was on January 28, 2002. Her first course of Accutane treatment commenced in January 1997, and her last course commenced in September 2003. Pursuant to *N.J.S.A.* 2A:14–21, she had until January 28, 2004, to commence suit for any injuries she reasonably attributed to her use of Accutane while a minor.

My colleagues have determined, however, that her complaint, which was not filed until December 21, 2005, was timely. They reach this result by concluding that the various warnings included with Accutane over the period of her use, each of which was approved by the federal Food and Drug Administration (FDA), did not provide adequate warning to plaintiff of the risk of developing ulcerative colitis. Based upon what they perceive to be inadequate FDA-approved warnings, they conclude that plaintiff is entitled to a further tolling of the period of limitations under the discovery rule. *See Lopez v. Swyer*, 62 *N.J.* 267, 300 *A.*2d 563 (1973). I am unable to agree and therefore must dissent.

A review of the facts demonstrates that plaintiff had adequate notice of the risks of receiving Accutane. Plaintiff received her first prescription for Accutane from her treating dermatologist in January 1997 when she was twelve years old. At that time, the patient brochure that accompanied each prescription included the following warnings regarding side-effects of the treatment:

• YOU SHOULD BE AWARE THAT ACCUTANE MAY CAUSE SOME LESS COMMON, BUT MORE SERIOUS SIDE EFFECTS. BE ALERT FOR ANY OF THE FOLLOWING:

• HEADACHES, NAUSEA, VOMITING, BLURRED VISION

• CHANGES IN MOOD

• SEVERE STOMACH PAIN, DIARRHEA, RECTAL BLEEDING

• PERSISTENT FEELING OF DRYNESS OF THE EYES

• YELLOWING OF THE SKIN OR EYES AND/OR DARK URINE

****558** IF YOU EXPERIENCE ANY OF THESE SYMPTOMS OR ANY OTHER UNUSUAL OR SEVERE PROBLEMS, DISCONTINUE TAKING ACCUTANE ***201** AND CHECK WITH YOUR DOCTOR IMMEDIATELY. THEY MAY BE THE EARLY SIGNS OF MORE SERIOUS SIDE EFFECTS WHICH, IF LEFT UNTREATED, COULD POSSIBLY RESULT IN PERMANENT EFFECTS.

Plaintiff's physician testified that he gave plaintiff a copy of the brochure when he gave her the first Accutane prescription. Plaintiff signed a consent form acknowledging that she received and read the patient brochure. Those same warnings were repeated on the blister packaging that contained the individual Accutane pills that plaintiff received when she filled the prescription. In addition, the package insert for Accutane included the following statement:

Inflammatory Bowel Disease: Accutane has been temporally associated with inflammatory bowel disease (including regional ileitis) in patients without a prior history of intestinal disorders. Patients experiencing abdominal pain, rectal bleeding or severe diarrhea should discontinue Accutane immediately.

The FDA had approved the contents of the patient brochure, the blister packaging, and the package insert.[FN1]

FN1. It is not immediately apparent from the record whether plaintiff received a package insert each time she had her prescriptions filled. There are two categories of package inserts: physician package inserts and patient package inserts. The examples contained in the record are not identified as to which category they belong.

Plaintiff's treating dermatologist gave her three more prescriptions for Accutane. She took the drug for three separate three-month periods: July to September 1997, February to April 1998, and July to September 1998. On each occasion, when she received the prescription from her physician and when she had it filled at the pharmacy, she received the same FDA-approved warnings. On each of the visits, as she had been on her first, she was accompanied by her mother.

Plaintiff began to suffer abdominal pain in approximately April 1998. In April 1999 she was hospitalized after experiencing a severe case of bloody diarrhea, abdominal pain, and cramping; and on April 14, 1999, her pediatric gastroenterologist diagnosed her as having severe ulcerative colitis. Thus, by 1999 plaintiff ***202** suffered symptoms, which were included in the FDA-approved

warnings that accompanied her receipt and use of Accutane.

Inflammatory bowel disease is a condition marked by chronic idiopathic inflammation of the small bowel and colon. *Stedman's Medical Dictionary* 414 (26th ed. 1995). It traditionally manifests itself as one of two diseases: Crohn's disease or ulcerative colitis. David B. Sachar & Aaron E. Walfish, *Overview of Inflammatory Bowel Disease*, *The Merck Manual Home Health Handbook*, Aug. 2006, http:// www. merckmanuals. com/ home/ digestive_ disorders/ inflammatory_ bowel_ diseases_ ibd/ overview_ of_ inflammatory_ bowel_ disease. html. The latter involves the chronic inflammation of the inner lining of the colon cells. Sachar & Walfish, *Ulcerative Colitis*, *The Merck Manual*, *supra*, http:// www. merckmanuals. com/ home/ digestive_ disorders/ inflammatory_ bowel_ diseases_ ibd/ ulcerative_ colitis. html. The symptoms of ulcerative colitis include frequent and often bloody bowel movements accompanied by cramping and abdominal pain, together with other symptoms. *Ibid*.

In October 2000, plaintiff returned to the physician who was treating her acne ****559** condition. He consulted with her pediatric gastroenterologist, who expressed no objection to plaintiff receiving another course of Accutane as long as plaintiff's liver enzymes were monitored. In December 2000, plaintiff began her fifth course of Accutane. By that time, the package insert that accompanied the pills stated:

> *Inflammatory Bowel Disease:* Accutane has been associated with inflammatory bowel disease (including regional ileitis) in patients without a prior history of intestinal disorders. In some instances, symptoms have been reported to persist after Accutane treatment has been stopped. Patients experiencing abdominal pain, rectal bleeding or severe diarrhea should discontinue Accutane immediately....

The only modification to that portion of the package insert from its previous iteration was the deletion of the word "temporally," which had preceded the word "associated" in the earlier package inserts. She again received the patient brochure with its various warnings. The pills were again dispensed in a blister package ***203** that also restated the warnings. All of the warnings had been approved by the FDA.

In August 2003, more than a year and a half after turning eighteen, plaintiff again returned to her treating dermatologist for her acne. He decided to prescribe yet another course of Accutane treatment. By this time, the FDA had directed that the warnings that accompanied a prescription of Accutane be strengthened.

In connection with her 2003 prescription, plaintiff received an expanded patient booklet. It stated in pertinent part:

> You should be aware that certain SERIOUS SIDE EFFECTS have been reported in patients taking Accutane. Serious problems do not happen in most patients. If you experience any of the following side effects or any other unusual or severe problems, stop taking Accutane right away and call your prescriber because they may result in permanent effects.
>
> ....
>
> Abdomen (stomach area) problems. Certain symptoms may mean that your internal organs are being damaged. These organs include the liver, pancreas, bowel (intestines), and esophagus .... If your organs are damaged, they may not get better even after you stop taking Accutane. Stop taking Accutane and call your prescriber if you get severe stomach, chest or bowel pain; have trouble swallowing or painful swallowing; get new or worsening heartburn, diarrhea, rectal bleeding, yellowing of your skin or eyes, or dark urine.

Plaintiff signed an acknowledgement that she received and read the information.

In addition, when she went to the pharmacy to have the prescription filled, she received a medication guide for Accutane. It stated in pertinent part:

> **What are the possible side effects of Accutane?**
>
> ....
>
> **Abdomen (stomach area) problems.** Certain symptoms may mean that your internal organs are being damaged. These organs include the liver, pancreas, bowel (intestines), and esophagus (connection between mouth and stomach). If your organs are damaged, they may not get better even after you stop taking Accutane. Stop taking Accutane and call your prescriber if you get

severe stomach, chest or bowel pain, trouble swallowing or painful swallowing, new or worsening heartburn, diarrhea, rectal bleeding, yellowing of your skin or eyes, or dark urine.

In addition to the various warnings delivered to plaintiff over the course of her ****560** Accutane treatment, defendants also delivered ***204** warnings to physicians prescribing the drug. For example, some years prior to plaintiff's initial prescription, defendants sent a "Dear Doctor" letter to physicians informing them that ten patients who had received Accutane treatment "experienced gastrointestinal disorders characteristic of inflammatory bowel disease." The letter said that defendants would continue to monitor the matter. In 1998, defendants issued another "Dear Doctor" letter warning dermatologists of the importance of monitoring patients on Accutane for inflammatory bowel disease. Plaintiff's dermatologist received those letters.

Plaintiff suffered symptoms of ulcerative colitis with varying intensity from the time she was initially diagnosed with the disease in 1999. It is characteristic of ulcerative colitis that its symptoms will wax and wane over the course of time. *The Merck Manual* 307 (17th ed. 1999). She acknowledged that her symptoms intensified after completing a course of treatment with Accutane. Indeed, plaintiff's expert with respect to causation, David B. Sachar, M.D., relied on the fact that her symptoms worsened after several courses of treatment in opining that Accutane was a cause of plaintiff's ulcerative colitis. Plaintiff also acknowledged that her diarrhea worsened with the 2003 treatment. Her symptoms progressively worsened and led to her decision in January 2006 to undergo a proctocolectomy.

In the face of the repeated FDA-approved warnings provided to plaintiff, the warnings provided to her physician, and the intensification of her symptoms, my colleagues have concluded that plaintiff was reasonably unaware by December 21, 2003, two years prior to the filing of her complaint, of a potential link between her ulcerative colitis and her use of Accutane. My colleagues stress that the material she received in 2003 did not use the terms inflammatory bowel disease or ulcerative colitis.

I cannot find that reasoning persuasive for several reasons. The 2003 material, in an effort to be more informative, refrained from diagnostic terms but clearly stated that an individual's intestines could be damaged and that an individual should stop ***205** taking the drug if he or she experienced diarrhea or rectal bleeding. Because plaintiff experienced both symptoms, she should have been aware of a potential link. *See, e.g.*, *Magistrini v. One Hour Martinizing Dry Cleaning*, 109 *F.Supp.*2d 306, 315 (D.N.J.2000) (holding that manufacturer of dry cleaning solvent was required to warn that the substance was carcinogenic rather than to warn of the risk of contracting a specific form of cancer). Further, plaintiff testified at the *Lopez* hearing that after receiving the diagnosis of ulcerative colitis in 1999, she engaged in research on the topic and knew that ulcerative colitis was a particular form of inflammatory bowel disease and was a medical term for damage to the bowels.

Plaintiff testified that she "skimmed" the material she received in 2003. At the beginning of the medication guide she received from the pharmacy in 2003, it noted the importance of a patient reviewing the entire document, even if the patient had received an earlier prescription for Accutane because the information may have changed in the interim. Plaintiff should not be relieved of having the information contained in that material imputed to her because she chose not to review it.

Further, I am unable to agree, for purposes of determining whether a complaint has been timely filed, that the statutory presumption contained in *N.J.S.A.* 2A:58C–4, which presumes FDA-approved labels are adequate, can be overcome by ****561** plaintiff's election not to review the material in which the warnings are set forth. Nor can I discern an analytical justification for according the statutory presumption set forth in *N.J.S.A.* 2A:58C–4 a different weight when the issue is timeliness of the filing of the complaint as opposed to the merits of the claim.

This Court recently recognized that the Legislature enacted *N.J.S.A.* 2A:58C–4 to "re-balance the law 'in favor of manufacturers.' " *Rowe v. Hoffman–La Roche, Inc.*, 189 *N.J.* 615, 623, 917 *A.*2d 767 (2007) (quoting William A. Dreier, *N.J. Prods. Liab. & Toxic Torts Law* § 15:4 (2007)). One of the underlying purposes of our product liability statute was " 'to establish clear rules with ***206** respect to specific matters as to which the decisions of the courts in New Jersey have created uncertainty.' " *Id.* at 624, 917 *A.*2d 767 (quoting Senate Judiciary Committee, *Statement to Senate Committee Substitute for S.B. No. 2805* at 1 (Mar. 23, 1987)). In my judgment, the approach adopted here by my colleagues does not further either of those legislative objectives.

As I noted at the outset, a cause of action accrues when a plaintiff knows or should know of a state of facts that possibly equates to a cause of action. The determination of when a cause of action accrues is a question of law for the court. *Baird v. Am. Med. Optics*, 155 *N.J.* 54, 65, 713 *A.*2d 1019 (1998) (citing *Fernandi v. Strully*, 35 *N.J.* 434, 439, 173 *A.*2d 277 (1961)). "The discovery rule delays the accrual of a cause of action until 'the injured party discovers, or by an exercise of reasonable diligence and intelligence should have discovered that he may have a basis for an actionable claim.' " *Id.* at 66, 713 *A.*2d 1019 (quoting *Lopez, supra*, 62 *N.J.* at 272, 300 *A.*2d 563). Medical certainty linking the harm and its cause is not the fulcrum for the analysis; rather, "reasonable medical information" suffices. *Vispisiano v. Ashland Chem. Co.*, 107 *N.J.* 416, 435, 527 *A.*2d 66 (1987). Certainly, all of the FDA-approved

material provided to plaintiff has to be considered "reasonable medical information." Giving plaintiff the most generous reading of the material provided to her, I conclude that she knew or should have known, no later than her August 2003 receipt of yet another prescription for Accutane, of a potential link between her use of the medication and her continuing gastrointestinal problems.

I note that my colleagues "take no position" whether advertisements placed by lawyers in January and April 2004 "should have spurred Kendall to action." *See ante* op. at 199, 36 *A.*3d at 557. Kendall testified that the advertisements caused her to think for the first time that there might be a link between her use of Accutane and her intestinal problems. My colleagues' omission is entirely understandable in light of the fact that the advertisements ***207** contained less information than defendants had provided her over the years as she took the medication.

In my judgment, plaintiff's complaint was untimely and should have been dismissed.

For affirmance—Chief Justice RABNER and Justices LONG, LaVECCHIA, ALBIN, and HOENS—5.
For reversal—Judge WEFING (temporarily assigned)—1.
Not Participating—Justice PATTERSON—1.

N.J.,2012.
Kendall v. Hoffman-La Roche, Inc.
209 N.J. 173, 36 A.3d 541, Prod.Liab.Rep. (CCH) P 18,799

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Superior Court of New Jersey,
Appellate Division.
John McDARBY and Irma McDarby, husband and wife, Plaintiffs-Respondents,
v.
MERCK & CO., INC., Defendant-Appellant.
Thomas Cona and Joyce Cona, Plaintiffs-Respondents,
v.
Merck & Co., Inc., Defendant-Appellant.

Argued Jan. 16, 2008.
Decided May 29, 2008.

Background: Two patients brought claims, under Product Liability Act (PLA) and Consumer Fraud Act (CFA), against manufacturer of rofecoxib, a prescription non-steroidal anti-inflammatory drug (NSAID) to treat acute pain and arthritis by specifically inhibiting cyclooxygenase-2 (COX-2), alleging defendant's inadequate warning of cardiovascular risks. After jury trial, the Superior Court, Law Division, Atlantic County, Carol E. Higbee, P.J. Cv., 2007 WL 2011773, entered judgment awarding first patient $15.7 million for compensatory and punitive damages as well as attorney fees and costs, and awarding second patient $2.27 million, consisting of $135 in compensatory damages and the remainder as attorney fees and costs. Defendant appealed.

Holdings: The Superior Court, Appellate Division, Payne, J.A.D., held that:
(1) inadequate-warning claims under Product Liability Act were not preempted by federal law;
(2) presumption of adequacy of defendant's warnings was rebutted;
(3) evidence established product-defect causation element of claim under Product Liability Act;
(4) evidence established medical causation element of claim under Product Liability Act;
(5) punitive damages provision of Product Liability Act was preempted by federal law; and
(6) Product Liability Act subsumed claims under Consumer Fraud Act.

Affirmed in part, reversed in part.

West Headnotes

[1] Products Liability 313A 225

313A Products Liability
313AIII Particular Products
313Ak223 Health Care and Medical Products
313Ak225 k. Drugs in general. Most Cited Cases
(Formerly 313Ak46.2)

States 360 18.65

360 States
360I Political Status and Relations
360I(B) Federal Supremacy; Preemption
360k18.65 k. Product safety; food and drug laws. Most Cited Cases

Federal Food, Drug, and Cosmetic Act (FDCA) does not preempt state-law tort remedies against drug manufacturers, under theories of express conflict preemption or implied preemption, in the duty-to-warn context. Federal Food, Drug, and Cosmetic Act, § 1 et seq., 21 U.S.C.A. § 301 et seq.

[2] Products Liability 313A 225

313A Products Liability
313AIII Particular Products
313Ak223 Health Care and Medical Products

313Ak225 k. Drugs in general. Most Cited Cases
(Formerly 313Ak46.2)

States 360 18.65

360 States
360I Political Status and Relations
360I(B) Federal Supremacy; Preemption
360k18.65 k. Product safety; food and drug laws. Most Cited Cases

Patients' inadequate-warnings actions against manufacturer of rofecoxib, a prescription non-steroidal anti-inflammatory drug (NSAID) to treat acute pain and arthritis by specifically inhibiting cyclooxygenase-2 (COX-2), asserted under the New Jersey Product Liability Act (PLA), were not preempted, under a theory of regulatory preemption, by rules promulgated by the federal Food and Drug Administration (FDA) under the Federal Food, Drug, and Cosmetic Act (FDCA); labeling changes sought by the patients did not conflict with federal requirements, and were in fact consonant with them, e.g., an FDA regulation permitted a drug manufacturer to add risk information to an FDA-approved New Drug Application (NDA) when hazards emerged, without securing FDA's prior approval. Federal Food, Drug, and Cosmetic Act, § 1 et seq., 21 U.S.C.A. § 301 et seq.; 21 C.F.R. §§ 201.56, 201.57(e), 314.70(c)(2)(i), (c)(6)(iii)(A); N.J.S.A. 2A:58C-2, 2A:58C-4.

[3] Administrative Law and Procedure 15A 419

15A Administrative Law and Procedure
15AIV Powers and Proceedings of Administrative Agencies, Officers and Agents
15AIV(C) Rules and Regulations
15Ak416 Effect
15Ak419 k. Retroactivity. Most Cited Cases

Retroactive application of an administrative rule is not favored.

[4] Products Liability 313A 225

313A Products Liability
313AIII Particular Products
313Ak223 Health Care and Medical Products
313Ak225 k. Drugs in general. Most Cited Cases
(Formerly 313Ak46.2)

Products Liability 313A 226

313A Products Liability
313AIII Particular Products
313Ak223 Health Care and Medical Products
313Ak226 k. Medical devices and appliances in general. Most Cited Cases
(Formerly 313Ak46.1)

States 360 18.65

360 States
360I Political Status and Relations
360I(B) Federal Supremacy; Preemption
360k18.65 k. Product safety; food and drug laws. Most Cited Cases

For purposes of federal regulatory preemption of state law claims, preamble to final rule of federal Food and Drug Administration (FDA) governing requirements for content and format of labeling for human prescription drug and biological products, stating that FDA believed that under existing preemption principles FDA approval of labeling under Federal Food, Drug, and Cosmetic Act (FDCA) preempted conflicting or contrary state law, did not constitute a regulation duly adopted after notice and comment, and

instead was merely an expression of opinion on the part of FDA, and thus, the preamble lacked preemptive force. Federal Food, Drug, and Cosmetic Act, § 1 et seq., 21 U.S.C.A. § 301 et seq.

[5] States 360 18.13

360 States
360I Political Status and Relations
360I(B) Federal Supremacy; Preemption
360k18.13 k. State police power. Most Cited Cases

There is a presumption against federal preemption in fields traditionally occupied by the states.

[6] Products Liability 313A 225

313A Products Liability
313AIII Particular Products
313Ak223 Health Care and Medical Products
313Ak225 k. Drugs in general. Most Cited Cases
(Formerly 313Ak77)

Products Liability 313A 347

313A Products Liability
313AIV Actions
313AIV(C) Evidence
313AIV(C)2 Presumptions and Burden of Proof
313Ak347 k. Warnings or instructions. Most Cited Cases
(Formerly 313Ak77)

Drug manufacturer's economically-driven manipulation of post-market regulatory process, with respect to manufacturer's prescription non-steroidal anti-inflammatory drug (NSAID), rofecoxib, to treat acute pain and arthritis by specifically inhibiting cyclooxygenase-2 (COX-2), rebutted the presumption, in inadequate-warnings action under New Jersey Product Liability Act (PLA), that two warning labels approved by federal Food and Drug Administration (FDA) under the Federal Food, Drug, and Cosmetic Act (FDCA), the first of which contained no precautions or warnings regarding cardiovascular risks, and the second of which contained a statement in the "Precaution" section that was limited to patients with history of ischemic heart disease, were adequate; for first label, manufacturer actively sought to dilute the labeling required as result of study showing increased cardiovascular risks, manufacturer's marketing personnel engaged in strenuous efforts to ensure that study's results were not communicated to prescribing physicians by sales persons, and increased cardiovascular risk was framed by manufacturer in terms of a comparatively decreased incidence of cardiovascular thrombotic events associated with traditional NSAIDs imbued with cardioprotective powers whose extent was unproven, and for second label, manufacturer opposed the inclusion of cardiovascular risk in "Warnings" section of label, despite universal opinion of FDA's advisory committee and medical reviewers that a warning was appropriate. Federal Food, Drug, and Cosmetic Act, § 1 et seq., 21 U.S.C.A. § 301 et seq.; N.J.S.A. 2A:58C-4.

[7] Products Liability 313A 225

313A Products Liability
313AIII Particular Products
313Ak223 Health Care and Medical Products
313Ak225 k. Drugs in general. Most Cited Cases
(Formerly 313Ak97)

Products Liability 313A 439

313A Products Liability
313AIV Actions
313AIV(E) Instructions

313Ak438 Presumptions and Burden of Proof
313Ak439 k. In general. Most Cited Cases
(Formerly 313Ak97)

Jury instruction, regarding rebuttal of presumption, under New Jersey Product Liability Act (PLA), of adequacy of warning labels approved by federal Food and Drug Administration (FDA) under the Federal Food, Drug, and Cosmetic Act (FDCA), was proper, in action against manufacturer of rofecoxib, a prescription non-steroidal anti-inflammatory drug (NSAID) to treat acute pain and arthritis by specifically inhibiting cyclooxygenase-2 (COX-2), alleging inadequate warning of cardiovascular risks; instruction adequately informed jury that the presumption of adequacy could be overcome only by "substantial evidence," thereby according the presumption a significance greater than would otherwise have been the case, while not according it conclusive effect. Federal Food, Drug, and Cosmetic Act, § 1 et seq., 21 U.S.C.A. § 301 et seq.; N.J.S.A. 2A:58C-4.

[8] Evidence 157 506

157 Evidence
157XII Opinion Evidence
157XII(B) Subjects of Expert Testimony
157k506 k. Matters directly in issue. Most Cited Cases

Proffered testimony of defendant drug manufacturer's regulatory expert witness in action under New Jersey Product Liability Act (PLA) alleging inadequate warning of cardiovascular risks of manufacturer's prescription non-steroidal anti-inflammatory drug (NSAID), rofecoxib, to treat acute pain and arthritis by specifically inhibiting cyclooxygenase-2 (COX-2), giving her interpretation of federal Food and Drug Administration (FDA) regulations, including regulation addressing labeling revision under Changes-Being-Effected (CBE) procedure, and stating that based upon applicable FDA regulations the manufacturer's revised label for the prescription drug was adequate, was inadmissible, because it expressed legal conclusions, thereby posing a risk of confusing the jury and of usurping the role of the judge in instructing the jury on the relevant law. 21 C.F.R. 314.70(c)(2)(i); N.J.S.A. 2A:58C-2.

[9] Evidence 157 555.10

157 Evidence
157XII Opinion Evidence
157XII(D) Examination of Experts
157k555 Basis of Opinion
157k555.10 k. Medical testimony. Most Cited Cases

The proffered testimony of defendant drug manufacturer's regulatory expert witness in action under New Jersey Product Liability Act (PLA) alleging inadequate warning of cardiovascular risks of manufacturer's prescription non-steroidal anti-inflammatory drug (NSAID), rofecoxib, to treat acute pain and arthritis by specifically inhibiting cyclooxygenase-2 (COX-2), that if manufacturer had submitted a warning-label change pursuant to federal Food and Drug Administration's (FDA) Changes-Being-Effected (CBE) procedure it would have been rejected, was speculative and lacking in foundation, and therefore was inadmissible. 21 C.F.R. 314.70(c)(2)(i); N.J.S.A. 2A:58C-2.

[10] Evidence 157 506

157 Evidence
157XII Opinion Evidence
157XII(B) Subjects of Expert Testimony
157k506 k. Matters directly in issue. Most Cited Cases

The trial court must limit expert testimony so as not to allow experts to testify regarding legal conclusions by offering opinions on what the law requires or by testifying as to the governing law.

[11] Evidence 157 506

157 Evidence
157XII Opinion Evidence

157XII(B) Subjects of Expert Testimony
157k506 k. Matters directly in issue. Most Cited Cases

The ruling barring expert witnesses from offering legal conclusions exists to avoid confusing the jury or usurping the role of the judge in instructing the jury on the relevant law.

[12] Evidence 157 146

157 Evidence
157IV Admissibility in General
157IV(D) Materiality
157k146 k. Tendency to mislead or confuse. Most Cited Cases

Probative value was substantially outweighed by danger of unfair prejudice, in action against manufacturer of rofecoxib, a prescription non-steroidal anti-inflammatory drug (NSAID) to treat acute pain and arthritis by specifically inhibiting cyclooxygenase-2 (COX-2), brought under New Jersey Product Liability Act (PLA) and alleging inadequate warning of cardiovascular risks, as to memorandum from federal Food and Drug Administration (FDA), offered by defendant manufacturer, in which two FDA scientists provided opinion that all NSAIDs, including defendant's drug, increased the risk of heart attacks, in absence of explanation for scientific basis for scientists' opinion and of expert witness who could support the opinion based on review not just of the memorandum but also of relevant clinical studies; validity of the opinion was unknown, and in order for jury to properly weigh the information in the memorandum supporting the opinion, the information had to be used by an expert who could explain it and be cross-examined on it. N.J.S.A. 2A:58C-2; N.J.S.A. 2A:84A, App. A, Rules of Evid., N.J.R.E. 403(a).

[13] Evidence 157 363

157 Evidence
157X Documentary Evidence
157X(C) Private Writings and Publications
157k360 Books and Other Printed Publications
157k363 k. Scientific and technical works; safety standards. Most Cited Cases

Admission, under hearsay exception for learned treatises, of peer-reviewed article in medical journal, encompassed, in action under New Jersey Product Liability Act (PLA) alleging inadequate warning of cardiovascular risks of defendant manufacturer's prescription non-steroidal anti-inflammatory drug (NSAID), rofecoxib, to treat acute pain and arthritis by specifically inhibiting cyclooxygenase-2 (COX-2), the article's extrapolation, from clinical trials conducted by defendant manufacturer, of estimated "excess" heart attacks probably caused by defendant's drug during five-year period; while such estimate was not directly derived from the epidemiological study that was the initial focus of the article, the article presented a proper foundation for the estimate, the estimate was directly related to article's conclusions that use of defendant's drug increased the risk of serious coronary heart disease compared with a second NSAID and that a third NSAID did not protect against serious coronary heart disease, and the estimate was integral to article's further conclusion, based upon results of author's epidemiological research, that public health consequences of failure to take earlier action to remove a drug from the market must be assessed. N.J.S.A. 2A:58C-2; N.J.S.A. 2A:84A, App. A, Rules of Evid., N.J.R.E. 803(c)(18).

[14] Products Liability 313A 225

313A Products Liability
313AIII Particular Products
313Ak223 Health Care and Medical Products
313Ak225 k. Drugs in general. Most Cited Cases
(Formerly 313Ak81.1)

Products Liability 313A 367

313A Products Liability
313AIV Actions
313AIV(C) Evidence

313AIV(C)3 Admissibility of Evidence
313Ak367 k. Warnings or instructions. Most Cited Cases
(Formerly 313Ak81.1)

Evidence of marketing practices of defendant manufacturer of rofecoxib, a prescription non-steroidal anti-inflammatory drug (NSAID) to treat acute pain and arthritis by specifically inhibiting cyclooxygenase-2 (COX-2), was relevant, in action under New Jersey Product Liability Act (PLA) alleging inadequate warning of cardiovascular risks, to showing defendant's failure to adequately warn of known dangers of its product and to showing defendant's conduct in obscuring scientific evidence of cardiovascular risks established by clinical studies, though such marketing practices had not been targeted to plaintiff patients or their physicians. N.J.S.A. 2A:58C-2.

[15] Products Liability 313A 225

313A Products Liability
313AIII Particular Products
313Ak223 Health Care and Medical Products
313Ak225 k. Drugs in general. Most Cited Cases
(Formerly 313Ak75.1)

Products Liability 313A 351(2)

313A Products Liability
313AIV Actions
313AIV(C) Evidence
313AIV(C)2 Presumptions and Burden of Proof
313Ak348 Proximate Cause
313Ak351 Warnings or Instructions
313Ak351(2) k. Heeding. Most Cited Cases
(Formerly 313Ak75.1)

In appropriate circumstances, a heeding presumption, that a patient's doctors would have heeded an adequate warning by the manufacturer of a prescription drug, may be applicable to a claim of the manufacturer's failure to warn of the dangers of a palliative drug for which potentially less harmful alternatives exist.

[16] Products Liability 313A 225

313A Products Liability
313AIII Particular Products
313Ak223 Health Care and Medical Products
313Ak225 k. Drugs in general. Most Cited Cases
(Formerly 313Ak77)

Products Liability 313A 351(2)

313A Products Liability
313AIV Actions
313AIV(C) Evidence
313AIV(C)2 Presumptions and Burden of Proof
313Ak348 Proximate Cause
313Ak351 Warnings or Instructions
313Ak351(2) k. Heeding. Most Cited Cases
(Formerly 313Ak77)

Use of a heeding presumption, that a patient's treating physician would have heeded an adequate warning by the manufacturer of a prescription drug, was not necessary, in action under New Jersey Product Liability Act (PLA) alleging manufacturer's inadequate warning of cardiovascular risks of rofecoxib, a prescription non-steroidal anti-inflammatory drug (NSAID) to treat acute pain and

arthritis by specifically inhibiting cyclooxygenase-2 (COX-2), where direct evidence existed, in the form of testimony of patient's treating physician, that if the physician had been informed of the cardiovascular risks of the drug, he would not have prescribed it to the patient. N.J.S.A. 2A:58C-2.

[17] Products Liability 313A 225

313A Products Liability
313AIII Particular Products
313Ak223 Health Care and Medical Products
313Ak225 k. Drugs in general. Most Cited Cases
(Formerly 313Ak83)

Products Liability 313A 392

313A Products Liability
313AIV Actions
313AIV(C) Evidence
313AIV(C)4 Weight and Sufficiency of Evidence
313Ak389 Proximate Cause
313Ak392 k. Warnings or instructions. Most Cited Cases
(Formerly 313Ak83)

Evidence established product-defect causation element of claim, under New Jersey Product Liability Act (PLA), of inadequate warning of cardiovascular risks of defendant manufacturer's prescription non-steroidal anti-inflammatory drug (NSAID), rofecoxib, to treat acute pain and arthritis by specifically inhibiting cyclooxygenase-2 (COX-2); plaintiff patient's treating physician testified that he had paid close attention to defendant's product literature for the drug, including package inserts and "Dear Doctor" letters, that when he had been informed by defendant that the drug posed a risk to patients with ischemic heart disease he had discontinued prescribing the drug to another patient, who had that condition, but he had determined such precaution did not apply to plaintiff, and that if he had known the drug "could" increase the risk of heart attack he would not have added to the cardiovascular risks confronting plaintiff, as result of patient's age, gender, and diabetic condition, by prescribing the drug, and patient testified that he would not have taken the drug if he had known of its cardiovascular risk and that he had relied on the physician for a determination of drug safety. N.J.S.A. 2A:58C-2.

[18] Damages 115 185(1)

115 Damages
115IX Evidence
115k183 Weight and Sufficiency
115k185 Personal Injuries and Physical Suffering
115k185(1) k. In general. Most Cited Cases

Evidence 157 571(9)

157 Evidence
157XII Opinion Evidence
157XII(F) Effect of Opinion Evidence
157k569 Testimony of Experts
157k571 Nature of Subject
157k571(9) k. Cause and effect. Most Cited Cases

Products Liability 313A 225

313A Products Liability
313AIII Particular Products
313Ak223 Health Care and Medical Products
313Ak225 k. Drugs in general. Most Cited Cases

(Formerly 313Ak83)

Products Liability 313A 392

313A Products Liability
313AIV Actions
313AIV(C) Evidence
313AIV(C)4 Weight and Sufficiency of Evidence
313Ak389 Proximate Cause
313Ak392 k. Warnings or instructions. Most Cited Cases
(Formerly 313Ak83)

Evidence established medical causation element of claim, under New Jersey Product Liability Act (PLA), of inadequate warning of cardiovascular risks of defendant manufacturer's prescription non-steroidal anti-inflammatory drug (NSAID), rofecoxib, to treat acute pain and arthritis by specifically inhibiting cyclooxygenase-2 (COX-2), relating to patient who suffered heart attack after taking the drug for 48 months; cardiologist testified that, among existing hypotheses, the scientific community was "most concerned about" and the "most evidence" supported a hypothesis that a COX-2 inhibitor upset the body's balance between prostacyclin and thromboxane by inhibiting prostacyclin production, thereby increasing clotting action of platelets in blood that would occur when plaque deposited in arteries ruptured, cardiologist testified that increased clotting could lead to blockage of normal blood flow and occurrence of heart attack, and second cardiologist, relying upon epidemiological studies, identified the presence of heart attack risk factors for the patient in addition to long-term use of the drug, consisting of his age, low levels of "good" cholesterol, weight, and diabetes, testified that conjoined effects of diabetes and use of the drug increased the patient's risk of heart attack, and concluded that the drug had been a substantial contributing factor to patient's heart attack. N.J.S.A. 2A:58C-2.

[19] Damages 115 87(1)

115 Damages
115V Exemplary Damages
115k87 Nature and Theory of Damages Additional to Compensation
115k87(1) k. In general. Most Cited Cases

States 360 18.15

360 States
360I Political Status and Relations
360I(B) Federal Supremacy; Preemption
360k18.15 k. Particular cases, preemption or supersession. Most Cited Cases

Provision of New Jersey Product Liability Act (PLA), allowing punitive damages to be awarded if manufacturer knowingly withheld or misrepresented information required to be submitted to the federal Food and Drug Administration (FDA), as exception to PLA's general rule that punitive damages cannot be awarded if the drug, device, food, or food additive that caused claimant's harm was subject to premarket approval or licensure by FDA and was so approved or licensed or if it was generally recognized as safe and effective pursuant to conditions established by FDA and applicable regulations, impinged upon federal statutes and regulations, and thus, such provision allowing punitive damages was impliedly preempted. Federal Food, Drug, and Cosmetic Act, § 1 et seq., 21 U.S.C.A. § 301 et seq.; Public Health Service Act, § 2 et seq., 42 U.S.C.A. § 201 et seq.; N.J.S.A. 2A:58C-5(c).

[20] Damages 115 15

115 Damages
115III Grounds and Subjects of Compensatory Damages
115III(A) Direct or Remote, Contingent, or Prospective Consequences or Losses
115III(A)1 In General
115k15 k. Nature and theory of compensation. Most Cited Cases

Damages 115 87(1)

115 Damages
115V Exemplary Damages
115k87 Nature and Theory of Damages Additional to Compensation
115k87(1) k. In general. Most Cited Cases

The purposes of punitive damages are to punish unlawful conduct and to deter its repetition, while the purpose of compensatory damages is to make the individual plaintiff whole.

[21] Antitrust and Trade Regulation 29T 282

29T Antitrust and Trade Regulation
29TIII Statutory Unfair Trade Practices and Consumer Protection
29TIII(E) Enforcement and Remedies
29TIII(E)1 In General
29Tk281 Exclusive and Concurrent Remedies or Laws
29Tk282 k. In general. Most Cited Cases

The New Jersey Product Liability Act (PLA), under which patients brought a claim of inadequate warnings, subsumed patients' economic-harm claims, under New Jersey Consumer Fraud Act, that manufacturer of rofecoxib, a prescription non-steroidal anti-inflammatory drug (NSAID) to treat acute pain and arthritis by specifically inhibiting cyclooxygenase-2 (COX-2), made misrepresentations that had the capacity to mislead concerning cardiovascular risks of the drug while marketing it to prescribing physicians, and intentionally suppressed, concealed, or omitted, with respect to prescribing physicians, material information about association between the drug and an increased risk of cardiovascular events, and thus, patients could not bring separate claims under CFA. N.J.S.A. 2A:58C-2, 56:8-1 et seq.

[22] Products Liability 313A 110

313A Products Liability
313AII Elements and Concepts
313Ak110 k. In general. Most Cited Cases
(Formerly 313Ak1)

By enacting the Product Liability Act (PLA), the New Jersey Legislature manifested its intent to replace all pre-existing claims by one unified, statutorily defined theory of recovery for harm caused by a product. N.J.S.A. 2A:58C-1 et seq.

[23] Products Liability 313A 110

313A Products Liability
313AII Elements and Concepts
313Ak110 k. In general. Most Cited Cases
(Formerly 313Ak1)

The New Jersey Legislature intended for the Product Liability Act (PLA) to limit the liability of manufacturers, so as to balance the interests of manufacturers, the public, and the individual, with a view towards economic reality. N.J.S.A. 2A:58C-1 et seq.

West Codenotes
PreemptedN.J.S.A. 2A:58C-5(c) ****229** Douglas S. Eakeley argued the cause for appellant in both cases (Lowenstein Sandler, attorneys; Mr. Eakeley, Michael Dore and Alan S. Modlinger, Roseland, on the brief).

Ellen Relkin, New York, NY, argued the cause for respondents John and Irma McDarby (Weitz & Luxenberg, attorneys; George W. Conk, South Orange, of counsel, Ms. Relkin and Stephen J. Riegel, New York, NY, on the brief).

Evan M. Janush (The Lanier Law Firm) of the New York bar, admitted pro hac vice, argued the cause for respondents Thomas and Joyce Cona (The Lanier Law Firm, attorneys; W. Mark Lanier, Mr. Janush, and Richard D. Meadow, Houston, TX, on the brief).

Before Judges AXELRAD, PAYNE and MESSANO.

The opinion of the Court was delivered by

PAYNE, J.A.D.

***20** Defendant, Merck & Co., Inc., appeals from a $15.7 million judgment, awarding compensatory and punitive damages, as well as attorneys' fees and costs, to plaintiffs, John and Irma McDarby, on claims of product liability and consumer fraud arising from Merck's sale of the prescription drug Vioxx, as well as from a $2.27 million judgment awarding damages of $135 and the remainder as attorneys' fees and costs to plaintiffs, Thomas and Joyce Cona, on claims of consumer fraud arising, likewise, from the sale of Vioxx. The claims of the McDarbys and Conas were tried together. We declined to consolidate Merck's appeals, but scheduled them to be heard back-to-back. This opinion addresses both appeals.

I.

We commence this opinion with a statement of facts that could reasonably have been considered by the jury in support of its verdict. Our factual statement is extended, but we regard it as ***21** necessary to place in perspective the issues regarding the applicability of the New Jersey Product Liability Act (PLA), *N.J.S.A.* 2A:58C-1 to -11, and the New Jersey Consumer Fraud Act (CFA), *N.J.S.A.* 56:8-1 to -156, that underlie this appeal. The record discloses the tension that existed between Merck's scientists and its marketers and, in plaintiffs' view, the pressure on Merck's employees to preserve market share and concomitant profits arising from the sale of Vioxx-a drug envisioned as re-establishing Merck as preeminent in the field of pharmaceutical development and manufacture-regardless of the cardiovascular risks posed by the drug. The record likewise discloses a spirited defense on behalf of Merck. However, as the result of the verdict in plaintiffs' favor, we do not focus on that defense.

A. *Background*

Scientists have known for some time that the enzyme cyclooxygenase (COX) catalyzes****230** the synthesis of prostaglandins, which affect pain and inflammation. Non-steroidal anti-inflammatory drugs (NSAIDs) are a class of compounds including ibuprofen (Advil and Motrin), naproxen (Aleve) and aspirin that exert an analgesic and anti-inflammatory effect by decreasing the production of prostaglandins through the inhibition of COX. For that reason, NSAIDs are widely used in the treatment of acute and chronic pain and inflammation, including that caused by rheumatoid arthritis and osteoarthritis. However, NSAIDs have been found to have a deleterious effect on the gastrointestinal (GI) tract, causing perforations, ulcers, and GI bleeding (collectively, PUBs).

In the early 1990s, scientists learned that prostaglandin synthesis in humans is catalyzed by two forms of cyclooxygenase, cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2). They postulated that COX-1 functions to protect the gastric mucosa and to promote normal platelet function, whereas COX-2 promotes painful inflammation. Development of a drug that could suppress ***22** COX-2, while not affecting COX-1, could be beneficial and potentially lucrative.

At the time of these discoveries, Merck was concerned by the forthcoming loss of patent protection for six of its major drugs, and it was actively seeking replacement products. In 1992, Merck synthesized the substance rofecoxib, later trade-named Vioxx®, a COX-2 inhibitor that the company posited would have potent analgesic and anti-inflammatory properties without associated GI toxicity. At this time, Pfizer was also actively seeking to develop a COX-2 inhibitor, and competition between the two companies for first entry into the market and an accordingly larger market share was intense.

B. *Federal Food and Drug Administration Approval of Vioxx*

In order to obtain Federal Food and Drug Administration (FDA) approval, Vioxx was required to undergo Phase I, II and III trials [FN1] designed to demonstrate safety and efficacy in humans for the uses proposed by the manufacturer. By 1995, Merck was actively involved in Phase II studies.

> FN1. Phase I trials normally involve a small group (20 to 80) of healthy volunteers who are utilized to assess the safety of a investigational new drug (IND) over a range of doses. Once initial safety has been confirmed in Phase I trials, Phase II trials are performed on larger groups (20 to 300) and are utilized to assess how well the drug functions. Phase II may be divided into Phase IIA, which studies dosing and Phase IIB, which studies efficacy. Phase III studies usually involve randomized controlled multicenter trials on large patient groups, which may continue while a new drug application is pending before the FDA. Such trials may also be used to demonstrate that the drug works for additional patients or conditions beyond the original use for which the drug was approved for marketing, to obtain additional safety data or to support marketing claims. Phase IV trials are conducted to provide safety surveillance and technical support after a drug is approved for sale.

At the time, it was known that two hormones, present in the body, affect blood clotting by causing or preventing aggregation of platelets. Thromboxane acts to induce platelet aggregation and to constrict blood vessels, whereas prostacyclin acts in a reverse fashion. The balance between the two hormones is a factor in ***23** preventing thromboses or clots. The actions of these substances had

been reported by Merck in its Merck's Manual, which described prostacyclin as the "most potent" anti-clotting substance in the body. However, at trial, plaintiffs demonstrated that this entry, potentially relevant to the ****231** risks of taking Vioxx, was absent from the 1999 version of the Manual.

In one of the clinical pharmacology studies conducted during the development of Vioxx, researchers noted that the administration of Vioxx to inhibit COX-2 vastly decreased the excretion of the metabolites of prostacyclin, and thus that it likely inhibited the production of prostacyclin itself.[FN2] Levels of the metabolites of thromboxane remained unchanged. In an article by Garret FitzGerald, the study's chief investigator, and others, received for publication on October 19, 1998, FitzGerald hypothesized that if COX-2 inhibitors suppressed prostacyclin generated within blood vessels without suppressing thromboxane, increased clotting, leading to heart attacks and strokes, would result.

> FN2. Merck's senior scientist, Dr. Nancy Santanello, testified that "Vioxx apparently has the effect of lowering prostacyclin such that there's less prostacyclin. I believe it is about a 50 percent decrease."

As early as April 13, 1998, Vioxx project team meeting minutes noted the unexpected effect of Vioxx on prostacyclin. Minutes of Merck's May 12, 1998 project team meeting reflect a May 1998 recommendation by Merck's independent board of scientific advisors to "[b]egin from this point onward to systematically collect data on CV [cardiovascular] events in all clinical trials [for Vioxx ...] utilizing predefined end points for MCI [myocardial infarction], stroke, TIA [transient ischemic attack], unstable angina etc. To accomplish this task, an adjudication committee [FN3] should be established and follow a formal plan." Such adjudication was commenced.

> FN3. An adjudication committee examines reported events to determine accuracy; for example, whether symptoms reported as angina instead reflect a heart attack.

***24** On November 23, 1998, Merck submitted a new drug application (NDA) for Vioxx to the FDA that included FitzGerald's study and a subsequent analysis of cardiovascular events in then-existing Phase II and partially completed Phase III studies. In its discussion of clinical safety, Merck admitted that "theoretically, there might be a risk for thromboembolic cardiovascular adverse experiences with long-term treatment with a COX-2-specific inhibitor compared to long-term NSAID therapy (where COX-1 inhibition inhibits platelet aggregation)." However, Merck stated that statistical analysis had not disclosed statistically significant differences in thromboembolic cardiovascular adverse experiences, regardless of seriousness, between Vioxx-treated patients and those treated with traditional NSAIDs or placebos. None of the trials submitted to the FDA specifically evaluated cardiovascular safety. Additionally, most were short-term in length and did not evaluate patients at high risk for cardiovascular disease.

The application was reviewed by FDA medical officer Dr. Maria Villalba who, in a report dated May 20, 1999, examined, among other things, the thromboembolic and vascular safety of Vioxx, noting that most of the serious adverse events observed in studies submitted in connection with the NDA were cardiovascular in nature, despite the exclusion of patients with a recent history of myocardial infarction or unstable angina, and of patients with a transient ischemic attack or cardiovascular accident within two years of entry into the study. Patients utilizing cardioprotective doses of aspirin were also excluded. Dr. Villalba noted that "[e]valuation of CV thromboembolic events regardless of seriousness shows a numerically higher incidence of ischemic/thromboembolic events (angina, myocardial infarction, CVA [cardiovascular accident], TIA [****232**transient ischemic attack])" in patients taking Vioxx as compared to those taking a placebo, and that there was "a trend toward an increased incidence in longer trials." However, the doctor determined that it was difficult to reach meaningful conclusions regarding this information because of the small number of events, differences in length of exposure and in dose, and ***25** lack of large-scale trials using a high (50 mg) dose of Vioxx. She concluded:

> *In summary:* With the available data, it is impossible to answer with complete certainty whether the risk of cardiovascular and thromboembolic events is increased in patients on rofecoxib. A larger database will be needed to answer this and other safety comparison questions.

Patients who need aspirin for cardiovascular reasons [FN4] should not stop aspirin when taking rofecoxib.

> FN4. Aspirin is recognized to be a cardioprotective drug because it prevents platelets from aggregating. Low dose aspirin is often recommended for patients at risk of heart attack.

Vioxx was approved by the FDA on May 20, 1999, the same day as Villalba's report, as safe and effective for use in the relief of the signs and symptoms of osteoarthritis, for the management of acute pain in adults, and for treatment of primary dysmenorrhea. The labeling required by the FDA did not contain any warnings or precautions regarding cardiovascular risks.

The FDA's letter informing Merck of its approval of Vioxx stated: "If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required."

C. *Merck's Product Launch*

The sale of Vioxx was launched at a million-dollar two-and-one-half-day launch meeting and party in San Francisco in June 1999. There, David Anstice, Merck's President for the Sale and Marketing of its Human Health Products in North America, described Vioxx as a "superstar" that would make Merck "own" the rheumatology market "once again." He announced that Merck would be distributing seventeen million units of Vioxx as samples between then and the end of a year, stating that the short-run cost was worth the opportunity to win market share. Merck employed its largest-ever sales force for the marketing effort, providing sales incentives and targeting over 10,000 physicians; funded a "Health Education Liaison" program at three million dollars per month; ***26** and paid doctors to speak about Vioxx. At trial, plaintiffs' counsel highlighted the money spent on advertising and promotion, and compared it with the absence of any funding for a cardiovascular safety study, which Raymond Gilmartin, Merck's Chief Executive Officer, testified that Merck was not required to perform.

During 1999, Merck compiled a substantial list of influential physicians across the country and their views about Vioxx. A chart introduced at trial indicated that some whose views were adverse to Merck were to be visited by upper management and provided with funding for programs or invited to prestigious meetings in "elegant" national or international locations. A number of other doctors were listed as "neutralized" by offers to participate in clinical trials, speaking engagements, or conferences. The legend "discredit" appeared by the name of one doctor, an advocate for Searle.

In addition to its extensive direct marketing of Vioxx to physicians, throughout the period that Vioxx was on the market, Merck engaged in significant direct-to-consumer marketing efforts, including magazine advertisements and television spots ****233** featuring ice skater Dorothy Hamill touting the drug and persons able to engage in leisure activities because of their use of Vioxx.

D. *The VIGOR Study*

In mid-1998, prior to the approval of Vioxx by the FDA, Merck commenced development of the protocols for a large-scale blinded study of persons with rheumatoid arthritis, given the acronym VIGOR,[FN5] to test whether Vioxx was associated with fewer gastrointestinal adverse events than a comparator NSAID, naproxen (sold in over-the-counter form as Aleve). Dr. Alise Reicin, who at the time of trial was a vice-president of clinical research at Merck, was a primary drafter of the protocols and the study's clinical monitor. The study utilized doses of 500 mg twice a day for naproxen and, at the FDA's request, a 50-mg dose of Vioxx, which ***27** was two times the recommended dose. Use of cardioprotective low-dose aspirin was not permitted. Because of the need of the patients for some form of analgesic, the study did not utilize a placebo. The study was monitored by an independent safety monitoring board that analyzed unblinded data at various points during the study's progress. Between January 1999 and July 1999, approximately 8,000 persons were enrolled in the study, and were divided equally into groups taking Vioxx and naproxen. The primary endpoint for the study was a specified number of clinical upper GI events (gastroduodenal perforation or obstruction, upper gastrointestinal bleeding, and symptomatic gastroduodenal ulcers). However, serious cardiovascular events were also noted and adjudicated for use with other studies in a projected pooled or meta-analysis.

FN5. VIGOR stands for Vioxx Gastrointestinal Outcomes Research study.

In its November 1999 and December 1999 meetings, the data safety monitoring board discussed the increase in deaths and adverse cardiovascular events that was appearing in patients taking Vioxx over those taking naproxen. Although the board did not recommend discontinuance of the trial as a result, it did recommend development of an analysis plan for adjudicated serious cardiovascular events in the VIGOR trial separate from any other planned analysis of that data. Dr. Reicin responded by providing such a plan and stating that the cutoff date for reporting serious vascular events to Merck would be February 10, 2000-a date that was maintained in a published report of the cardiovascular evidence obtained in the study, despite later-acquired evidence that suggested a further increase in cardiovascular risk.

At the conclusion of the gastrointestinal portion of the trial on March 9, 2000 (one month after the cardiovascular cut-off), the VIGOR study confirmed that Vioxx and naproxen had similar efficacy against rheumatoid arthritis, and that the use of Vioxx resulted in significantly fewer confirmed adverse gastrointestinal events, as Merck had projected. However, it also demonstrated an alarming four-fold increase in the incidence of non-acute ***28**myocardial infarctions. Inclusion of three additional myocardial infarctions, reported shortly after the study's thromboembolic event cut-off date, would have created a five-fold increase.

On March 9, 2000, Dr. Edward Scolnick, the President of Merck's Research Division, wrote an e-mail about the VIGOR data that stated: "The CV events are clearly there." Scolnick continued: "It is a shame but it is a low incidence and it is mechanism based as we worried it was." In a April 12, 2000 e-mail to Dr. Reicin, Dr. Scolnick stated:

****234** I will tell you my worry quotient is high. I actually am in minor agony. What I really want to do is a 10000 vs 10000 patient study in mild-moderate OA [osteoarthritis] Tylenol vs Vioxx with prn [as needed] low dose asa [aspirin] for those judged to need it. [S]afety first primary endpoint and efficacy secondary or co-primary. WE WILL NOT KNOW FOR SURE WHAT IS GOING ON UNTIL WE DO THIS STUDY. PLEASE THINK HARD ABOUT THE DESIGN BEFORE THE PAC MEETING.

The results of the VIGOR study were reported by Merck to the FDA on March 27, 2000. In a section captioned "Cardiovascular Safety," Merck stated that the VIGOR study "provided an opportunity to determine if the NSAID naproxen, which inhibits platelet aggregation, reduced cardiovascular risk compared with the COX-2 inhibitor rofecoxib, which has no effect on platelet aggregation." Merck then reported: "The overall incidence of serious thromboembolic cardiovascular adverse events was low in both treatment groups. However, the incidence of such events was significantly lower in patients on naproxen compared to rofecoxib." The greatest difference was for non-acute myocardial infarctions, with sixteen for Vioxx and five for naproxen. Additionally, fourteen patients treated with Vioxx sustained strokes, whereas only six of the naproxen-treated patients were thus affected. Merck stated further: "The differences in the incidences of cardiovascular SAEs [significant adverse events] between patients who received rofecoxib and patients who received naproxen was observed consistently between men and women, in patients above and below the age of 65, in patients with and without a history of ***29**atherosclerotic cardiovascular disease, [FN6] and in patients with or without classic risk factors for cardiovascular disease."

> FN6. Nonetheless, the precaution set forth in the 2002 FDA-approved label related only to persons with known ischemic heart disease.

Merck continued its analysis by stating that "VIGOR is the only study to demonstrate a difference in the incidence of serious cardiovascular adverse events in patients treated with rofecoxib compared with another treatment (placebo or NSAID comparator)" and was inconsistent with previous results of Phase II osteoarthritis studies, which showed identical rates of these events in patients on Vioxx and on NSAID comparitors. Merck explained the VIGOR results to the FDA by stating that: "Non-specific COX-1/COX-2 inhibitors such as naproxen may have cardioprotective effects through COX-1 mediated inhibition of platelet aggregation. The longer duration of therapy with naproxen in VIGOR and the size of the trial may have provided a sufficient sample size and period of observation to demonstrate the cardiovascular protective effects of naproxen." Alternatively, Merck noted that therapy with COX-2 selective inhibitors had been shown to cause "moderate" reductions in the synthesis of prostacyclin, a platelet aggregation inhibitor, without COX-1 mediated inhibition of platelet aggregation. "The resulting imbalance could theoretically have mildly pro-aggregatory platelet effects" that were noticeable in rheumatoid arthritis patients at higher risk for thrombotic events. As a consequence of the VIGOR findings, Merck signaled to the FDA its intent to amend its ongoing trials so as to allow low dose aspirin treatment for patients who may be at risk for cardiovascular events.

On the same day as its submission to the FDA, March 27, 2000, Merck also issued a ****235** news release on VIGOR, stressing the gastrointestinal safety of Vioxx by proclaiming that: "Among patients treated with Vioxx, there was a significantly reduced incidence of serious gastrointestinal events compared to patients treated with naproxen." Merck also reported the cardiovascular results of the ***30** study, but stated that there were "significantly fewer thromboembolic events" in patients taking naproxen, which it stated was "consistent with naproxen's ability to block platelet aggregation." As a consequence, the news release stated, investigators were being notified to permit the use of low-dose aspirin when appropriate.

Evidence at trial demonstrated that before the announcement was made, Merck's scientists had been unable to locate appropriately focused studies that supported its theory that naproxen had such a pronounced cardioprotective effect, despite the fact that the drug had been on the market for twenty years. Merck did not admit to the possibility that Vioxx was increasing cardiovascular risks.

E. *Merck's Supplemental New Drug Application Based on VIGOR*

On June 29, 2000, Merck submitted a supplemental new drug application to add the VIGOR results to the Vioxx label. Primarily, Merck sought to disclose that the results of the VIGOR study had provided "conclusive evidence of the improved GI safety of rofecoxib compared with a nonselective NSAID, naproxen." However, in its transmittal letter, Merck also stated: "Other findings in the VIGOR study reinforce the need for aspirin therapy in patients where cardio-protective use of low dose aspirin is indicated."

On August 7, 2000, Merck requested expedited review of its supplemental new drug application, stating:

> We believe that the results of the VIGOR trial establish a significant GI safety advantage for rofecoxib over non-selective NSAIDs which is not conveyed in the currently approved product labeling for this drug. Therefore, MRL [Merck Research Laboratories] is concerned that a standard review classification will delay the availability of this important safety information to prescribers and delay our dissemination of this information in a form consistent with the Agency's appraisal of the data.

However, the FDA denied the request because the maker of Celebrex had submitted a similar supplemental new drug application***31** for label changes, which caused the FDA to decide to review both with a public advisory committee that included outside experts.

On October 13, 2000, Merck submitted a safety update report to the FDA, which included data on the eleven additional patients in the VIGOR study who experienced cardiovascular serious adverse experiences eligible for adjudication that were reported after the pre-specified cut-off date. The adjudicated data disclosed three confirmed myocardial infarctions and one confirmed peripheral venous thrombosis on rofecoxib and one confirmed ischemic cerebrovascular accident on naproxen. However, Merck stated: "Inclusion of these patients in the analysis did not meaningfully alter the findings or conclusions of the study." An accompanying table indicated a substantial difference in the relative risk for all thrombotic events among users of Vioxx and naproxen. Divergence between the two groups commenced at one month. The incidence of confirmed acute myocardial infarctions rose from 0.4% to 0.5% in patients treated with Vioxx.

****236** Merck proposed a label change to reflect the VIGOR findings that included the following:

> In this study, in order not to confound the analysis of PUBs [perforation, ulcers, bleeding], patients were not permitted to use concomitant aspirin or other anti-platelet drugs.... The incidence of confirmed acute myocardial infarction was 0.4% 0.5% in patients treated with VIOXX 50 mg daily and 0.1% in patients treated with naproxen 500 mg twice daily.... This is consistent with the known anti-platelet effects of naproxen.

Merck also sought to include language stating that when the four percent of patients for whom aspirin therapy was indicated were removed from the study,

> the incidence of confirmed acute myocardial infarction was 0.2% 0.3% in patients treated with VIOXX 50 mg daily and 0.1% in patients treated with naproxen.... In other controlled clinical trials, spontaneous reports of these cardiovascular events were similar between VIOXX and nonselective NSAID comparators (ibuprofen, diclofenac and nabumetone). VIOXX is not a substitute for aspirin for cardiovascular prophylaxis.

Merck proposed adding a precaution that Vioxx lacked an anti-platelet effect that could substitute for aspirin, and thus that "[p]atients who require low dose aspirin therapy for cardiovascular ***32** prophylaxis should continue on aspirin during therapy with VIOXX."

The results of Merck's VIGOR trial were published in the New England Journal of Medicine on November 23, 2000.[FN7] However, the article omitted the adjudicated myocardial infarctions reported after the study's end date, and thus reported that the incidence of myocardial infarction was 0.1% in the naproxen group and 0.4% in the Vioxx group. Again, the difference was cast as a decrease among the naproxen-treated group, rather than an increase among the Vioxx-treated group. As in the labeling proposed by Merck, the authors of the article attributed the difference in rates of myocardial infarction primarily to the incidence of heart attacks among the four percent of patients who should have been taking cardioprotective doses of aspirin, but were not. After citing a meta-analysis of 7,535 patients comparing Vioxx with placebo and other NSAIDs (diclofenac, ibuprofen, and nabumetone) that revealed similar rates of myocardial infarctions in all groups, the article stated that "our results are consistent with the theory that naproxen has a coronary protective effect and highlight the fact that rofecoxib does not provide this type of protection owing to its selective inhibition of cyclooxygenase-2 at its therapeutic doses and at higher doses. The finding that naproxen therapy was associated with a lower rate of myocardial infarction needs further confirmation in larger studies."

> FN7. Claire Bombardier et al., *Comparison of Upper Gastrointenstinal Toxicity of Rofecoxib and Naproxen in Patients with Rheumatoid Arthritis*, 343 *New Eng. J. Med.* 1520 (2000).

In an editorial dated December 29, 2005,[FN8] published in the New England Journal of Medicine, the authors noted that "Three ***33** myocardial infarctions, all in the ****237** rofecoxib group, were not included in the data submitted to the *Journal.*" Although initially thought to have been unknown to the study's authors at the time of publication,

> FN8. Gregory D. Curfman et al., *Expression of Concern: Bombardier et al., "Comparison of Upper Gastrointestinal Toxicity of Rofecoxib and Naproxen in Patients with Rheumatoid Arthritis," New Eng. J. Med.2000; 343:1520-8*, 353 *New Eng. J. Med.* 2813 (2005). A response by the non-Merck authors of the initial article, Claire Bombardier et al., *Response to Expression of Concern Regarding VIGOR Study*, 354 *New Eng. J. Med.* 1196, appeared on March 16, 2006, followed by Curfman et al., *Expression of Concern Reaffirmed*, 354 *New Eng. J. Med.* 1193 (2006).

[i]t now appears ... that at least two of the authors knew about the three additional myocardial infarctions at least two weeks before the authors submitted the first of two revisions and 4 1/2 months before publication of the article.

* * *

Lack of inclusion of the three events resulted in an understatement of the difference in risk of myocardial infarction between the rofecoxib and naproxen groups (presented in the article as a reduction in the risk with naproxen but shown here as an increase in the risk with rofecoxib). It also resulted in the misleading conclusion that there was a difference in the risk of myocardial infarction between the aspirin indicated and aspirin not indicated groups.

Plaintiff's expert, Dr. Topol,[FN9] criticized the VIGOR article for advocating the "naproxen hypothesis" in the absence of data from any other study to support it, let alone to show that its effect was strong enough to account for the entire differential in cardiovascular event rates; particularly, since aspirin was known to cause only a twenty-five percent reduction in heart attacks. He testified that naproxen had been available for twenty years, and if a cardioprotective effect existed, it should have been noted. Additionally, Dr. Topol observed that the VIGOR study had been conducted on patients with rheumatoid arthritis, but without heart disease. He speculated that the thrombotic effects could be worse in an undifferentiated population suffering from osteoarthritis. Dr. Topol further criticized the authors of the published VIGOR ***34** study for their failure to include a chart, provided to the FDA, that showed the divergence between Vioxx and naproxen in terms of heart attacks and serious thrombolic events commencing at four to six weeks.

FN9. Dr. Topol's deposition was played to the jury. At the time of the deposition, the doctor was Provost of the Cleveland Clinic Lerner College of Medicine, Chief Academic Officer of the Cleveland Clinic, and Chair of the Department of Cardiovascular Medicine of the Cleveland Clinic. He is an outspoken critic of the conduct of Merck and the FDA in connection with Vioxx whose criticisms have been published in journals including the Journal of the American Medical Association.

Additionally, Dr. Topol noted that an excess of serious cardiovascular events was found in two other studies comparing Vioxx with NSAIDs: Protocol 090, which used a low dose (12.5 mg) of Vioxx for only six weeks on osteoarthritis patients and ADVANTAGE,[FN10] which was a twelve-week trial using a 25-mg dose of Vioxx in comparison to a 1,000 mg naproxen dose in osteoarthritis patients. Dr. Topol also cited a 2004 study by Peter Juni that demonstrated that a progressive meta-analysis of the combined patient populations of the VIGOR and the 090 study would have disclosed a statistically significant cardiovascular risk for Vioxx earlier than Merck recognized.

FN10. *A*ssessment of *D*ifferences Between *V*ioxx *A*nd *N*aproxen *T*o *A* scertain *G* astrointestinal Tolerability and *E*ffectiveness.

Plaintiff's expert, Dr. Krumholz, a cardiologist, epidemiologist, and a member of the faculty of the Yale Medical School, provided similar testimony, concluding that Merck should have responded to the VIGOR findings by adding a cardiovascular safety warning to the label, even though the VIGOR results were not definitive, because the five-fold difference between****238** Vioxx and naproxen in the rate of heart attacks was "important and consequential" to the decision whether or not to take Vioxx. Additionally, Dr. Krumholz noted that in the ADVANTAGE study, where low dose aspirin was permitted, an excess of myocardial infarctions and sudden deaths, likely from myocardial infarctions, still appeared among patients taking Vioxx. Because aspirin was at least as cardioprotective as naproxen, these results undermined the theory that VIGOR's results were attributable to naproxen's effects.

On November 23, 2000, Merck issued a news release regarding the New England Journal of Medicine article on the VIGOR study, which led with the statement: "In a study of Vioxx published***35** in *The New England Journal of Medicine*, Vioxx significantly reduced the risk of serious gastrointestinal side effects by half compared to naproxen." The cardiovascular results of the VIGOR study were reported on page three of the news release, which again noted that "significantly fewer heart attacks were seen in patients taking naproxen" and attributed the lowered incidence to naproxen's cardioprotective effect, which was claimed to be "similar to low-dose aspirin." It was noted that "[p]atients taking low-dose aspirin did not participate in VIGOR."

On December 8, 2000, FDA medical officer, Dr. Shari Targum, issued her medical review of the cardiovascular safety of Vioxx based upon VIGOR, two other protocols,[FN11] clinical trial data and prior FDA reviews. She concluded with respect to VIGOR that "there is an increased risk of cardiovascular thrombotic events, particularly myocardial infarction, in the rofecoxib group compared with the naproxen group." However, she observed that "[m]ore difficult is the question of a safety signal for rofecoxib" because of the absence of a placebo group. Although she noted that Merck had claimed that the difference in myocardial infarctions between the Vioxx and naproxen groups was primarily the result of the antiplatelet effects of naproxen, "[t]his hypothesis is not supported by any prospective placebo-controlled trials with naproxen. One can further argue that, no matter what the attribution, the results (from a cardiovascular standpoint) are favorable for naproxen." Dr. Targum rejected Merck's claims that the majority of the cardiovascular

events in the VIGOR study occurred in those patients who should have been on aspirin, finding that "[t]he VIGOR data are consistent (i.e., increased events in the rofecoxib group) even in patients who did not fall into the 'aspirin-indicated'***36** subgroup." She dismissed the theory that the results occurred because patients with rheumatoid arthritis were at an increased risk for cardiovascular events stating that, "one is *still* faced with the difference in cardiovascular events between rofecoxib and naproxen." She observed that, given that premise, "could one not extend this argument to any patient at increased risk of cardiovascular events?" Finally, Dr. Targum rejected results of other studies involving osteoarthritis and Alzheimers disease patients because the dose of Vioxx and length of exposure had not been stated, and the cardiovascular events were not adjudicated.

> FN11. (1) Study 085, a randomized placebo-controlled study to evaluate the efficacy and safety of low-dose (12.5 mg) Vioxx against the NSAID nabumetone in patients with osteoarthritis of the knee, with use of low-dose aspirin permitted and (2) Study 090, a similar study that disclosed numerically more myocardial infarctions in the Vioxx group compared with nabumetone and placebo, as well as more cardiovascular adverse experiences and discontinuances due to cardiovascular adverse experiences in the Vioxx group.

****239** On December 28, 2000, the FDA asked Merck for a cardiovascular meta-analysis of studies lasting six months or longer that compared Vioxx to placebo, naproxen and other NSAIDs and with separate treatment of Vioxx at 12.5 mg, 25 mg, and 50 mg. It also sought a meta-analysis of the "composite of all active NJSAID comparators" for the most serious cardiothrombic events. A response was provided on January 8, 2001, which concluded that the risk of sustaining a thrombotic cardiovascular event was similar in patients treated with rofecoxib, placebo and non-naproxen non-selective NSAIDs that lack potent inhibition of platelet function. The risk of sustaining a thrombotic cardiovascular event was reduced in patients treated with naproxen as compared to Vioxx. However, Merck again attributed the reduction with naproxen as "likely due to its ability to maintain near maximal inhibition of platelet function throughout its dosing interval." Significantly, the incidence of heart attacks was elevated both when compared to naproxen and to other non-selective NSAIDs, but that fact was not discussed by Merck.

F. *Revised Labeling*

Over the next sixteen months, various events occurred of relevance to the labeling that Merck had proposed. In early February 2001, the Arthritis Advisory Committee convened by the FDA met to discuss, on succeeding days, the VIGOR trials with Vioxx ***37** and the CLASS trials with Celebrex. On January 31, 2001, just prior to the Committee's meeting with Merck's representatives on February 8, Dr. Scolnick e-mailed Gilmartin and Anstice, stating in part:

> On Monday, I will show you the essence, an update, of the data that supports Vioxx is safe in the CV sense. But I want to point out to all of you at one time that 1. there is no way to prove that in patients with rheumatoid arthritis that ALL of the difference between Vioxx and naproxen is due to the benefit of naproxen. IT IS IMPOSSIBLE TO PROVE THIS; IT IS IMPOSSIBLE TO KNOW THIS WITH CERTAINTY. It is likely if not certain that our label will state the data from VIGOR. It is even likely that words will be used to say that it is not clear if the effect is purely d[ue] to a protective effect of naproxen in this RA [rheumatoid arthritis] patient population. When the study results came out last year, this fact was patently clear. Since then we have reduced the uncertainty to this very salient point. But it is impossible to dismiss the point. The FDA will NEVER allow it to be fully dismissed. Ther [e] will be great adverse publicity at the meeting.... In any case, we need to face the reality of the situation and manage it. Knowing what is about to happen, managing the short term fall out, and facing and managing any longer term consequences.

However, in a February 5, 2001 e-mail to Dr. Reicin and others who would be presenting Merck's position to the FDA, Dr. Scolnick expressed relief about the results, stating: "We all worried to death about the CV events last Spring. Merck is of course always an issue. But I was sick at the thought we might be doing harm to patients.... With all the data now available I am no longer worried." And after the meeting, Dr. Scolnick sent his congratulations, stating: "I bit my nails all day. You were FANTASTIC. You made them look like grade d high school students and you won big huge and completely."

After hearing presentations from Merck representatives, including Dr. Reicin, the advisory committee recommended the inclusion of the VIGOR data, including its cardiovascular component, on the label. It thought the fact that Vioxx was not an ****240** inhibitor of platelet clumping should be highlighted, and it suggested further research on the cause of the adverse thromboembolic findings, the significance of which was unclear.

On February 8, Merck issued a press release about the advisory committee meeting declaring its belief that the data presented at ***38** the meeting "support the excellent safety profile of Vioxx." It then collectively referred to the pre-approval clinical trials and the ongoing Alzheimer's and ADVANTAGE trials as "clinical trials with Vioxx [at] 12.5 mg, 25 mg and 50 mg in 30,000 patients," and declared that they exhibited "no difference in the incidence of CV events, such as heart attacks, among patients taking Vioxx, other NSAIDs and placebo."

On the following day, Merck sent a bulletin for Vioxx regarding the advisory committee meeting to all sales personnel with responsibility for Vioxx that commenced:

> DO NOT INITIATE DISCUSSIONS ON THE FDA ARTHRITIS ADVISORY COMMITTEE (ADVISORY COMMITTEE) REVIEW OR THE RESULTS OF THE Vioxx® GI OUTCOMES RESEARCH (VIGOR) STUDY. YOU MAY RESPOND TO CUSTOMER INQUIRIES ONLY AS OUTLINED BELOW.

The bulletin then instructed sales personnel to "Stay Focused On Efficacy" and, in its summary conclusion stated: "*Do not proactively discuss the Advisory Committee Meeting or VIGOR.*[FN12] Respond to questions about the study by requesting a PIR [physician information report] and in accordance with the obstacle-handling guide." Physician inquiry twenty-three on the "Obstacle Response Guide" was "I am concerned about the cardiovascular effects of Vioxx." If the inquiry was specific to heart attacks, the sales person was instructed to state:

> FN12. Anstice testified that the sales people were not permitted to discuss VIGOR because its results were not set forth on Vioxx's label.

> Doctor, once daily Vioxx has no effect on platelet aggregation, and therefore would not be expected to demonstrate reductions in MI or other CV events. Agents such as low-dose aspirin are routinely prescribed for CV patients for their effect on the inhibition of platelet aggregation. Therefore, once daily Vioxx® is not a substitute for aspirin for cardiovascular prophylaxis.
> After assuring the physician that Vioxx and aspirin could be taken together, the sales person was instructed to transition back to the positive messages for the drug. If probed further by the physician, the sales person was instructed to offer to submit a physician information request.

***39** An updated proposed label was sent by Merck to the FDA in March 2001 that placed the cardiovascular results of the VIGOR study in a "precautions" section, rather than in a more prominent and more significant "warnings" section. In July 2001, Merck predicted that Vioxx sales for 2002 would be approximately $1.6 to $2.1 billion. Another July long-range planning document projected that Vioxx sales would peak in 2003 before declining, and it stated that if the upcoming cardiovascular labeling were "milder; no prothrombic language," an "upside" estimate of a 25% increase over projected sales for 2006 over baseline projections could be expected; that the "base" earnings assumed that cardiovascular effects would be detailed in the "precautions" section of the labels of all COX-2 inhibitors; and that if cardiovascular effects were placed in the "warnings" ****241** section, a 50% decrease in projected sales in 2006 would result.

On March 30, 2001, FDA reviewer Villalba issued a review of Vioxx, reporting that the VIGOR study had revealed a relative risk of developing serious CV/thrombotic events that was more than twice that in the Vioxx group as compared to the naproxen group, mainly because of the difference in the number of myocardial infarctions: 20 with Vioxx and 4 with naproxen. Significantly, she also observed that Merck's proposed theory of the cardioprotective effect of naproxen (58% decrease in the risk of serious CV thrombotic events over a nine-month period) "exceeds that reported in the literature for an anti-platelet agent in a primary or secondary prevention setting." She additionally noted that Merck had completed a twelve-week, 5,500 patient safety study known as ADVANTAGE comparing 25 mg Vioxx with 500 mg naproxen twice daily in a population that did not exclude the use of low-dose aspirin. Although the study had been completed in March 2000, it had not been submitted to the FDA for review, but had been requested. Villalba was interested in determining whether the ADVANTAGE study, which had permitted the use of low-dose aspirin, similarly disclosed a higher cardiovascular risk from use of Vioxx.

***40** An April 6, 2001 letter from the FDA, stating that Merck's supplemental new drug application was "approvable," but requiring the ADVANTAGE data and a safety update report, was met with dismay by Dr. Scolnick, who feared that "our competitor would get a better label now, while Merck was required to provide additional data." In an e-mail dated April 5, 2001, he stated:

> I am going in 2 weeks to an FDA Science Board I am on and I have been asked to give a talk on how they can keep their scientists up to date. I have already told them I think their review system is an anachronism because they cannot possibly keep up with science given their hiring constraints. I will be making quite radical suggestions. They have said they will allow me to speak on them.

Dr. Scolnick stated further that, if necessary, he would go to contacts he had made in the Department of Health and Human Services, regarding the labeling situation. In an e-mail of April 9, Dr. Scolnick stated:

> I think giving them Advantage was not wise. The Alzheimer's data vs placebo is helpful. Advantage is not, numbers are too small. They will data dredge as they did on original submission and we will end up with bad labeling. If they are data dredging Advantage I would argue for giving them the safety data in Alzheimer's since it is much more supportive.

On May 22, 2001, the New York Times published an article on the first page of its business section, captioned "Doubts Are Raised on the Safety of 2 Popular Arthritis Drugs," that noted the higher risk of heart attacks among users of Vioxx revealed by the VIGOR study. A May 2001 "Dear Doctor" letter, sent by Merck in response, stressed the safety of the drug, as did a widely-used "CV Card" utilized to overcome what Merck characterized as the "cardiovascular obstacle," that did not include the VIGOR data. Sales personnel were instructed not to leave the CV Card with physicians, but merely to show it to them. Additionally, a "Dodge Ball Vioxx" documents instructed sales representatives how to "dodge" obstacles that included questions about Vioxx's risk for edema, hypertension, and myocardial infarction by use of Merck's "obstacle handler."

An August 28, 2001 form letter, sent by Merck in response to a physician's request ****242** for safety information, stated that the cardiovascular event rate was 0.4 or 0.5% depending on the reporting ***41** date. However, at trial, Anstice admitted that this figure related only to heart attacks, and that the cardiovascular event rate, including hypertension and other conditions, was 14.6%, and that the 0.4-0.5% figure was "inaccurate."

On August 22, 2001, the Journal of the American Medical Association published a "special communication" authored by Drs. Debabrata Mukherjee and Steven Nissen, both members of the FDA's Arthritis Steering Committee, and by Dr. Topol,[FN13] that evaluated Merck's VIGOR study and Pfizer's CLASS study involving Celebrex, concluding that "[t]he available data raise a cautionary flag about the risk of cardiovascular events with COX-2 inhibitors." The authors continued: "Given the remarkable exposure and popularity of this new class of medications, we believe that it is mandatory to conduct a trial specifically assessing cardiovascular risk and benefit of these agents. Until then, we urge caution in prescribing these agents to patients at risk for cardiovascular morbidity." Shortly after the publication of this article, Merck responded with an August 2001 "Dear Doctor" letter that criticized the data utilized by the article's authors and stated that Merck stood behind the overall and cardiovascular safety profile of Vioxx.

> FN13. Debabrata Mukherjee et al., *Risk of Cardio-vascular Events Associated with Selective COX-2 Inhibitors,* 286 *JAMA* 954 (2001).

Also in August 2001, FitzGerald published an study in the New England Journal of Medicine [FN14] in which he speculated on the cause of the elevated incidence of major cardiovascular events with the use of Vioxx in the VIGOR trials and the dissimilar results obtained in the CLASS trial and ***42** urged additional research in this area. Significantly, FitzGerald stated that: "There is no convincing evidence from epidemiologic studies that NSAIDs, including naproxen, protect against cardiovascular events." FitzGerald urged additional research on the cardiovascular effects of the COX-2 inhibitors.

> FN14. Garret A. FitzGerald & Carlo Patrono, *The Coxibs, Selective Inhibitors of Cyclooxygenase-2,* 345 *New Eng. J. Med.* 433 (2001).

The need for further study was echoed by Dr. Scolnick in a September 13, 2001 memo that stated, in relevant part,

> [Merck Research Laboratories] has just completed its annual planning meeting. As most of you know we reviewed strategy for each franchise.... I want to give you a list of the only studies that I regard as ESSENTIAL. Essential means just that ESSENTIAL. Not preferred, not useful, not helpful; ESSENTIAL....
>
> 1. For Vioxx: Only the CV outcome study ONLY ESSENTIAL STUDY!
>
> [Spelling and punctuation modified.]

While Dr. Scolnick was urging more research, on September 13, 2001, Anstice sent a voice-mail message to Merck's sales force, in response to complaints, that reminded the sales persons that they had received a "cardiovascular letter" and press release in response to the negative article in the New York Times, published in May, and similar material in response to the negative article in the Journal of the American Medical Association, published in August. The voice mail continued:

> I can understand why people are confused about the results of VIGOR that showed differences in heart attacks of .1 versus .5 if they don't understand the data. I can even understand why doctors, why Wall Street, why maybe even lawyers might be confused. To understand****243** VIGOR you must understand Naproxen is cardioprotective.

However, four days later, on September 17, 2001, Merck received a warning letter from the FDA that stated, on the basis of its review of promotional audio conferences given on Merck's behalf by a named physician, a press release, and oral representations

made by Merck sales representatives to promote Vioxx, the FDA had concluded that Merck's promotional activities and materials were "false, lacking in fair balance, or otherwise misleading in violation of the Federal Food, Drug, and Cosmetic Act (the Act) and applicable regulations. *See* 21 U.S.C. §§ 331(a) and (b), 352(a),(f), and (n), and 355(a)." Specifically, the letter stated:

> You have engaged in a promotional campaign for Vioxx that minimizes the potentially serious cardiovascular findings that were observed in the Vioxx Gastrointestinal Outcomes Research (VIGOR) study, and thus, misrepresents the safety profile for Vioxx. Specifically, your promotional campaign discounts the fact that in the VIGOR study, patients on Vioxx were observed to have a four to five ***43** fold increase in myocardial infarctions (MIs) compared to patients on the comparator non-steroidal anti-inflammatory drug (NSAID), Naprosyn (naproxen).
>
> Although the exact reason for the increased rate of MIs observed in the Vioxx treatment group is unknown, your promotional campaign selectively presents the following hypothetical explanation for the observed increase in MIs. You assert that Vioxx does not increase the risk of MIs and that the VIGOR finding is consistent with naproxen's ability to block platelet aggregation like aspirin. That is a possible explanation, but you fail to disclose that your explanation is hypothetical, has not been demonstrated by substantial evidence, and that there is another reasonable explanation, that Vioxx may have pro-thrombotic properties.
>
> * * *
>
> Your minimizing these potential risks and misrepresenting the safety profile for Vioxx raise significant public health and safety concerns. Your misrepresentation of the safety profile for Vioxx is particularly troublesome because we have previously, in an untitled letter, objected to promotional materials for Vioxx that also misrepresented Vioxx's safety profile.
> The FDA required Merck to cease all violative promotional activity and to provide a detailed response by October 1, 2001, including a "Dear Healthcare Provider" letter to correct false or misleading impressions and information. [FN15]

> FN15. Anstice responded by stating that the FDA had mistakenly focused on VIGOR, not on a review of all available data which disclosed no significant risks for Vioxx when compared to a placebo. Anstice further stated that Merck's agreement with the offending speaker had been terminated, and he explained Merck's press releases as an appropriate response to "media and analyst activity." He sought to defer the "Dear Healthcare Provider" letter until labeling was finalized.

Merck reacted to the warning letter by providing, on October 1, 2001, further, superseding directions to its sales persons with respect to VIGOR, with the instruction that "[y]ou may not discuss or respond to any questions about VIGOR, except as *specifically* set forth in this Bulletin." The document then stated that if asked about Merck's GI safety study, the results of its rheumatoid arthritis study, or why Vioxx had a higher rate of heart attacks than naproxen, the sales person should identify the VIGOR ****244** study, refuse to discuss its details "[b]ecause the study is not in the label" and to offer to refer the question to Merck's Medical Services department. The instructions continued: "if you are ***44** asked any other questions about VIGOR by a health care professional or a customer, you may not answer the question. You may respond to unsolicited questions only by offering to submit a [physician information request]." If asked about the FDA's warning letter, sales persons were instructed to respond, only: "The Warning Letter is from FDA's Advertising Division and relates to Vioxx. We are responding to FDA. Merck continues to stand behind the overall and cardiovascular safety of Vioxx."

Minutes of an FDA regulatory briefing meeting held on September 21, 2001 disclose Villalba's conclusion that in VIGOR, "there was no overall safety advantage for rofecoxib when compared to naproxen," and that "[f]indings in ADVANTAGE, RA safety database and Alzheimer's studies were not inconsistent with findings in VIGOR." The minutes also reflect the recommendation that "FDA should strengthen the WARNINGS section of Vioxx, and deemphasize the safety advantage information in the label. Naproxen should be used as a comparison in the label."

On October 15, 2001, the FDA sent Merck a draft label for Vioxx. In the "Warnings" section of the label, the FDA proposed:

> Cardiovascular Disease
>
> VIOXX should be used with caution in patients at risk of developing cardiovascular thrombotic events such as those with a history of myocardial infarction and angina and in patients with pre-existent hypertension and congestive heart failure.
>
> The risk of developing myocardial infarction in the VIGOR study was five-fold higher in patients treated with VIOXX 50-mg (0.5%) as compared to patients treated with naproxen (0.1%) (See Special studies, VIGOR). The finding was consistent in a smaller and shorter study using VIOXX 25 mg that allowed the use of low dose ASA [aspirin] (See Special Studies, ADVANTAGE). Prospective, well-powered, long term studies required to compare the incidence of serious CV events in patients taking VIOXX versus NSAID comparators other than naproxen have not been performed.

Because of its lack of platelet effect, VIOXX is not a substitute for aspirin for cardiovascular prophylaxis. The impact of VIOXX on the cardiovascular prophylactic benefit of ASA is unknown. (See special studies, Platelets: PRECAUTIONS, Drug Interactions, Aspirin).

In an October 15, 2001 e-mail sent upon receipt of the FDA's proposed label, Merck's Dr. Scolnick stated to Anstice:

***45** David. Be assured we will not accept this label. If we need to we will ask to go to an advisory committee meeting.

Anstice replied:
... We knew it would be UGLY and it is. We'll fight back and see where we get. I agree that we should ask for an advisory committee if necessary.

To which Scolnick responded:
It is ugly cubed. thye [sic] are bastards.

Merck proposed relocation of the FDA's text to the Precautions section of the label, and to modify the text to de-emphasize the risk of Vioxx by stating as follows:

Cardiovascular Effects

The following data should be taken into consideration when prescribing VIOXX in patients at risk of developing cardiovascular thrombotic events.

****245** The risk of developing a serious cardiovascular thrombotic event in the VIOXX study was significantly different in patients treated with VIOXX 50 mg once daily as compared to patients treated with naproxen 500 mg twice daily. This was largely due to the significant difference in the incidence of myocardial infarction between patients taking VIOXX 50 mg once daily (0.5%) and naproxen 500 mg twice daily (0.1%). (See CLINICAL STUDIES, Special Studies, VIGOR). In other controlled clinical trials, the incidence of all serious cardiovascular thrombotic events, including myocardial infarction, was similar between VIOXX, nonselective NSAID comparators (ibuprofen, diclofenac and nabumetone) and placebo. Prospective, well powered, long term studies specifically designed to compare the incidence of serious CV events in patients taking VIOXX versus NSAID comparators have not been performed.

Because of its lack of platelet effects, VIOXX is not a substitute for aspirin for cardiovascular prophylaxis [sentence will appear bold?] (See CLINICAL STUDIES, Special Studies, Platelets and PRECAUTIONS, Drug Interactions, Aspirin).

On November 28, 2001, FDA reviewer Villalba provided an analysis of Merck's response to the FDA's approvable letter, issued on April 7, 2001, which required that Merck submit data from the ADVANTAGE study-a twelve-week comparison of Vioxx, taken at 25 mg per day, with naproxen, taken at 500 mg twice per day in 5,400 patients with osteoarthritis-a Safety Update Report on the long-term follow up of patients in Merck's original osteoarthritis program, and safety data from studies not previously submitted to the FDA. The summary of clinical findings relating to safety was not favorable to Merck. Dr. Villalba divided her analysis into three categories: (1) findings that applied to ***46** ADVANTAGE and the VIGOR databases; (2) cardiovascular safety of Vioxx compared to NSAIDs other that naproxen; and (3) cardiovascular safety of Vioxx compared to placebo. With respect to the first category, the doctor found that Vioxx at 25 and 50 mg doses showed no overall safety advantage over naproxen as measured by total deaths, serious adverse events, hospitalizations, or discontinuations due to adverse events and common adverse events; that Vioxx was associated with a nominally higher incidence of discontinuations due to hypertension, edema and congestive heart failure-related events; and it was associated with a nominally higher cardiovascular thrombotic risk, particularly heart attacks. The doctor found no adequate long-term data comparing the cardiovascular risk of Vioxx to traditional NSAIDs other than naproxen. Finally, she found that existing studies did not provide adequate evidence that Vioxx has a cardiovascular safety profile similar to placebo. In that connection, she reported that the Alzheimer's studies disclosed a higher incidence of cardiovascular thrombotic deaths with Vioxx that with placebo (nine vs. four), and also noted that "although this was an elderly population (mean age 75 years), patients at high cardiovascular risk were not enrolled." Additionally, the doctor found the trend of excess serious cardiac thrombotic events in the ADVANTAGE study and discontinuances resulting from such events was consistent with VIGOR and "of concern" because ADVANTAGE was only a twelve-week study, used a lower dose of Vioxx, and permitted the use of aspirin for cardiovascular prophylaxis.

On January 12, 2002, Dr. Wayne Ray, a professor of preventive medicine, published an article describing his observational and

retrospective analysis of Tennessee ****246** Medicaid patients for the years 1987 to 1998, before the widespread use of COX-2 inhibitors.[FN16] In the article, he identified the patients who had been taking only aspirin and those who had been taking a non-aspirin ***47** NSAID. He found no indication that naproxen had a cardioprotective effect.

> FN16. Wayne A. Ray et al., *Non-steroidal Anti-inflammatory Drugs and Risk of Serious Coronary Heart Disease: An Observational Cohort Study*, 359 *Lancet* 118 (2002).

While approval of a new label remained pending, Merck was negotiating an agreement with Brigham and Women's Hospital in Boston to perform the cardiovascular risk study urged by Dr. Scolnick, entitling it "A Randomized, Double Blind, Parallel, Placebo-Controlled Trial to Evaluate the Cardiovascular Safety and Efficacy of Rofecoxib on Cardiovascular Events in Patients with Recent Acute Coronary Syndromes"-(VALOR)." By February 13, 2002, a letter of intent was sent by Dr. Alan Nies, Senior Vice-President for Clinical Sciences at Merck Research Laboratories to the Harvard Medical School with respect to the study. Despite Dr. Scolnick's urging, the study was never performed.

The revised label for Vioxx was approved on April 11, 2002, two years after the results of the VIGOR study were known, and a "Dear Doctor" letter substantially incorporating the information set forth in the label was circulated by Merck that same month. A review of the label demonstrates that Merck successfully obtained the FDA's consent to use of a revised label that contained no mention of cardiovascular risks in the "Warnings" section, but instead, contained a "Precaution" that limited use of Vioxx only among patients "with a medical history of ischemic heart disease"-patients whose already-diagnosed coronary artery disease was symptomatic. However, the label set forth the results of the VIGOR trials in detail, and it stated that "the risk of developing a serious cardiovascular thrombolic event was significantly higher in patients treated with Vioxx 50 mg once daily (n=45) as compared to patients treated with naproxen 500 mg twice daily (n=19)." It did not express the results in terms of a lower incidence among those taking naproxen, and it did not contain Merck's thesis that naproxen was cardioprotective. Instead, the "Precautions" section stated:

> The significance of the cardiovascular findings from these 3 studies (VIGOR and two placebo-controlled studies) is unknown. Prospective studies specifically designed to compare the incidence of serious CV events in patients taking Vioxx versus NSAID comparators or placebo have not been performed.

***48** Because of the lack of platelet effects, Vioxx is not a substitute for aspirin for cardiovascular prophylaxis.

G. *Product Withdrawal*

Following approval of the revised label, Vioxx continued to be marketed until September 30, 2004, when evidence of adverse cardiovascular events resulting from Merck's APPROVe study [FN17] led to the voluntary****247** withdrawal of the drug from the market. During the period between FDA approval of a revised label for Vioxx in April 2002 and Merck's withdrawal of the product, scientists, including Merck's Dr. Reicin, published, in October 2003, a meta-analysis of the clinical trials, VIGOR, and the Alzheimer's trials, [FN18] concluding that "rofecoxib was not associated with excess CV thrombotic events compared with either placebo or non-naproxen NSAIDs. Again, naproxen appeared to be the outlier, suggesting a cardioprotective benefit of naproxen." The authors concluded additionally that "among the predominantly elderly, male population participating in Alzheimer trials, both ***49** rofecoxib-and placebo-treated patients had similar rates of CV thrombotic events. The totality of data is not consistent with an increased CV risk among patients taking rofecoxib."

> FN17. The APPROVe study (Adenomatous Polyp Prevention on Vioxx), for which patient enrollment commenced in February 2000, was proposed as a three-year trial of Vioxx at 25 mg against placebo in patients with a history of colorectal adenomas or polyps. The primary endpoint was whether Vioxx could match aspirin's known effectiveness in reducing the recurrence of polyps while maintaining GI safety. It was also designed to assess CV safety prospectively. The study excluded patients who were expected to need long-term NSAID therapy, those who had experienced significant cardiovascular events or conditions during the preceding year, or a stroke or transient ischemic attack during the preceding two years. The study was initially reported as Robert S. Bresalier et al., *Cardiovascular Events Associated with Rofecoxib in a Colorectal Adenoma Chemoprevention Trial,* 352 *New Eng. J. Med.* 1092 (2005). The article stated that the relative risk of a confirmed thrombotic event with Vioxx was 1.92, and the difference between Vioxx and placebo was primarily due to an increase in myocardial infarctions and strokes. In a correction printed on July 13, 2006, statements that the increased relative risk became apparent after eighteen months of treatment and that the event rates were similar between groups in the first eighteen months were deleted. *Correction,* 355 *New Eng. J. Med.* 2.

> FN18. Matthew R. Weir, Rhoda S. Sperling, Alise Reicin, & Barry J. Gertz, *Selective COX-2 Inhibition and Cardiovascular Effects: A Review of the Rofecoxib Development Program,* 146 *Am. Heart J.* 591 (2003).

However, in an editorial published in *The Lancet* in August 2004, [FN19] Dr. Topol commented on a study demonstrating the small protective effect of naproxen (less than half that of aspirin) and concluded as a result that the continued commercial availability of Vioxx without a black-box warning was "indeed troubling."

FN19. Eric J. Topol and Gary W. Falk, *A Coxib a Day Won't Keep the Doctor Away*, 364 *Lancet* 639 (2004).

Additionally, in an article published in *The Lancet* in November 2004, [FN20] Peter Juni and his co-authors demonstrated how the cardiovascular risk of Vioxx could have been discovered earlier by appropriate cumulative statistical meta-analysis. The article concluded:

FN20. Peter Juni et al., *Risk of Cardiovascular Events and Rofecoxib: Cumulative Meta-analysis*, 364 *Lancet* 2021 (2004).

> Our cumulative meta-analysis of randomised controlled trials indicates that an increased risk of myocardial infarction was evident from 2000 onwards. At the end of 2000, the effect was both substantial and unlikely to be a chance finding.
>
> We found an increased risk of myocardial infarction in trials of both short and long duration, which is in contrast to the unpublished results from the APPROVe trial. Our findings thus indicate that patients are at risk even if rofecoxib is taken for a few months only. Therefore, the reassuring statement by Merck, that there is no excess risk in the first 18 months, is not supported by our data. Similarly, we recorded no evidence to support the notion that rofecoxib's cardiovascular toxicity is dose-dependent.
>
> [Footnotes omitted.]
>
> Additionally, the authors challenged the naproxen hypothesis, concluding:
> The possible cardioprotective effect of naproxen has also been examined in several observational, pharmaco-epidemiological studies. Taken together, the data from these studies indicate that if a protective effect of naproxen exists, it is ****248** probably small, and, as pointed out earlier, not large enough to explain the findings of VIGOR.
>
> [Footnotes omitted.]

***50** Although the Juni study was severely challenged by Merck at trial, plaintiffs' expert, Dr. Krumholz, spoke approvingly of the article and stated that the authors had used proper statistical techniques in reaching their conclusions, which were consistent with the FitzGerald hypothesis.

II.

Plaintiffs John McDarby and Thomas Cona both took Vioxx for osteoarthritic pain commencing prior to the FDA's approval of Merck's revised label in April 2002.

McDarby [FN21] sustained a heart attack and fractured hip on April 15, 2004 at the age of 75. He was prescribed Vioxx by his family physician, Dr. John Braun, on March 21, 2000, as treatment for osteoarthritis in the hands and knee, and he took it daily until his heart attack on April 15, 2004. Prior to 2000, McDarby had not heard of Vioxx; thereafter, he saw a number of Merck's commercials for the product on television, which solidified his thinking that Vioxx was a "good prescription." McDarby read the drug's package insert at the time of his first purchase, but could recall none of the contents, and did not read the insert thereafter, relying on his physician to determine whether it was safe. McDarby testified that he would not have taken the drug if he had been told it could cause heart attacks. At the time of his treatment by Dr. Braun, McDarby was a diabetic whose condition was controlled by oral medicine. He had sustained a brief loss of vision that might have resulted from a transitory ischemic attack, and therefore took low-dose aspirin. However, the amount of plaque in his carotid arteries was found to be normal. Additionally, McDarby was "slightly" overweight. Dr. Braun found that he did not suffer from hypertension.

FN21. We do not discuss Cona's medical history, since the jury did not accept his claim of physical injury as the result of taking Vioxx.

Dr. Braun's videotaped deposition testimony was played for the jury. In it, he confirmed that he had treated McDarby in the ***51** period from September 9, 1998 to November 18, 2003, and that he had prescribed Vioxx at a 25 mg dose as McDarby had stated. The doctor testified that as a matter of practice, he reads the entire package insert for a drug before prescribing it for the first time "so I know what to expect from a drug and who I can use it in, who I can't use it in, if it's contraindicated in a certain patient population, if it's going to cause risk factors in patients with renal insufficiency or heart disease or whatever, to get a better understanding of the drug

and its ... side effects." He also discussed Vioxx with Merck's sales representatives, who visited his office at least twice a week. As one sales representative acknowledged, the doctor was targeted because of the high volume of his prescriptions for pain relievers. Dr. Braun was familiar with the VIGOR study CV results, but he testified that he was told that they were attributable to naproxen's cardioprotective effects, and that representatives assured him that Vioxx was safe for patients with CV risks so long as they continued to take aspirin. On three to four occasions after the VIGOR results became known, Dr. Braun was also shown Merck's "CV Card," entitled "Chemical Profile, Osteoarthritis Studies" that indicated no elevated risk of heart attack and, according to Dr. Braun, showed Vioxx to be safer than a ****249** placebo. Additionally, Dr. Braun testified to having received and relied upon Merck's May 2001 "Dear Doctor" letter that referred to media reports regarding the safety profile of Vioxx and "place[d] the information in the news reports in context by setting forth the results of Merck's osteoarthritis studies as also summarized on the CV Card." Dr. Braun testified that he understood the letter as "reaffirm[ing] that the drug was safe."

Although the doctor testified additionally that he had read Dr. Topol's article in the Journal of the American Medical Association, which indicated that VIGOR's CV results theoretically could be attributed to the prothrombic effect of Vioxx, the antithrombic effect of naproxen, or both, he understood the article to be suggesting the need for additional studies, not that use of Vioxx be suspended. Additionally, he was reassured by Merck's statements in an August 2001 "Dear Doctor" letter that was critical of the ***52** Topol data and stated that Merck stood by the cardiovascular safety profile of its drug. Although Dr. Braun understood that Vioxx was not cardioprotective, he testified that he was never told by a Merck representative that use of Vioxx increased clotting risks.

Dr. Braun testified that if he had been informed of the cardiovascular risks of Vioxx, he would not have prescribed it to McDarby. In this connection, the following exchange occurred:

> Q. If you had been told by Merck that Vioxx could increase the risk of a heart attack, would you have prescribed Vioxx to Mr. McDarby?
>
> THE WITNESS: Of course not.
>
> Q. Why not?
>
> A. My ... job as a doctor is to try to prevent things from happening, try to prevent strokes, try to prevent heart attacks.
>
> He [McDarby] has one risk factor that we know of, which is diabetes. His second risk factor is being a male. And his third risk factor is being elderly for having heart disease. So why would I give him another risk factor? Why would I give him a thromboembolic drug, a drug that caused clots?
>
> That's not my job.

Dr. Braun testified further that, after the April 2002 revised label was issued, he understood Vioxx to be contraindicated in patients with ischemic heart disease, and he had in fact stopped prescribing the drug to a patient for whom the use was contraindicated. However, McDarby did not have that condition, and thus the prescription was continued.

III.

Merck has challenged the jury's verdict in favor of plaintiff McDarby on his product liability claim, arguing first that the trial judge failed to give proper effect to the PLA's presumption of adequacy for prescription drug warnings approved by the FDA and, second, that the Federal Food Drug and Cosmetic Act (FDCA), 21 *U.S.C.A.* §§ 301 to 399, preempts McDarby's claims challenging the adequacy of the FDA-approved Vioxx labels. McDarby responds (1) that state law imposes a duty upon manufacturers of prescription drugs to warn of the drug's dangers as soon as knowledge of those dangers exists; (2) that the trial judge ***53** properly applied the rebuttable presumption of warning adequacy contained in the PLA; and (3) that the judge was correct in her rulings and instructions that, as a matter of law, Merck had a duty to warn of the cardiovascular risks of Vioxx without seeking FDA approval. McDarby also argues that the PLA, as applicable to claims of inadequate warnings by pharmaceutical manufacturers,****250** is not preempted by the FDCA or by a 2006 preamble to revised federal prescription drug regulations containing preemptive language.

A. *Statutory Preemption*

We are satisfied that principles of preemption do not require dismissal of the McDarbys' action under the PLA. In reaching this conclusion, we are mindful of the decision by the United States Supreme Court in *Riegel v. Medtronic, Inc.*, 552 *U.S.* ----, 128 *S.Ct.* 999, 169 *L.Ed.*2d 892 (2008).[FN22] However, *Riegel* concerned the proper interpretation of an express preemption provision contained in the Medical Device Amendments of 1976 to the FDCA, set forth at 21 *U.S.C.A.* § 360k(a),[FN23] that is inapplicable to ***54** prescription drugs. Additionally, whereas in *Riegel*, the Court held that common-law claims challenging the safety and effectiveness

of the device at issue, a balloon catheter used in cardiovascular surgery, conflicted with premarket approval requirements under federal law, in the present case the McDarbys' challenge is consistent with, and indeed relies upon, FDCA regulations that, at the time, required labeling to be revised "to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved." 21 *C.F.R.* § 201.57(e) [FN24]; *see also* 21 *C.F.R.* § 314.70(c)(2)(i) [FN25] (permitting labeling changes to "add or strengthen a contraindication, warning, precaution, or adverse reaction"); U.S. Dep't of Health & Human Servs., FDA, Ctr. for Drug Evaluation & Research (CDER), *Guidance for Industry, Changes to an Approved NDA or ANDA* 24-25 (Nov. 1999) (referencing 21 *C.F.R.* § 314.70(c)(2)(i)). Thus, Merck's duty in this case, as found by the trial court, and its violation, as found by the jury, are premised upon a federal obligation, mirrored by state tort law, as expressed initially in *Feldman v. Lederle Labs. (Feldman I)*, 97 *N.J.* 429, 456, 479 *A.*2d 374 (1984) (requiring communication of a new warning based upon subsequently-acquired actual or constructive knowledge of danger ****251** "as soon as reasonably feasible"), and are not simply state-law constructs.

FN22. We recognize as well the affirmance by an equally-divided Court, in *Warner-Lambert Co. v. Kent*, 552 *U.S.* ----, 128 *S.Ct.* 1168, 170 *L.Ed.*2d 51 (2008), of the decision of the United States Court of Appeals for the Second Circuit in *Desiano v. Warner-Lambert & Co.*, 467 *F.*3d 85 (2d Cir.2006), *amended*, 2006 *U.S.App. LEXIS* 32377 (January 18, 2007) (recognizing a fraud-based exception to Michigan law immunizing pharmaceutical companies from products liability claims) and the pendency in the Supreme Court of an appeal from the decision of the Supreme Court of Vermont in *Levine v. Wyeth*, 944 *A.*2d 179 (Vt.2006), *cert. granted*, --- *U.S.* ----, 128 *S.Ct.* 1118, 169 *L.Ed.*2d 845 (2008) (affirming verdict against defendant Wyeth in a pharmaceutical failure-to-warn case, and finding no preemption by the FDCA). *See also Good v. Altria Group, Inc.*, 501 *F.*3d 29 (1st Cir.2007), *cert. granted*, --- *U.S.* ----, 128 *S.Ct.* 1119, 169 *L.Ed.*2d 846 (2008) (holding that state-law consumer fraud claims based on the marketing of "light" cigarettes were not preempted by the Federal Cigarette Labeling and Advertising Act).

FN23. It provides that "no State ... may establish or continue in effect with respect to a device intended for human use any requirement (1) which is different from, or in addition to, any requirement applicable under this chapter to the device, and (2) which relates to the safety or effectiveness of the device or to any other matter included in a requirement applicable to the device under this chapter."

FN24. The regulation presently provides that "labeling must be revised to include a warning about a clinically significant hazard as soon as there is reasonable evidence of a causal association with a drug; a causal relationship need not have been definitely established". 21 *C.F.R.* § 201.57(c)(6).

FN25. Presently, 21 *C.F.R.* § 314.70(c)(6)(iii)(A).

[1] Existing New Jersey precedent clearly supports the conclusion that the FDCA does not preempt state-law tort remedies under theories of express conflict or implied preemption in this duty-to-warn context. *See* ***55***Feldman v. Lederle Labs. (Feldman II)*, 125 *N.J.* 117, 133-56, 592 *A.*2d 1176 (1991), *cert. denied*, 505 *U.S.* 1219, 112 *S.Ct.* 3027, 120 *L.Ed.*2d 898 (1992); *see also Feldman I, supra*, 97 *N.J.* at 459-61, 479 *A.*2d 374. Indeed, in *Feldman II*, the Court specifically noted that, as the result of the adoption of the federal regulations now contained in 21 *C.F.R.* § 201.57(c)(6), requiring that labeling be revised to include a warning about "a clinically significant hazard as soon as there is reasonable evidence of a causal association with a drug," regardless of whether a causal relationship had been proven, the defendant, Lederle, was not faced with "the Hobson's choice of either complying with federal regulations and continuing to be subject to damages in state tort actions or providing additional warnings and thereby violating federal law." 125 *N.J.* at 153, 592 *A.*2d 1176. Moreover, the Court recognized that granting immunity to a drug manufacturer from liability in this circumstance would "conflict with Congress' well-recognized purpose in enacting the FDCA," *id.* at 154, 592 *A.*2d 1176, which was "to protect consumers from dangerous products." *Id.* at 148, 592 *A.*2d 1176 (quoting *United States v. Sullivan*, 332 *U.S.* 689, 696, 68 *S.Ct.* 331, 335, 92 *L.Ed.* 297, 303 (1948)). As the Court stated in *Feldman II:* "We continue to believe, as we stated in *Feldman I*, that for the FDA to have prevented a drug manufacturer from warning the public of a newly-discovered danger pending development of unequivocal factual evidence of adverse reaction in man 'would seem anomalous.' " *Ibid.* (quoting *Feldman I, supra*, 97 *N.J.* at 459, 479 *A.*2d 374).

The position taken by the *Feldman II* Court on the issue of preemption is mirrored by the decisions of a wide range of courts. *See, e.g., Desiano v. Warner-Lambert & Co.*, 467 *F.*3d 85, 97 & n. 9 (2d Cir.2006); *Tobin v. Astra Pharm. Prods., Inc.*, 993 *F.*2d 528, 537-38 (6th Cir.1993); *Hill v. Searle Labs.*, 884 *F.*2d 1064, 1068 (8th Cir.1989); *Hurley v. Lederle Labs. Div. of Am. Cyanamid Co.*, 863 *F.*2d 1173, 1176-78 & n. 2 (5th Cir.1988); *Abbot v. Am. Cyanamid Co.*, 844 *F.*2d 1108, 1111-14 (4th Cir.1988); *Osburn v. Anchor Labs., Inc.*, 825 *F.*2d 908, 911-13 (5th Cir.1987); *Brochu v. Ortho Pharm. Corp.*, 642 *F.*2d 652, 658 (1st Cir.1981); ***56***In Re Vioxx Prods. Liab. Litig.*, 501 *F.Supp.*2d 776, 783-88 (E.D.La.2007); *In Re Zyprexa Prods. Liab. Litig.*, 489 *F.Supp.*2d 230, 274-75 (E.D.N.Y.2007); *Witczak v. Pfizer Inc.*, 377 *F.Supp.*2d 726, 729-32 (D.Minn.2005); *Cartwright v. Pfizer Inc.*, 369 *F.Supp.*2d 876, 882 (E.D.Tex.2005); *Caraker v. Sandoz Pharm. Corp.*, 172 *F.Supp.*2d 1018, 1032-44 (S.D.Ill.2001); *Motus v. Pfizer Inc.*, 127 *F.Supp.*2d

1085, 1096-1100 (C.D.Cal.2000); *Levine v. Wyeth*, 2006 Vt. 107, 944 *A.*2d 179, 183-91 (2006); *Kurer v. Parke, Davis & Co.*, 272 *Wis.*2d 390, 679 *N.W.*2d 867, 874-75 (App.2004); *Bell v. Lollar*, 791 *N.E.*2d 849, 854-55 (Ind.Ct.App.2003).

B. *Regulatory Preemption*

[2][3] We are likewise satisfied that the McDarbys' inadequate warnings action, asserted under the New Jersey PLA, is not preempted by statements contained in "D. Comments on Product Liability Implications" found in the Preamble to a final rule governing "Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products," 71 *Fed.Reg.* 3922, 3933-36 (Jan. 24, 2006) ****252** (Preamble or 2006 Preamble), [FN26] effective June 30, 2006.[FN27] There, the FDA, in a reversal of long-standing policy,[FN28] asserted:

> FN26. Labeling requirements appear in 21 *C.F.R.* §§ 201.56 and 201.57.
>
> FN27. "[R]etroactive application of an administrative rule," assuming the Preamble to be such, "is not favored." *Citizens for Equity v. N.J. Dep't of Envtl. Prot.*, 252 *N.J.Super.* 62, 76, 599 *A.*2d 516 (App.Div.1990), *aff'd*, 126 *N.J.* 391, 599 *A.*2d 507 (1991).
>
> FN28. See, e.g., discussion in David A. Kessler and David C. Vladeck, *A Critical Examination of the FDA's Efforts to Preempt Failure-To-Warn Claims*, 96 *Geo. L.J.* 461, 462-63, 474 & n. 59 (Jan. 2008), noting also, "[s]tate damages litigation helps uncover and assess risks that are not apparent to the agency during a drug's approval process." *Id.* at 463. *See also Levine, supra*, 944 *A.*2d at 190-91 (finding an express congressional purpose not to preempt state law remedies unless in direct conflict with federal law).

> FDA believes that under existing preemption principles, FDA approval of labeling under the act, whether it be in the old or new format, preempts conflicting or contrary State law.

***57** [*Id.* at 3934.]

As we have illustrated earlier in this opinion, the labeling changes sought by plaintiffs at trial do not conflict with federal requirements, but are in fact consonant with them. *See, e.g.*, 21 *C.F.R.* § 314.70(c), which permits the addition of risk information to a label by a manufacturer. Indeed, the Preamble specifically acknowledges a regulatory foundation for such label changes, stating:

> FDA permits two kinds of labeling supplements: (1) Prior approval supplements, which require FDA approval before a change is made ... and (2) "changes being effected" (CBE) supplements, which may be implemented before FDA approval, but after FDA notification (§§ 314.70(c) and 601.12(f)(2)). While a sponsor is permitted to add risk information to the FPI [full prescribing information] without first obtaining FDA approval via a CBE supplement, FDA reviews all such submissions and may later deny approval of the supplement, and the labeling remains subject to enforcement action if the added information makes the labeling false or misleading under section 502(a) of the act (21 U.S.C. 352).[FN29]
>
> FN29. Commentators and courts have noted that strengthened warnings have never been the subject of an FDA enforcement action. *See, e.g.*, *Feldman II, supra*, 125 *N.J.* at 148, 592 *A.*2d 1176; Kessler & Vladeck, *supra*, 96 *Geo. L.J.* at 479 & n. 80.

[*Ibid.*]

See also ibid. ("A manufacturer may, under FDA regulations, strengthen a labeling warning.").[FN30] In an article critical of the FDA's preemption position, written by David A. Kessler (who served as Commissioner of the FDA from November 1990 until March 1997) and Georgetown University Professor David C. Vladeck, the authors observe:

> FN30. A manufacturer must promptly inform the FDA of the change and submit a Supplemental New Drug Application for the FDA's review after-the-fact. 21 *C.F.R.* § 314.70(c).

> The FDA's pro-preemption arguments are based on a reading of the FDCA that, in our view, understates the ability of drug manufacturers to change labeling unilaterally to respond to newly discovered risks, or to seek labeling changes from the FDA. In fact, drug manufacturers have significant authority-and indeed, a responsibility-to modify labeling when hazards emerge and may do so without securing the FDA's prior approval.

58** [David A. Kessler & David C. Vladeck, ****253A Critical Examination of the FDA's Efforts to Preempt Failure-To-Warn Claims*, 96 *Geo. L.J.* 461, 464-65 (Jan. 2008)(hereafter, Kessler & Vladeck).]

See also *Feldman I, supra*, 97 *N.J.* at 459, 479 *A.*2d 374 ("It would seem anomalous for the FDA to have prevented a drug manufacturer from advising the public immediately of a newly discovered danger while waiting for FDA approval.").

A similar recognition of the ability of manufacturers, pursuant to 21 *C.F.R.* § 314.70(c), to strengthen warnings without creating a conflict with FDA regulations appears in *Vioxx Products Liability Litigation, supra,* where the court stated:

> The FDCA regulations also set forth detailed guidelines that drug manufacturers must follow when seeking to make changes to an approved NDA [New Drug Application]. *See* 21 *C.F.R.* § 314.70. In general, prior to making any "major changes," a supplemental NDA must be submitted and approved by the FDA. *See* 21 *C.F.R.* § 314.70(b). Certain "moderate changes" may also require FDA approval, although merely submitting notice of such changes may suffice depending on the circumstances. *See* 21 *C.F.R.* § 314.70(c). Prior FDA approval is not required, however, where the manufacturer seeks to "add or strengthen a contraindication, warning, precaution, or adverse reaction" to the labeling. 21 *C.F.R.* § 314.70(c)(6)(iii)(A). "Thus, it is apparent that 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." Although the FDA's regulations "do grant it the power to later disapprove a label strengthened pursuant to [21 *C.F.R.*] § 314.70 ... the power to disapprove does not retroactively make the manufacturer's strengthened label a violation of any law. Rather, if the FDA exercises its power to disapprove, the manufacturer simply stops distributing the new label." *Witczak v. Pfizer, Inc.*, 377 *F.Supp.*2d 726, 729 (D.Minn.2005).
>
> [501 *F.Supp.*2d at 782-83 (citation omitted).]

See also *Zyprexa Prods. Liab. Litig., supra,* 489 *F.Supp.*2d at 276-77; *Jackson v. Pfizer Inc.*, 432 *F.Supp.*2d 964, 965 (D.Neb.2006). The FDA concedes in this regard that its "regulation of drug labeling will not preempt all State law actions. The Supreme Court has held that certain State law requirements that parallel FDA requirements may not be preempted." 2006 Preamble, *supra*, 71 *Fed.Reg.* at 3936 (citing *Medtronic, Inc. v. Lohr*, 518 *U.S.* 470, 495, 116 *S.Ct.* 2240, 2255, 135 *L.Ed.*2d 700, 722 (1996)).

The Preamble further suggests that the FDA's concerns were focused upon circumstances in which state law appeared to mandate***59** warnings "that FDA had specifically considered and rejected as scientifically unsubstantiated"; to foster interpretations of the act and FDA regulations "that conflict with the agency's own interpretations"; to view FDA labeling requirements as "a minimum safety standard" [FN31]; or to "undermine safe and effective use in other ways." *Id.* at 3934-35. None of these possibilities exists here. The "balance of risks and benefits set by the FDA when it approves a drug label," Kessler & Vladeck, *supra*, 96 *Geo. L.J.* at 465, is not affected in the present context.

> FN31. In *Feldman II*, the Court construed federal regulations as establishing minimum standards. 125 *N.J.* at 141, 592 *A.*2d 1176. The PLA has elevated their significance in the context of FDA-approved warnings by establishing a presumption of adequacy.

[4] Moreover, we note, as have other courts considering this issue, that the ****254** Preamble does not constitute a regulation, duly adopted after notice and comment, but is merely an expression of opinion, reflective of current Administration views, on the part of the FDA. *See, e.g., Vioxx Prods. Liab. Litig., supra*, 501 *F.Supp.*2d at 786-87 (declining to grant deference to preamble, which "actually *conflict[s]* with statements made in the original notice of proposed rulemaking out of which the 2006 Final Rule grew," and determining that "[a]t best, the preamble merely offers an opinion on the viability of the plaintiffs' state-law claims given the existence of the federal regulatory scheme as a whole"); *Zyprexa Prods. Liab. Litig., supra*, 489 *F.Supp.*2d at 272 ("If an agency interpretation lacks the 'power to control'-because it was not promulgated in the exercise of congressionally-delegated authority ... or does not resolve an ambiguity in a previously issued regulation ...-it serves as guidance for litigants, but will only be respected by the court to the extent that it has the 'power to persuade' "); *Levine, supra*, 944 *A.*2d at 194 (finding after an analysis of legislative history and applicable precedent that "the FDA's statement is neither an authoritative interpretation of an ambiguous statutory provision entitled to deference ... nor a ***60** persuasive policy statement entitled to respect"). That the Preamble cites specific instances in which the "FDA has previously preempted State law requirements relating to drugs in rulemaking proceedings," 71 *Fed.Reg.* at 3935, but can identify no such regulation pertaining to preemption in the area of prescription drug labeling, reinforces this point.

It cannot be ignored that Merck's withdrawal of Vioxx from the market and ensuing congressional scrutiny of the roles of drug manufacturers and the FDA in prescription drug labeling and marketing led to marked revisions in the FDCA (*see* Food and Drug Administration Amendments Act of 2007 (FDA Amendments Act)), Pub.L. No. 110-85, 121 *Stat.* 823,[FN32] and the promulgation of the regulations that this Preface precedes. Yet, in contrast to the Medical Device Act, no preemption provision was adopted by statute or by regulation. Instead, the FDA Amendments Act contains a "Rule of Construction" that provides the FDA's new authority over

labeling "shall not be construed to effect the responsibility" of the manufacturer "to maintain its label in accordance with existing requirements, including subpart B of part 201 and sections 314.70 and 601.12 of title 21, *Code of Federal Regulations* (or any successor regulations)." 28 FDA Amendments Act, tit. IX, sec. 901(a), 121 *Stat.* at 925-26 (to be codified at 21 *U.S.C.A.* § 505(*o*)(4)(I)).

FN32. Of particular relevance here are Titles VIII, expanding existing clinical trial and clinical trial results data banks, and IX, providing enhanced authority to the FDA to mandate postmarket studies and clinical trials, as well as postmarket labeling changes.

[5] We thus join those courts that have held that the Preamble lacks preemptive force in cases such as this on the basis of (1) the well-recognized presumption against preemption in fields traditionally occupied by the states; (2) the absence of any requirement of deference to the preamble under principles set forth in ***61***Chevron, U.S.A., Inc. v. Natural Res. Def. Council, Inc.*, 467 *U.S.* 837, 843, 104 *S.Ct.* 2778, 2782, 81 *L.Ed.*2d 694, 703 (1984), and *United States v. Mead Corp.*, 533 *U.S.* 218, 226-27, 121 *S.Ct.* 2164, 2171, 150 *L.Ed.*2d 292, 303 (2001) (affording deference to agency interpretations promulgated in exercise of congressionally delegated authority), or in *Auer v. Robbins*, 519 *U.S.* 452, 461, 117 *S.Ct.* 905, 911, 137 *L.Ed.*2d 79, 90 (1997) (affording deference to agency statements clarifying ambiguities****255** in its own regulations); (3) the failure to provide notice and an opportunity for comment as required to properly promulgated regulations and the acknowledgement that such a sea change should be accomplished through more definitive action than can be found in a regulatory preamble; (4) the conflict between the Preamble and longstanding FDA policy, as set forth in statute, regulations and case law, which has permitted state-law failure-to-warn claims and federal regulation to coexist except in instances of actual conflict; (5) the recognition that the sweeping preemption espoused by the FDA would eliminate state police power as a means of protecting the health and safety of their citizens and would leave many injured citizens remediless; and (6) the absence of any actual conflict between the FDCA or FDA regulations and plaintiffs' failure-to-warn cause of action. *See, e.g.*, *Desiano, supra*, 467 *F.*3d at 86-87; *Vioxx Prods. Liab. Litig., supra*, 501 *F.Supp.*2d at 786-88; *Zyprexa Prods. Liab. Litig., supra*, 489 *F.Supp.*2d at 270-78; *Jackson, supra*, 432 *F.Supp.*2d at 968 & n. 3; *Levine, supra*, 944 *A.*2d at 191-94; *see also* Kessler & Vladeck, *supra*, 96 *Geo. L.J.* at 481-83.

We decline to follow the reasoning of *Colacicco v. Apotex, Inc.*, 432 *F.Supp.*2d 514, 537-38 (E.D.Pa.2006), which we regard as according unfounded deference to the Preamble's preemption position. Further, we distinguish *Sykes v. Glaxo-SmithKline*, 484 *F.Supp.*2d 289, 316-18 (E.D.Pa.2007), as involving a direct conflict between state tort law and an FDA determination that a particular vaccine ingredient was non-toxic and as applying a different regulation making the label on a biological product ineffective unless FDA-approved.

***62** C. *The PLA's Presumption of Adequacy*

The PLA, enacted in 1987,[FN33] codified liability on the part of a manufacturer for failure to provide adequate warnings, *N.J.S.A.* 2A:58C-2, and defined an adequate product warning as "one that a reasonably prudent person in the same or similar circumstances would have provided with respect to the danger and that communicates adequate information on the dangers and safe use of the product, ... in the case of prescription drugs, taking into account the characteristics of, and the ordinary knowledge common to, the prescribing physician." *N.J.S.A.* 2A:58C-4. That latter provision additionally establishes a rebuttable presumption that a warning, approved or prescribed by the FDA under the FDCA, is adequate. *Ibid.*

FN33. The PLA was not applicable in *Feldman*, which was initiated long before the Act's passage.

This presumption was construed, prior to Merck's withdrawal of Vioxx, in *Perez v. Wyeth Labs. Inc.*, 161 *N.J.* 1, 734 *A.*2d 1245 (1999), a case alleging failure to directly warn consumers of the difficulty of removing implants of the contraceptive Norplant. When reversing summary judgment in Wyeth's favor, the Court recognized a duty to warn in direct-to-consumer advertising of pharmaceuticals, but held that the presumption set forth in *N.J.S.A.* 2A:58C-4 was applicable in this context as well. *Id.* at 21-25, 734 *A.*2d 1245. The Court found that in this consumer context, "the same rebuttable presumption should apply when a manufacturer complies with FDA advertising, labeling and warning requirements." *Id.* at 24, 734 *A.*2d 1245. The court continued:

> That approach harmonizes the manufacturer's duty to doctors and to the public when it chooses to directly advertise its products, and simultaneously recognizes the public interest in informing patients ****256** about new pharmaceutical developments. Moreover, a rebuttable presumption that the duty to consumers is met by compliance with FDA regulations helps to ensure that manufacturers are not made guarantors against remotely possible, but not scientifically-verifiable, side-effects of prescription drugs, a result that could have a "significant anti-utilitarian effect."
>
> [*Id.* at 24-25, 734 *A.*2d 1245.]

***63** In language upon which defendant Merck strongly relies, the Court then stated:

> We believe that this standard is fair and balanced. For all practical purposes, absent deliberate concealment or nondisclosure of after-acquired knowledge of harmful effects, compliance with FDA standards should be virtually dispositive of such [failure to warn] claims. By definition, the advertising will have been "fairly balanced."

[*Id.* at 25, 734 *A.*2d 1245.]

See also *Rowe v. Hoffman-La Roche, Inc.*, 189 *N.J.* 615, 626, 917 *A.*2d 767 (2007) (utilizing this language from *Perez* in a case concerning choice-of-law).

[6] Merck claims on appeal that the language of *Perez* limiting exceptions to the rebuttable presumption of adequacy set forth in the PLA to instances of deliberate concealment or nondisclosure, precludes liability in this case, because the results of its studies, particularly, VIGOR, were provided by Merck in a timely fashion to the FDA and constituted a basis for the FDA's approval of the revised Vioxx label. However, we are unwilling to construe the presumption as Merck urges, finding the record in this case to be sufficient to support the recognition of an additional basis for overcoming the presumption of adequacy set forth in the PLA, applicable to Merck in the post-market warning context presented here. Specifically, we do not rest our decision to recognize this compensatory damage claim as one of "those rare cases when the presumption [of warning adequacy] is overcome," *Perez*, *supra*, 161 *N.J.* at 25, 734 *A.*2d 1245, upon any claim of fraud on the FDA, thereby implicating the punitive damage aspects of the PLA.[FN34] Our focus rests solely upon plaintiffs' claims of Merck's economically-driven manipulation of the post-market regulatory process.

> FN34. In this regard, we note that the Court in *Perez* recognized that there could be circumstances in which a compensatory damage award was appropriate, because the presumption of warning adequacy was overcome, but that a basis for punitive damages would not exist. *Ibid.*

In concluding that a hitherto unrecognized legal basis for an award of compensatory damages under the PLA exists here, we ***64** note that close scrutiny of the FDA and its regulatory power in a labeling context commenced only after *Perez* was decided, and that scrutiny disclosed flaws in the regulatory system, existing at least until the time of the 2007 Amendments, [FN35] that render the dictum of *Perez* less all-encompassing than it might then have appeared. Commentators and courts have since recognized that, whereas pre-market approvals of drugs are generally thorough in nature, the ability of the FDA, post-market, "to detect unforeseen adverse effects of [a] drug and to take prompt and effective remedial action" is considerably less. Kessler & Vladeck, *supra*, 96 *Geo. L.J.* at 465. It is these flaws in that post-marketing oversight process that provide the foundation for the further exception to ****257** the presumption of adequacy that we find applicable to this case. Kessler and Vladeck have stated: "Recent regulatory failures, such as the agency's ineffectual response to Vioxx, have demonstrated the FDA's shortcomings in this regard." *Ibid. See also* Thomas N. Tiedt, *The Drug Safety System Conundrum*, 62 *Food & Drug L.J.* 547, 551-55 (2007) (summarizing criticisms of the FDA's post-market oversight). Thus, Kessler and Vladeck have asserted that on the day of new drug approval, "and that day only, we agree that the FDA's determinations about labeling ought not be subject to re-examination by courts or juries in failure-to-warn cases." 96 *Geo. L.J.* at 465. Although, in light of the PLA's statutory presumption, we do not take so extreme a position, we regard the scientific and regulatory conditions upon which the authors then focus to be highly relevant to our consideration of whether the jury in this case could, on the basis of the evidence presented and applicable law, determine that the presumption of adequacy had been overcome.

> FN35. We express no opinion whether the strengthening of the FDA's powers in 2007 will be adequate to alleviate earlier-detected problems.

In this regard, Kessler and Vladeck first observe:

> At the time of approval, the FDA's knowledge-base may be close to perfect, but it is also highly limited because, at that point, the drug has been tested on a relatively small population of patients. Once the drug enters the marketplace, risks that are ***65** relatively rare, that manifest themselves only after an extended period of time, or that affect vulnerable subpopulations, begin to emerge. These are often not risks foreseen by the drug's manufacturer or the FDA and, for that reason, are not addressed on the label.

[*Id.* at 466 (footnotes omitted).]

See also U.S. Gov't Accountability Office, *Drug Safety: Improvement Needed in FDA's Postmarket Decision-Making and Oversight Process*, GAO 06-402 (2006) (hereafter, *GAO Report*) at 26 (discussing weaknesses in clinical trials); Comm. on the Assessment of the U.S. Drug Safety Sys., Inst. of Med. of the Nat'l Acads., *The Future of Drug Safety: Promoting and Protecting the Health of the Public*, 37-39, 153 (Alina Baciu, Kathleen Stratton & Sheila P. Burke eds., 2006) (hereafter *IOM Report*); Tiedt, *supra*,

62 *Food & Drug L.J.* at 553. As the IOM Report's authors found: "It is worth underscoring that the fundamental design of the drug approval system ...-separate from the quality of the data that sponsors generate in compliance with it-inevitably puts drugs on the market when safety information is incomplete." *IOM Report, supra,* at 59.

Further, until the 2007 Amendments were passed, the FDA "did not have the [statutory] authority to compel labeling changes, but instead had to negotiate changes with the drug's sponsor." Kessler & Vladeck, *supra,* 96 *Geo. L.J.* at 466. As Kessler and Vladeck note in opposing preemption:

> Manufacturers often *resist* labeling changes the FDA believes are needed due to emerging safety concerns. For instance, the FDA acknowledges that it took over a year to force Merck, the manufacturer of Vioxx, to add a warning of the risks of heart attack and stroke to Vioxx's label. During the lengthy negotiations, no change was made to Vioxx's label, and in the end, the FDA settled for a weaker warning than it had proposed. As noted, at the time of the Vioxx controversy, the FDA did not have statutory authority to compel manufacturers to make labeling changes, but instead had to rely on its power of persuasion, backed up by the FDA's authority to seek withdrawal of the drug's NDA or to file a misbranding action. The FDA generally got its way, but ****258** negotiations with manufacturers are often quite lengthy and frequently result in compromise decisions, as was the case with Vioxx.
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> [*Id.* at 480 (footnotes omitted).]

The FDA's Deputy Director of its Office of New Drugs, Dr. Sandra Kweder, testified in a Senate hearing held after the ***66** withdrawal of Vioxx that safety concerns over the drug prompted the FDA to convene an advisory committee meeting in 2001 to determine whether it increased the risk of heart attacks and strokes. Although the panel advised a change in the label to reflect that risk, the change was delayed. Additionally, Dr. Kweder acknowledged the lack of regulatory authority recognized by Kessler and Vladeck, stating:

> [W]e don't have the authority to tell a company, ["T]his is how your label has to look. This is the language that needs to go into your label. Here is where it goes, end of story.["] We have to negotiate with the company the specific language of how things should be worded, the placement, those kinds of things....
>
> * * *
>
> [In connection with Vioxx, Merck] rejected many of our proposals, and we similarly rejected many of the proposals-most of the proposals they sent us.
>
> [*FDA's Drug Approval Process: Up to the Challenge?: Hearing Before the S. Comm. on Health, Educ. Labor and Pensions,* 109th Cong. 10, 26-27 (2005) (hereafter, *Up to the Challenge*)].

See also GAO Report, supra, at 10; *IOM Report, supra,* at 157-58.

Dr. Kweder also acknowledged that the FDA lacked the power to compel additional post-marketing randomized clinical trials or epidemiological studies.

> We don't have the authority to tell them, you must do this particular trial. That is an authority we don't have.
>
> Now, we certainly have a fair amount of influence in convincing them to do some of these studies, and we are, for the most part, reasonably successful. But we don't have the authority to say, you must do the trial.
>
> [*Up to the Challenge, supra,* at 23.]

See also GAO Report, supra, at 11, 27-28; *IOM Report, supra,* at 155-57.

Given these admitted flaws in the FDA's control over postmarket labeling in the years that Vioxx was on the market, we are unwilling to accept Merck's position that the presumption of adequacy of a prescription drug's label can be overcome only upon proof of deliberate concealment or nondisclosure. Facts unavailable to the Supreme Court at the time of the *Perez* decision demonstrate that such a restriction is too narrow.

***67** The FDCA requires federal approval of new drugs, and mandates that, in order to obtain FDA approval, a manufacturer must demonstrate that adequate, well-controlled studies have demonstrated the drug to be both safe and effective. 21 *U.S.C.A.* § 355. The

"Indications and Usage" section of Merck's initial label stated that Vioxx was indicated for relief of the signs and symptoms of osteoarthritis, for the management of acute pain in adults and for the treatment of primary dysmenorrhea. Neither the "Warnings" section nor the "Precautions" section mentioned any adverse cardiovascular effects.

At trial, plaintiffs took the position, supported by sufficient evidence, that by 1997, as the result of FitzGerald's 023 study, Merck knew that Vioxx suppressed prostacyclin and thus upset the balance between clotting and anti-clotting agents in the body. It also knew that FitzGerald had postulated that the imbalance could lead to ****259** an increased risk of thrombotic events. [FN36] Studies at the time of new drug approval in 1999 arguably were insufficient to verify whether an increased cardiovascular risk existed for patients taking Vioxx. But even then, the FDA's medical review officer, Dr. Villalba, recognized a numerical increase in ischemic/thromboembolic events, and she recommended further cardiovascular testing. Such cardiovascular testing was also urged by Dr. Scolnick. However, despite preparatory steps, it was not conducted. Instead, the company focused on clinical trials intended to expand the market for its product, including the VIGOR trials.

> FN36. We regard it to be immaterial whether the FitzGerald hypothesis was correct, finding greater significance in the patent evidence of increased CV risk from use of Vioxx-whatever its cause. We note that the lack of specific CV studies by Merck has likely contributed to the absence of specific knowledge of causative factors.

Merck's VIGOR study confirmed the existence of the feared elevated thrombotic risk, as acknowledged by company officials in e-mails. Although Merck reported the VIGOR study results to the FDA on June 29, 2000 as support for its supplemental new ***68** drug application and supplemented its report on October 13, 2000, Merck's focus was on Vioxx's gastrointestinal safety as compared with nonselective NSAIDs. At that time, Merck sought to explain the adverse cardiovascular effects disclosed by the study as consistent with the "known" anti-platelet effects of naproxen. However, no such effects, particularly effects of the magnitude required to explain the difference in cardiovascular incidents, had been scientifically validated.

Further, although the FDA determined in February 2001 that the results of the VIGOR study should be incorporated into the label for Vioxx and that a warning regarding cardiovascular risks should be expressed, an almost two-year period elapsed between the time that Merck submitted its supplemental new drug application, intended to tout the GI benefits of Vioxx over traditional NSAIDs, and the approval of the new label in April 2002. The time span is even longer when calculated from March 27, 2000, the date that Merck initially reported the results of the VIGOR study to the FDA.

The record provides evidence sufficient to conclude that, during this period of time, Merck actively, and to an extent successfully, sought to dilute the labeling required as a result of the VIGOR study. Moreover, during this time, Merck's marketing personnel engaged in strenuous efforts to ensure that the results of the VIGOR study were not communicated to prescribing physicians by sales persons, and there is some evidentiary support for a claim of misrepresentation by Merck in responding to individual physician inquiries. Additionally, although the VIGOR results were published during this period, the increased CV risk evident upon examination of events occurring just after the study's CV cut-off date was not disclosed in the published article. Further, the increased risk was not described as such, but rather framed in terms of the decreased incidence of cardiovascular thrombotic events associated with naproxen-a traditional NSAID imbued with cardioprotective powers whose extent, to date, remains unproven.

69** The fact that the label was finally revised in April 2002 to reflect VIGOR's results, known to Merck at least by March 9, 2000 when Dr. Scolnick acknowledged that "the CV events are clearly there," provides powerful evidence that the label approved in May 1999, which contained no precautions or warnings regarding cardiovascular*260** risks, was inadequate, at least from March 9, 2000 onward.

We additionally find the evidence at trial sufficient to have permitted a jury to conclude that plaintiffs had overcome the presumption of adequacy relating to the revised label approved in April 2002. In this regard, we particularly note evidence of Merck's strenuous, economically driven, opposition to the inclusion of cardiovascular risk in the "Warnings" section of the Vioxx label, despite the universal opinions of the FDA's advisory committee and medical reviewers-and indeed, initially, the FDA regulators, themselves-that a warning was appropriate. That a lesser "Precaution," limited only to patients with a history of ischemic, or patent, heart disease, was approved can best be attributed to the dominant power of drug companies in a regulatory process that permitted, and indeed required, efforts to resolve scientific disputes through conciliatory processes.

IV.

At the conclusion of the trial, the trial judge instructed the jury at length regarding Merck's duty to warn, incorporating in her instructions the PLA's rebuttable presumption of adequacy and applicable federal labeling regulations, by stating:

You have heard a lot about the FDA's role. Under the Product Liability Act of New Jersey, which sets forth the law for failure to

warn claims, there is a provision that states that in the case of a claim for failure to warn involving a prescription drug that there's a rebuttable presumption that a label approved by the FDA is adequate. Therefore, we start with the presumption that if the FDA approved a drug label, then the warnings in the label are adequate.

However, if plaintiffs produce substantial evidence that the [approved] label is not an adequate warning, then the presumption can be overcome.

If plaintiffs produce such evidence, then you, the jury, must weigh all the evidence produced by both plaintiffs and the defendant on the issue of the ***70** adequacy of the warning and decide if plaintiffs have met [their] burden of proving that Merck failed to provide an adequate warning to physicians. This presumption applies only to the label and only where the FDA has approved the label as adequate.

However, if you find that the plaintiffs have proven by a preponderance of the evidence that after a label was approved there was new information that changed the known or knowable cardiovascular risks of VIOXX, then under FDA regulations, Merck had a duty to warn physicians of any newly discovered risks of the drug.

The FDA requires a drug manufacturer to warn the medical community as soon as there's reasonable evidence of an association of a serious hazard with a drug, and that language comes from the FDA requirements and regulations.

There need not be proof of causation, only association. In other words, if there's reasonable evidence of association between taking a drug and certain harm occurring without proof of exactly how the drug causes the harm, the FDA still requires the warning be given to the physicians of the risk.

Merck could, if it chooses to, without prior FDA approval send letters to physicians, take out ads, publish in journals, or send out sales representatives in order to advise physicians of a newly known risk of VIOXX. There is a procedure under the regulations, also, where a manufacturer of a drug like Merck can change their label to add risk information and submit [it to] the FDA ****261** for approval within 30 days. If the FDA doesn't object to the change in that time, the new warning can be used.

* * *

It is up to you to decide what Merck knew or should have known about whether there were potential cardiovascular risks of VIOXX based upon the reasonable evidence and when. It is up to you to then determine whether in light of all the information that Merck knew or should have known, it acted reasonably and adequately warned physicians of any serious cardiovascular risks that they should have been warned about based on all the facts that you find to be true in the time period where they could have gotten the information to the prescribing physician before the plaintiffs' heart attacks.

On appeal, Merck reiterates objections to this instruction that it made at trial, claiming that the charge does not reflect the Court's holding in *Perez;* asserting that the judge erred in permitting the jury to consider the timeliness of the 2002 label; and arguing further that the judge's instructions "seriously misconstrued the FDA regulations" and, as the Court found in *Feldman v. Lederle Labs. (Feldman III)*, 132 *N.J.* 339, 346-47, 625 *A.*2d 1066 (1993), essentially directed a verdict against Merck on the issue of its breach of a duty to warn.

***71** [7] We do not accept Merck's arguments. The instruction at issue adequately informed the jury that the presumption of adequacy could only be overcome by "substantial evidence," thereby according the presumption a significance greater than would otherwise be the case, while not according it conclusive effect. *See Perez, supra*, 161 *N.J.* at 24, 734 *A.*2d 1245 (citing *Feldman II, supra*, 125 *N.J.* at 156-57, 592 *A.*2d 1176); *compare Shim v. Rutgers*, 191 *N.J.* 374, 386, 924 *A.*2d 465 (2007) ("[A] presumption has the effect of compelling a particular conclusion in the absence of contrary evidence. To overcome a presumption, evidence that 'tends to' disprove the presumed fact, thereby raising a debatable question regarding the existence of the presumed fact, must be adduced."); *N.J.R.E.* 301. Although the instruction did not contain language restricting rebutting evidence to that relating to "deliberate concealment or nondisclosure," as Merck requested, for the reasons that we have previously explained, we do not accept that restriction as applicable in the present case.

Merck argues that the instruction improperly introduced the factor of the "timeliness" of the 2002 label into the case. But, in light of the labeling requirements of 21 *C.F.R.* § 314.70(c)(2)(i) (permitting labeling changes "[t]o add or strengthen a contraindication, warning, precaution, or adverse reaction") and 21 *C.F.R.* § 201.57(e) (specifying that a label "shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug"), that issue was, properly, a principal focus of plaintiffs' proofs. *See Feldman II, supra*, 125 *N.J.* at 157, 592 *A.*2d 1176 (noting that the rebuttable presumption of the PLA "was enacted in the context of present FDCA, PHSA [Public Health Service Act], and regulatory provisions that explicitly require warning

of possible adverse side effects as soon as reasonably feasible and based on 'reasonable evidence.' "). Federal regulations, as well as the holding of *Feldman II*, were accurately described by the trial judge in an instruction that focused both on the nature of the scientific evidence that would trigger a duty to warn and the means by which such a warning could be conveyed.

****262 *72** We also reject Merck's argument that the instruction was fatally akin to that in *Feldman III*. There, the trial court instructed the jury that: "The Federal Food and Drug Administration regulations and requirements are minimal standards and the defendant still owes a duty to warn its users in the exercise of reasonable care." *Feldman v. Lederle Labs.*, 257 *N.J.Super.* 163, 168, 608 *A.*2d 356 (App.Div.1992). The Supreme Court, agreeing with our analysis of the issue, determined that "[t]he trial court's error lay in telling the jury outright that Lederle had a 'duty to warn.' " *Feldman III*, *supra*, 132 *N.J.* at 347, 625 *A.*2d 1066. Such language does not appear in the charge given in this case, which properly placed upon plaintiffs the burden of establishing Merck's failure to provide an adequate warning and appropriately directed the jury to consider what Merck knew or should have known, when facts sufficient to require a warning became known, and whether it acted reasonably, given the information that it possessed.

V.

Merck additionally raises a number of evidentiary arguments that we review under an abuse of discretion standard. *Benevenga v. Digregorio*, 325 *N.J.Super.* 27, 32, 737 *A.*2d 696 (App.Div.1999) (discussing admission of evidence), *certif. denied*, 163 *N.J.* 79, 747 *A.*2d 287 (2000); *see also State v. Torres*, 183 *N.J.* 554, 572, 874 *A.*2d 1084 (2005) (discussing expert testimony); *Carey v. Lovett*, 132 *N.J.* 44, 64, 622 *A.*2d 1279 (1993) (same).

A. *Limitation on testimony of Lisa Rarick, M.D.*

[8][9] Merck argues that the trial judge erred in limiting the scope of the testimony of the company's regulatory expert, Lisa Rarick, M.D., a specialist in obstetrics, gynecology and women's health who had worked for the FDA from 1988 to 1995 in various capacities in its Center for Drug Evaluation and Research and in the Office of the Commissioner. Dr. Rarick proposed to testify, among other things, that:

> ***73** [i]t would have been inappropriate for Merck to change the prescribing information for Vioxx to incorporate the results of the VIGOR trial without the prior approval of FDA. With limited exception, a drug manufacturer must obtain prior FDA approval before making changes to the prescribing information for its drug. A drug manufacturer may change its prescribing information without FDA's prior approval only in certain limited circumstances under a procedure called the Changes-Being-Effected ("CBE") [the procedure authorized by 21 *C.F.R.* 314.70(c)(2)(i)]. FDA practice and policy, and FDA guidances, however, make clear that major labeling changes-such as the incorporation of the results of a study like VIGOR, which produced a complex dataset and which was conducted in a population for which the drug was not yet indicated taking an unapproved chronic dose-must be approved by the FDA prior to being effected. Indeed, as FDA has recently made clear, the industry practice and FDA's preferred procedure is for sponsors to consult with FDA before any labeling change. Had Merck submitted prescribing information for Vioxx incorporating the results of VIGOR pursuant to the CBE procedure, FDA would have rejected it. Merck acted appropriately in submitting proposed labeling incorporating the results of VIGOR for FDA approval.

The judge barred Dr. Rarick from testifying regarding her interpretation of FDA regulations, including 21 *C.F.R.* 314.70(c)(2)(i), because their construction ****263** was a legal issue that the judge reserved for her own determination, finding the law to be "very clear." Additionally, the judge barred Dr. Rarick from stating that if Merck had submitted a label change pursuant to the CBE process, it would have been rejected, ruling that the opinion lacked a proper foundation and was speculative.[FN37] The judge also barred the doctor from testifying that, based upon applicable regulations, the April 2002 label was appropriate and adequate, given the information known at the time, and from speculating about the FDA's reactions to Merck's various submissions. The judge found that Dr. Rarick was not authorized to be a spokesperson for the FDA regarding its drug approval process, that her training and employment were in fields other than osteoarthritis and cardiology, and that she had no first-hand experience with Merck's Vioxx submissions.

> FN37. It is significant that the doctor never opined that the CBE process would have been inappropriate for Merck to use to warn of a cardiovascular risk, but only that the CBE process would have been an inappropriate vehicle for inclusion in the label of the VIGOR study which, we note, Merck sought to utilize to demonstrate Vioxx's GI benefits.

***74** However, the judge indicated that she would permit Dr. Rarick to respond to testimony suggesting that the FDA was dysfunctional by describing FDA staffing, pay, and level of achievement. The judge also ruled that the doctor would be permitted to testify as to the FDA's requirements for a new drug application, to evaluate Merck's compliance with those requirements, and to explain the manner in which the FDA reviews a new drug application. The doctor was additionally permitted to testify about the FDA's post-market evaluations of safety. The court's determinations on the scope of Dr. Rarick's testimony did not prevent Merck from eliciting her opinion on whether Merck acted properly after obtaining significant information regarding Vioxx's CV safety. Thus, contrary to Merck's position on its motion for a new trial and on appeal, she was free to counter opinions by plaintiffs' expert, Dr.

Krumholz, that Merck should have issued a warning upon analyzing the results of the VIGOR study by testifying, for instance, that the VIGOR study data was uncertain and that Merck acted appropriately by reporting that data to the FDA, publishing it, and educating the medical community, commencing with its press release of March 27, 2000. Nonetheless, allegedly as the result of the judge's ruling, Merck did not call Dr. Rarick as a witness in the compensatory damage portion of the trial.

We discern no abuse of discretion on the judge's part in limiting the testimony of Dr. Rarick in the fashion that she did. The Supreme Court has long recognized that FDA regulations do not "prevent a drug manufacturer from adding an additional warning as soon as it was aware of its necessity." *Feldman I, supra*, 97 *N.J.* at 459, 479 *A.*2d 374. Moreover, as the trial judge noted in her opinion denying Merck's motion for a new trial, the FDA agreed with the Supreme Court's position at the time of the VIGOR trial. In the preface to the 1979 FDA Final Rule on Labeling and Prescription Drug Advertising: Content and Format for Labeling for Human Prescription Drugs, the FDA responded to a comment requesting the FDA to state that the finding of a panel of experts be required before an association between a drug ***75** and a serious hazard would require a warning. The FDA responded:

> The Commissioner rejects these comments. A serious hazard must be included in the "Warnings" section of the ****264** labeling of a drug when evidence exists on the basis of which experts qualified by scientific training and experience can reasonably conclude that the hazard is associated with the use of the drug. A causal relationship need not be proved ... [The Act] requires labeling to include warnings about both potential and verified hazards. Accordingly, when medical information justifies a warning, the act requires that it be included in drug labeling.
>
> The Commissioner also advises that these labeling regulations do not prohibit a manufacturer, packer, relabeler, or distributor from warning health care professionals whenever possibly harmful adverse effects associated with the use of the drug are discovered. The addition to labeling and advertising of additional warnings, as well as contraindications, adverse reactions, and precautions regarding the drug, or the issuance of letters directed to health care professionals (e.g. "Dear Doctor" letters containing such information) is not prohibited by these regulations. [The Act] and FDA regulations require a warning in drug labeling as soon as a hazard is associated with the use of a drug.... In considering these regulations in a product liability case, at least one court has held that an NDA holder may have a duty to add a warning before FDA approval of a supplemental application. *See McEwen v. Ortho Pharmaceutical Corp.*, [270 *Or.* 375] 528 *P.*2d 522 (Ore.1974).
>
> [44 *Fed.Reg.* 37,434, 37,447 (1979).] FN38

FN38. The judge noted that the FDA had expressed a contrary position in 2006. *See*, Preamble, 71 *Fed.Reg.* 3922, 3934 (Jan. 24, 2006).

[10][11] In light of FDA regulations and its expressed position, if Dr. Rarick intended to testify that the CBE process would have been inappropriate for adoption of a warning of CV risk, that statement likely would have been incorrect and would have misled the jury. A statement that the CBE process would have been inappropriate for incorporation of the entire results of the VIGOR trial into the label would likely have been correct, but misleading, since plaintiffs did not suggest that Merck utilize the CBE process for that purpose. To the extent that Dr. Rarick sought to express a legal conclusion, her testimony would have been improper. As the court stated in *Suter v. Gen. Accident Ins. Co. of Am.*, 424 *F.Supp.*2d 781 (D.N.J.2006): "The rule against the admissibility of legal conclusions is well-settled. 'The district court must limit expert testimony so as to not allow experts to opine on "what the ***76** law required" or "testify as to the governing law." ' " *Id.* at 791 (quoting *Casper v. SMG*, 389 *F.Supp.*2d 618, 621 (D.N.J.2005) (quoting *U.S. v. Leo*, 941 *F.*2d 181, 196-97 (3d Cir.1991)). This rule exists "to avoid confusing the jury or usurping the role of the judge in instructing the jury on the relevant law." *Id.* at 793. *See also, e.g.*, *Boddy v. Cigna Prop. & Cas. Cos.*, 334 *N.J.Super.* 649, 659, 760 *A.*2d 823 (App.Div.2000).

We concur with the judge's further conclusion that the remainder of the barred testimony lacked foundation and was speculative in nature. *Tormenia v. First Investors Realty Co.*, 251 *F.*3d 128, 136 (3rd Cir.2000) (observing that appellants were correct, in principle, in noting that an expert's masters degree in civil engineering and experience as a professor do not "qualify him to provide expert testimony on any subject associated, however tangentially, with such engineering disciplines."); *Landrigan v. Celotex Corp.*, 127 *N.J.* 404, 413, 605 *A.*2d 1079 (1992) (requiring, among other things, that an expert have ****265** sufficient expertise to offer the intended testimony); *Newell v. Hudson*, 376 *N.J.Super.* 29, 47, 868 *A.*2d 1149 (App.Div.2005) (rejecting speculative expert testimony).

B. *Exclusion of April 6, 2005 FDA Memorandum*

[12] Merck claims additional error by the trial judge in excluding an April 6, 2005 FDA memorandum concerning the cardiovascular risks of other NSAIDs pursuant to *N.J.R.E.* 403(a), because its probative value was substantially outweighed by the risk of undue prejudice. In that memorandum, two FDA scientists, the Director of the Office of New Drugs and the Director of the

Office of Pharmacoepidemiology and Statistical Science concluded, among other things, that all three approved COX-2 inhibitors (Vioxx, Celebrex and Bextra) "are associated with an increased risk of serious adverse CV events compared to placebo"; data from trials that have included a comparison of COX-2 and non-selective NSAIDs "do not clearly demonstrate that the COX-2 selective agents confer a greater risk"; that available data on CV ***77** risk was best interpreted as being consistent with a class effect for all NSAIDs; short-term use of NSAIDs to relieve acute pain did not appear to confer a greater risk of adverse CV events; the three COX-2 inhibitors reduced the incidence of GI ulcers; and that valdecoxib (Bextra) was associated with an increased rate of serious and potentially life-threatening skin reactions and should be withdrawn from the market.

On appeal, Merck argues that the memorandum should have been admitted because it rebutted "almost every important scientific proposition in plaintiffs' case," including the FitzGerald hypothesis.

In her new trial opinion, the judge explained her ruling as follows:

> The court advised the defense it would admit the Memorandum into evidence if Merck put forth an expert who, based on a review not just of the FDA's Memorandum but of relevant clinical studies, held the opinion that *all* NSAIDs, including VIOXX®, increased the risk of heart attacks. The validity of the FDA statements w[as] unknown at that time. The memorandum did not explain the scientific basis for its opinion and no expert at that time was produced who could support the opinion. It was not just the validity of the FDA's conclusions that led the court to condition admission of the document; rather, in order for the jury to properly weigh the information contained in the Memorandum, it had to be used by an expert who could explain it and be cross examined on it.

We find no reversible error in the judge's conclusion in this regard.

C. *Admission of 2005 Lancet Article*

[13] At trial and on appeal, Merck objects to the admission, through the testimony of plaintiff's expert, Dr. Krumholz, of that portion of an article in the European medical journal, *The Lancet*, written by David Graham (an FDA employee speaking independently) and others,[FN39] that assumed issuance of an estimated 106.7 ***78** million Vioxx prescriptions between 1999 and September 2004 and, extrapolating from evidence provided by Merck's clinical trials, gave an estimate of the "excess" heart attacks probably caused by Vioxx as ****266** 88,000 to 144,000, forty-four percent of which were allegedly fatal.

> FN39. David J. Graham et al., *Risk of Acute Myocardial Infarction and Sudden Cardiac Death in Patients Treated with Cyclo-oxygenase-2 Selective and Non-selective Non-steroidal Anti-inflammatory Drugs: Nested Case-control Study*, 365 *Lancet* 475 (2005).

The evidence was admitted by the trial judge as an opinion contained in a peer-reviewed learned treatise upon which Dr. Krumholz relied. *See* *N.J.R.E.* 803(c)(18); *Jacober v. St. Peter's Med. Ctr.*, 128 *N.J.* 475, 493-97, 608 *A.*2d 304 (1992). Merck argues that the estimates were "commentary" unrelated to the published study of the incidence of serious coronary heart disease among patients treated through Kaiser Permanente in California with Vioxx, Celebrex, and non-selective NSAIDs, and that they were thus inadmissible. Additionally, it argues that the methodology utilized in arriving at the estimates was flawed and thus that the computation was grossly misleading and speculative.

At trial, the evidence was utilized by Dr. Krumholz to illustrate the "valid point" that, although the number of heart attacks among Vioxx users in the VIGOR and APPROVe studies was small, the incidence is magnified when considered in relation to the number of Vioxx prescriptions issued while the drug was on the market. We find no abuse of discretion on the part of the trial judge in permitting this evidence to be presented to the jury by Dr. Krumholz in this context. Although Merck is correct that the challenged numbers are not directly derived from the epidemiological study that is the initial focus of the article, they relate directly to Graham's conclusion that Vioxx use increases the risk of serious coronary heart disease compared with Celebrex and that naproxen use does not protect against serious coronary heart disease. Moreover, the estimates, for which a proper foundation is presented in the article, are integral to Graham's further conclusion, based upon the results of his epidemiological research, that the public health consequences of a failure to take earlier action to remove a drug from the market must be assessed. We find that ***79** Merck's further challenge to the validity of Graham's calculations merely affects their weight, not their admissibility.

D. *Admission of Evidence with "No Nexus" to Plaintiffs' Claims*

[14] In its final evidentiary argument, Merck asserts that the trial judge erred in admitting evidence of its marketing practices with respect to Vioxx that did not target McDarby, Cona, or their physicians. Merck specifically refers to (1) the September 17, 2001 warning letter from the FDA, which we previously described, that charged Merck with minimizing the potentially serious cardiovascular findings of the VIGOR study; (2) a prior June 16, 1998 FDA warning letter regarding a number of products other than Vioxx that expressed serious concern "that the dissemination of the above listed promotional materials demonstrate[s] a continuing

pattern and practice of widespread corporate behavior to avoid compliance with the regulations concerning the disclosure of risk information"; (3) the "CV card," minimizing risk, that, in fact, McDarby's physician recalled studying; (4) the internal document identifying doctors to be "neutralized" by sales staff; and (5) a puerile video, called "Be the Power," that trained sales representatives to meet obstacles such as users of Celebrex or non-specific NSAIDs and persons fearful of a heart attack, hypertension or edema by stressing the efficacy and gastrointestinal safety of Vioxx.

With the possible exception of the FDA warning letter relating to products other than Vioxx, we find all of the cited evidence to have been relevant to the issue of Merck's failure to adequately warn of the known dangers of its product and to its ****267** conduct in obscuring the scientific evidence of cardiovascular risk established by VIGOR and other studies.

Although we might disagree with the trial judge's decision to admit the FDA warning letter regarding marketing practices on products other than Vioxx as evidence of habit or custom, ***80** *N.J.R.E.* 406, we find any abuse of discretion in that regard insufficient to have constituted reversible error.

VI.

At the conclusion of the evidence, the trial judge directed a verdict for plaintiffs on the issue of whether Dr. Braun would have determined not to prescribe Vioxx to McDarby if adequately warned of its cardiovascular risks (product-defect causation), recognizing the applicability of a heeding presumption in this pharmaceutical context and determining that the presumption had not been overcome. The judge instructed the jury:

> If you find that Merck failed to provide an adequate warning, then the law requires you to presume that plaintiffs' doctors would have heeded that adequate warning and not have prescribed VIOXX to [plaintiffs]. However, to recover damages for their heart attacks, [plaintiffs] must still prove that their taking VIOXX was a proximate cause of their heart attacks.

In its new trial motion and on appeal, Merck argues that the heeding presumption is inapplicable to pharmaceuticals and, if applicable, it was overcome. Accordingly, the trial judge erred.

[15] Merck's arguments regarding the adoption of a heeding presumption in a pharmaceutical failure-to-warn context essentially mirror those rejected by Judge Walsh when presented by Wyeth, Inc., in phen-fen litigation pending before him. *See In re Diet Drug Litig.*, 384 *N.J.Super.* 525, 895 *A.*2d 480 (Law Div.2005). We agree in principle with Judge Walsh that in appropriate circumstances,[FN40] a heeding presumption may be applicable to claims of failure to warn of the dangers of pharmaceuticals, as well as other products. In doing so, we find no basis to conclude that the Court's reasoning in *Coffman v. Keene Corp.*, 133 *N.J.* 581, 595-603, 628 *A.*2d 710 (1993), and *Theer v. Philip Carey Co.*, 133 *N.J.* 610, 618-24, 628 *A.*2d 724 (1993), should necessarily be inapplicable to a claim of failure to warn of the dangers of a ***81** palliative drug for which potentially less harmful alternatives exist. [FN41] As the Court stated in *Coffman:*

> FN40. In light of the analysis that follows, we do not find it necessary to establish in this opinion what such circumstances would be.
>
> FN41. Although, as Merck argues, the cardiovascular risk to McDarby from continued use of Vioxx was "unavoidable," the use of a different palliative agent provided an alternative means for pain relief.

> The heeding presumption ... serves to reinforce the basic duty to warn-to encourage manufacturers to produce safer products, and to alert users of the hazards arising from the use of those products through effective warnings. The duty to warn exists not only to protect and alert product users but to encourage manufacturers and industries, which benefit from placing products into the stream of commerce, to remain apprised of the hazards posed by a product. The use of the heeding presumption provides a powerful incentive for manufacturers to abide by their duty to provide adequate warnings. *See Nissen Trampoline Co. v. Terre Haute First Nat'l Bank*, 332 *N.E.*2d 820, 826 (Ind.Ct.App.1975) (holding that heeding presumption****268** "would discourage those manufacturers who would rather risk liability than provide a warning which would impair the marketability of the product"), *rev'd on procedural grounds*, [265 *Ind.* 457] 358 *N.E.*2d 974 (1976).
>
> [133 *N.J.* at 599, 628 *A.*2d 710.]

That comment is equally apt in a pharmaceutical context.

We attribute no particular significance to the fact that the heeding presumption was not mentioned by the Court in *Strumph v.*

Schering Corp., 133 *N.J.* 33, 626 *A.*2d 1090 (1993), reversing for the reasons expressed by Judge Skillman in his dissent, 256 *N.J.Super.* 309, 323, 606 *A.*2d 1140 (App.Div.1992), a prescription drug case alleging failure to warn that was decided in the same term as *Coffman* and *Theer.* In light of testimony in *Strumph* by both treating physicians that they were aware of the risks of the drug that they prescribed and, having conducted a risk-benefit analysis, nonetheless determined its use to be warranted, *Strumph, supra*, 256 *N.J.Super.* at 323-24, 606 *A.*2d 1140, use of such a presumption would not have been factually sustainable or, analyzed otherwise, the presumption would have been rebutted as a matter of law.

Merck argues additionally that, because of the risk-benefit analysis that physicians undertake when prescribing medications, "one cannot 'presume' that additional risk information would lead a prescribing physician to avoid the drug." Recognition of that ***82** circumstance is incorporated into the generally rebuttable nature of the heeding presumption, permitting a drug manufacturer to counter a plaintiff's causation argument with contrary evidence, as in fact occurred in *Strumph.* Thus, the heeding presumption does not stifle innovation, as Merck suggests, but merely fosters the disclosure of accurate information regarding risk on new, as well as established, pharmaceutical products.

[16] However, we do agree with Merck that, in McDarby's case, the judge's use of the heeding presumption in her legal analysis and jury instructions was not legally required. That presumption, precedent demonstrates, is primarily applicable in circumstances in which plaintiff lacks the ability to prove by direct evidence that a proper warning, if given, would have been heeded. *Coffman, supra*, 133 *N.J.* at 600, 628 *A.*2d 710. But here, direct evidence in the form of the deposition testimony of McDarby's treating physician existed, rendering use of a presumption unnecessary. Nonetheless, we do not regard the judge's use of presumption language to have resulted in reversible error, since we are satisfied that directing a verdict on this causation issue was proper. As the Court has held, "in the absence of any countervailing evidence, 'a trial judge need not submit the issue of proximate cause from the absence of a warning to the jury but may determine as a matter of law that the warning would have been heeded.' " *Coffman, supra*, 133 *N.J.* at 595, 628 *A.*2d 710 (quoting *Coffman v. Keene Corp.*, 257 *N.J.Super.* 279, 290, 608 *A.*2d 416 (App.Div.1992)). That is essentially what the trial judge did here in directing a verdict in plaintiffs' favor on this causation issue.

[17] Our review of the record satisfies us that the judge ruled appropriately in this regard. Dr. Braun's deposition testimony discloses his close attention to Merck's product literature, including its package inserts, "Dear Doctor" letters, and the CV card, and his reliance upon Merck's assurances of safety in the face of the published results of the VIGOR trial and the questions regarding the cardiovascular risks of Vioxx posed by Dr. Topol. The doctor's testimony also demonstrates that, when informed by ***83** Merck that ****269** Vioxx posed a risk to patients with ischemic heart disease, the doctor discontinued prescribing the drug to a patient with that condition. He thus followed Merck's instructions where applicable, demonstrating his willingness to cease the use of a popular and effective medication, but on the basis of his treatment records, determined the inapplicability of Merck's precautions to McDarby. As a final matter, Dr. Braun testified unequivocally that he would not have added to the cardiovascular risks confronting McDarby as the result of his age, gender and diabetic condition if he had known Vioxx "could" increase the risk of a heart attack. Similarly, McDarby testified that he would not have taken the drug if he had known of its cardiovascular risk, and he stated that he relied on his doctor for a determination of drug safety.

Merck argues, nonetheless, that Dr. Braun was never asked whether he would have ceased prescribing Vioxx to McDarby if adequately warned of an "association" between Vioxx and an increased risk of serious cardiovascular events. While we recognize the scientific distinction between a causal relationship and an associative one, we do not regard this linguistic quibble as sufficient to have raised a jury issue, given the strength of Dr. Braun's testimony in this case. Additionally, Merck argues that a jury could have found that, after April 2002, Dr. Braun would have continued to prescribe a drug that had proven effective, noting that McDarby needed pain relief, he had taken the drug without problems for two years, he was taking cardioprotective aspirin, and debates still existed regarding the cardiovascular safety of Vioxx. However, this argument is wholly speculative, and finds no support in the unequivocal testimony given by Dr. Braun.

VII.

[18] At trial, testimony was presented by plaintiffs' experts, Dr. Krumholz, and cardiologist Dr. Nicholas DePace [FN42] to establish ***84** that Vioxx was a substantial contributing factor in the heart attack suffered by McDarby on April 14, 2004. Dr. Krumholz testified, in accordance with the FitzGerald hypothesis, that Vioxx's action as a COX-2 inhibitor was thought [FN43] to upset the body's balance between prostacyclin and thromboxane by inhibiting prostacyclin production, thereby increasing the clotting action of platelets in the blood that would occur when plaque deposited in arteries ruptured, and that the increased clotting could lead to blockage of the normal blood flow and the occurrence of a heart attack. Dr. Krumholz testified further that the risk that such clotting would lead to a heart attack was increased in patients with other elevated risk factors such as atherosclerosis, elevated "bad" cholesterol levels, or diabetes, utilizing a graphic illustration from a 2005 article in the journal *Circulation*[FN44] to demonstrate the impact of COX-2 inhibition on clotting in patients with atherosclerotic blood vessels.

FN42. Dr. DePace is board-certified in cardiology. He serves as a clinical professor at the Thomas Jefferson Medical School

in Philadelphia and a physician at the Jefferson Heart Center.

FN43. The doctor recognized the existence of other hypotheses, but found this was supported by the "most evidence," had "gotten the most attention" and was the one that the scientific community was "most concerned about."

FN44. Elliott M. Antman, David DeMets & Joseph Loscalzo, *Cyclooxygenase Inhibition and Cardiovascular Risk,* 112 *Circulation,* 759 (2005).

In additional testimony, Dr. Krumholz described the results of the APPROVe study, which disclosed a relative risk of adverse thrombotic cardiovascular events from use of Vioxx of 1.92. The doctor ****270** testified that the risk would be further elevated in diabetics, stating:

> It is reasonably probable that diabetics are at greater risk from VIOXX because they have an underlying higher risk of disease. Diabetes is a risk factor for heart disease .... VIOXX ... would be more dangerous in that group in absolute terms than it would be in the other group.

Whereas studies had shown an elevated risk of heart disease among diabetics of 1.5, it was Dr. Krumholz's opinion that a "conservative estimate" would place the increased risk to a diabetic taking Vioxx at "at least two times the risk." Although the doctor testified that the precipitating cause of a heart attack ***85** whether age, diabetes, low "good" cholesterol, or Vioxx) could not be physically identified, the existing scientific studies had demonstrated that a forty-eight-month history of use of Vioxx would constitute a substantial contributing factor to its occurrence.

Dr. DePace, who had examined McDarby, confirmed the presence of risk factors in addition to long-term use of Vioxx, consisting of his age, low levels of "good" cholesterol, weight, and diabetes, and he also concluded that Vioxx had been a substantial contributing factor to his heart attack. In reaching this conclusion, the doctor relied upon the existing epidemiological studies, including VIGOR and APPROVe. In addition to the general results of the APPROVe study, indicating a 1.92 relative risk of a serious thrombotic event, the doctor noted that the authors of the APPROVe study had conducted a subgroup analysis of patients taking Vioxx who had a history of diabetes that disclosed a relative risk of 6.10 or a 510% increase in risk. Although the doctor recognized that the *post hoc* subgroup analysis had limitations, he nonetheless found the findings to be significant.

Merck's expert, Dr. Barry Rayburn, conceded on cross-examination that McDarby had taken Vioxx for forty-eight months before his heart attack and, whereas the APPROVe study indicated an overall relative risk of 1.92 for serious thrombotic events, a *post hoc* analysis showed an elevation of that relative risk to 4.45 in patients taking the drug for nineteen to thirty-six months, for a 345% increase in risk.

On appeal, Merck contends that evidence of an increase in relative risk such as that to which the experts testified was insufficient to establish causation. Merck particularly challenges any reliance on the subgroup analysis performed by its scientists on the APPROVe data. However, that evidence did not constitute the sole basis for the opinions of either of plaintiffs' experts, and the potential lack of reliability of the subgroup analysis was exhaustively demonstrated to the jury. Ample evidence supported an increased risk resulting from the conjoined effects of diabetes and Vioxx, whether the jury accepted the more conservative ***86** estimates of Dr. Krumholz or the higher estimates that Dr. DePace considered in reaching his opinion. That epidemiological evidence, combined with the explanatory opinions of both Dr. Krumholz and Dr. DePace were sufficient to create the jury issue regarding causation. *Landrigan, supra,* 127 *N.J.* at 412-23, 605 *A.*2d 1079; *see also Grassis v. Johns-Manville Corp.*, 248 *N.J.Super.* 446, 454-56, 591 *A.*2d 671 (App.Div.1991).

We reject Merck's argument, premised on the Court's decision in *Cruz-Mendez v. ISU/Ins. Servs. of San Francisco,* 156 *N.J.* 556, 722 *A.*2d 515 (1999), that the jury had to find "but for" causation and that the judge erred in not giving that instruction. In *Cruz-Mendez*, a case involving the misuse by plaintiff of fireworks found after a display, an issue existed whether the fireworks****271** display was the proximate cause of the plaintiff's injury or whether plaintiff's conduct after finding the fireworks constituted an intervening cause so unforeseeable that the causal chain was broken. *Id.* at 576, 722 *A.*2d 515. In this circumstance, the Court reversed a determination that as a matter of law, plaintiff had demonstrated causation "because the firework that injured his hand 'was attributable to a fireworks display that was put on approximately five days earlier.' " *Id.* at 574, 722 *A.*2d 515. The Court held that plaintiff must show both that "defendant's act or omission was the factual, or 'but for,' cause of the injury" and that this factual cause was a proximate cause of the injury. *Ibid.*

However, as the Court explained in *Verdicchio v. Ricca,* 179 *N.J.* 1, 843 *A.*2d 1042 (2004):

[T]he "but for" test has its limitations in situations where two or more forces operate to bring about a certain result and "any one of them operating alone would be sufficient." Indeed, the "but for" test has been characterized as a potentially "insurmountable obstacle" for a plaintiff in a case in which "unrelated factors may have contributed to the same injury."

In response to the apparent limitation of the "but for" test in concurrent causation cases, New Jersey, like many jurisdictions, has adopted a modified standard-the substantial factor standard-"limited to that class of cases in which a defendant's negligence combines with a preexistent condition to cause harm-as distinguished from cases in which the deviation alone is the cause of the harm."

[*Id.* at 24, 843 *A.*2d 1042 (citations omitted).]

***87** Thus, the language of *Cruz-Mendez* is inapplicable in a case such as this in which multiple factors could be found by a jury to have contributed to McDarby's condition. In this matter, medical causation was appropriately demonstrated by proof that exposure to the defendant's product "was a substantial factor in causing or exacerbating the disease." *James v. Bessemer Processing Co.*, 155 *N.J.* 279, 299, 714 *A.*2d 898 (1998) (quoting *Sholtis v. Am. Cyanamid Co.*, 238 *N.J.Super.* 8, 30-31, 568 *A.*2d 1196 (App.Div.1989)) (adopting standard in toxic tort context); [FN45] *see also Model Jury Charge (Civil)*, 612, "Proximate Cause-Where There is Claim that Concurrent Causes of Harm Were Present" (1998). In sum, in this case there was adequate proof of McDarby's continued, long-term use of Vioxx and "medical and/or scientific proof of a nexus between [that use] and ... plaintiff's condition." *James, supra*, 155 *N.J.* at 304, 714 *A.*2d 898. Thus, the jury could properly conclude, as it did, that medical causation had been demonstrated. We thus affirm the compensatory damage award by the jury in connection with McDarby's cause of action for failure to warn in violation of the PLA.

FN45. To the extent that the requirement in *James* of proof of frequency, regularity and proximity, *id.* at 302-04, 714 *A.*2d 898, is imported into this drug context, we find that standard met by the uncontroverted proof of use by McDarby of Vioxx for a period of forty-eight months.

VIII.

[19] The PLA provides:

Punitive damages shall not be awarded if a drug or device ... which caused the claimant's harm was subject to premarket approval ... by the federal Food and Drug Administration ... and was approved .... However, where the product manufacturer knowingly withheld****272** or misrepresented information required to be submitted under the agency's regulations, which information was material and relevant to the harm in question, punitive damages may be awarded.

[*N.J.S.A.* 2A:58C-5c.]

In permitting the jury to consider punitive damages as the result of fraud on the FDA, the trial judge found that the remedy was not preempted by the FDCA. Additionally, she found that evidence***88** of a meta-analysis of the incidence of myocardial infarctions in Vioxx studies, conducted by Merck in 2000 and not submitted to the FDA in connection with a meta-analysis provided to the FDA on January 8, 2001, could be considered by the jury as the basis for plaintiffs' punitive damage claim.

On appeal, Merck claims error in the judge's failure to recognize on the basis of *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 *U.S.* 341, 121 *S.Ct.* 1012, 148 *L.Ed.*2d 854 (2001) and other cases that McDarby's punitive damages claim was preempted. Merck argues additionally that plaintiffs failed to adduce evidence of regulatory fraud. Finally, it argues that a new trial is warranted because of error in the judge's instruction to the jury, in which she stated that deterrence of persons or entities other than the defendant was a purpose of punitive damages.[FN46] We are persuaded by Merck's preemption argument.

FN46. The recent affirmance of our majority opinion in *Tarr v. Bob Ciasulli's Mack Auto Mall, Inc.*, 390 *N.J.Super.* 557, 916 *A.*2d 484 (App.Div.2007) demonstrates that Merck is correct in this regard. *See* *Tarr v. Bob Ciasulli's Mack Auto Mall, Inc.*, 194 *N.J.* 212, 216, 943 *A.*2d 866 (2008). Were we not to reverse the award of punitive damages, we would be required to order a new trial on this issue.

In *Buckman*, plaintiffs claiming injury as the result of use of orthopedic bone screw devices in spinal surgery sued a consulting company that aided the manufacturer of the devices in obtaining market clearance for their use under § 510(k) of the Medical Device Amendments of 1976, applicable to manufacturers asserting that their devices were substantially equivalent to ones already on the market at the time of passage of the Amendments, and therefore full FDA review for safety and efficacy was unnecessary. Plaintiffs claimed that, in the course of gaining § 510(k) clearance, Buckman had fraudulently represented to the FDA that the elements of the bone screw devices would be used for fixation of the long bones of the arms and legs and were substantially equivalent to existing

devices used for that purpose, when in fact the manufacturer intended to market the devices for use in spinal ***89** surgery-a use for which § 510(k) clearance had been previously denied.

Reversing the decision of a divided panel of the United States Court of Appeals for the Third Circuit, the Supreme Court found that plaintiffs' fraud claims were impliedly preempted by federal statute. In doing so, the Court declined to recognize a presumption against preemption, determining that "[p]olicing fraud against federal agencies is hardly 'a field which the States have traditionally occupied.' " *Id.* at 347, 121 *S.Ct.* at 1017, 148 *L.Ed.*2d at 860 (quoting *Rice v. Santa Fe Elevator Corp.*, 331 *U.S.* 218, 230, 67 *S.Ct.* 1146, 1152, 91 *L.Ed.* 1447, 1459 (1947)). The *Buckman* Court observed:

> The relationship between a federal agency and the entity it regulates is inherently federal in character because the relationship originates from, is governed by, and terminates according to federal law .... Accordingly-and in contrast to situations implicating "federalism concerns and the historic primacy of state regulation of matters of health and safety,"****273** *Medtronic, [Inc. v. Lohr, supra,]* 518 *U.S.* at 485, [116 *S.Ct.* at 2250, 135 *L.Ed.*2d at 715]-no presumption against pre-emption obtains in this case.

[*Id.* at 347-48, 121 *S.Ct.* at 1017, 148 *L.Ed.*2d at 860-61.]

In this circumstance, the Court held that principles of implied preemption applied to bar the plaintiffs' claims. Significantly, it declined to determine whether express preemption pursuant to 21 *U.S.C.A.* § 360k was also applicable. The Court found:

> The conflict stems from the fact that the federal statutory scheme amply empowers the FDA to punish and deter fraud against the Agency, and that this authority is used by the Agency to achieve a somewhat delicate balance of statutory objectives. The balance sought by the Agency can be skewed by allowing fraud-on-the-FDA claims under state tort law.

[*Id.* at 348, 121 *S.Ct.* at 1017, 148 *L.Ed.*2d at 861.]

In support of its position, the Court noted that the MDA's disclosure requirements were accompanied by a substantial number of provisions designed to detect, deter and punish false statements made during the approval process. ***90** *Id.* at 349, 121 *S.Ct.* at 1017-18, 148 *L.Ed.*2d at 861-62. Further, the Court observed that the DFCA "leaves no doubt that it is the Federal Government rather than private litigants who are authorized to file suit for noncompliance with the medical device provisions." *Id.* at 349 n. 4, 121 *S.Ct.* at 1018 n. 4, 148 *L.Ed.*2d at 862 n. 4. Flexibility in the use by the FDA of these remedies was characterized by the Court as "a critical component" in the statutory and regulatory framework within which the FDA fulfilled its purpose of ensuring safety and efficacy without, in the context of off-label use, interfering with medical decision-making by physicians. *Id.* at 349-50, 121 *S.Ct.* at 1018, 148 *L.Ed.*2d at 862.

Although the decision in *Buckman* must be read in light of the recent affirmance, by an equally divided Court, of the Second Circuit's decision in *Desiano v. Warner-Lambert & Co.*, 467 *F.*3d 85 (2d Cir.2006), *see Warner-Lambert Co. v. Kent*, --- *U.S.* ----, 128 *S.Ct.* 1168, 170 *L.Ed.*2d 51 (2008), we nonetheless find *Buckman* to be controlling precedent in this case. We reach this conclusion because we perceive a difference between the purposes of compensatory and punitive damages that renders the distinctions drawn by the *Desiano* court between the fraud claims before it and those in *Buckman* inapplicable in the present context.

[20] An award of punitive damages has a purpose that is entirely different from a compensatory award. As we stated in *Tarr v. Bob Ciasulli's Mack Auto Mall, Inc.*, 390 *N.J.Super.* 557, 916 *A.*2d 484 (App.Div.2007), *aff'd*, 194 *N.J.* 212, 943 *A.*2d 866 (2008), when discussing the scope of the New Jersey Punitive Damages Act, *N.J.S.A.* 2A:15-5.9 to -5.17 [FN47]:

> FN47. The Punitive Damages Act is applicable to the present case in concert with the punitive damage provisions of the PLA. *See DePalma v. Bldg. Inspection Underwriters*, 350 *N.J.Super.* 195, 223-26, 794 *A.*2d 848 (App.Div.2002).

The State has a legitimate interest "in punishing unlawful conduct and deterring its repetition." *BMW of N. Am., Inc. v. Gore*, 517 *U.S.* 559, 568, 116 *S.Ct.* 1589, 1595, 134 *L.Ed.*2d 809, 822 (1996). The Act provides that the purpose of a punitive damage award is "to punish the defendant and to deter that defendant from repeating such conduct." *N.J.S.A.* 2A:15-5.14. The Act defines punitive damages as "exemplary ... damages awarded against a party in a civil action ****274** because of aggravating circumstances in order to penalize and to provide additional deterrence against a defendant to discourage similar conduct in the future." *N.J.S.A.* 2A:15-5.10.

[*Id.* at 565, 916 *A.*2d 484.]

***91** In contrast, the purpose of compensatory damages is to make the individual plaintiff whole. *Caldwell v. Haynes*, 136 *N.J.*

422, 433, 643 *A.*2d 564 (1994). That purpose, in a personal injury compensation context, "is neither to reward the plaintiff, nor to punish the defendant, but to replace plaintiff's losses." *Ibid.* (quoting *Domeracki v. Humble Oil & Ref. Co.*, 443 *F.*2d 1245, 1250 (3d Cir.), *cert. denied*, 404 *U.S.* 883, 92 *S.Ct.* 212, 30 *L.Ed.*2d 165 (1971)).

With these distinctions in mind, we discuss *Desiano,* which concerned whether the compensatory damage provisions of Michigan's products liability statute were preempted by federal law as the result of *Buckman.* The Michigan statute affords a conclusive presumption that compliance with FDA standards on labeling of a federally-approved drug demonstrates due care. *Mich. Comp. Laws* § 600.2946(5).[FN48] However, the statute provides that the section precluding suit against the manufacturer of a regulatorily compliant drug "does not apply" if there is evidence that the manufacturer "[i]ntentionally withh[eld] from or misrepresent[ed] to the [FDA] information concerning the drug that [was] required to be submitted under the [FDCA] and the drug would not have been approved, or the [FDA] would have withdrawn approval for the drug if the information were accurately submitted." *Id.* § 600.2946(5)(a). The compensatory damage provisions of the Michigan Act bear similarities to the punitive damage provisions of *N.J.S.A.* 2A:58C-5c, which bar punitive damages if the drug has received FDA approval, but grant an exception "where the product manufacturer knowingly withheld or misrepresented information required to be submitted under the agency's regulations, ***92** which information was material and relevant to the harm in question."

FN48. The statute provides:

> In a product liability action against a manufacturer or seller, a product that is a drug is not defective or unreasonably dangerous, and the manufacturer or seller is not liable, if the drug was approved for safety and efficacy by the United States food and drug administration, and the drug and its labeling were in compliance with the United States food and drug administration's approval at the time the drug left the control of the manufacturer or seller.

In finding that *Buckman* 's implied preemption holding was not controlling, the *Desiano* court distinguished the cause of action before it-a preexisting common-law claim that had overcome the immunity provisions of Michigan law-from the claim at issue in *Buckman*-a specific cause of action premised upon fraud on the FDA. 467 *F.*3d at 92-93. The court acknowledged that it was "undoubtedly true," as stated in *Buckman,* that "[p]olicing fraud against federal agencies is hardly a field which the States have traditionally occupied" and, as a result, the presumption against preemption was inapplicable to fraud-on-the-FDA claims. *Id.* at 93 (quoting *Buckman, supra,* 531 *U.S.* at 347, 121 *S.Ct.* at 1017, 148 *L.Ed.*2d at 860). In the absence of a presumption against preemption, the Buckman Court could reasonably determine that a conflict between plaintiff's cause of action (derivative of federal law) and federal statute existed because "*policing fraud on the FDA* through a tort action could interfere with how the FDA might wish to police that kind of fraud itself." *Ibid.*

In contrast, the court held that, in *Desiano,* plaintiffs' cause of action was premised upon the common law, which survived ****275** statutory immunity by virtue of the fraud exception, and thus the presumption against preemption was applicable. *Id.* at 93-94. Although statutory immunity could be claimed by a manufacturer as an affirmative defense, *id.* at 96, if immunity were overcome by evidence of fraud, a plaintiff's entire common-law claim would then be recognized. *Id.* at 95. Thus, unlike "the unusual and narrow claim before the *Buckman* Court," *ibid.*, the court observed that the *Desiano* plaintiffs' cause of action could not "reasonably be characterized as a state's attempt to police fraud against the FDA." *Id.* at 94. The court concluded:

> Significantly, all of the claims advanced by Appellants in this case are premised on traditional duties between a product manufacturer and Michigan consumers. None of them derives from, or is based on, a newly-concocted duty between a manufacturer and a federal agency. As a result, were we to conclude that Appellants' claims were preempted, we would be holding that Congress, without ***93** any explicit expression of intent, should nonetheless be taken to have modified (and, in effect, gutted) traditional state law duties between pharmaceutical companies and their consumers. We see no reason, nor can we identify any precedent, to justify such a result.

[*Id.* at 94-95 (footnote omitted).]

Although, as we have previously noted, the language of the punitive damage provisions of the PLA resembles that of the compensatory damage provisions of the Michigan product liability act, in that each contains an immunity provision that can be overcome by evidence of fraud on the FDA, that fact does not require the two statutes to be construed similarly for preemption purposes. Significantly, *N.J.S.A.* 2A:58C-5c is designed to effectuate the State's interest in punishing unlawful conduct. *Tarr, supra,* 390 *N.J.Super.* at 565, 916 *A.*2d 484 (citing *Gore, supra,* 517 *U.S.* at 568, 116 *S.Ct.* at 1595, 134 *L.Ed.*2d at 822). In that context, a plaintiff bringing a product liability action acts in a fashion akin to a private attorney general, since any damages awarded on his punitive damage claim do not compensate him for his injury, but instead vindicate societal interests. *See, e.g., Jackson v. Johns-Manville Sales Corp.*, 781 *F.*2d 394, 403 (5th Cir.1986); *Walker v. Sheldon*, 10 *N.Y.*2d 401, 223 *N.Y.S.*2d 488, 179 *N.E.*2d 497, 498

(1961). And in this context, the statutory focus, like that in *Buckman,* is narrowly drawn upon a defendant's act of knowingly withholding from or misrepresenting to the FDA information material to the harm alleged. This limited claim for punitive damages, focused upon deterring a manufacturer's knowingly inadequate response to FDA informational requirements, thus differs from the common law compensatory claims at issue in *Desiano,* as to which a strong presumption against preemption applies.

Although there are differences between the fraud-on-the-FDA claim asserted in *Buckman* and McDarby's punitive damage claim premised on the withholding of information regarding the incidence of myocardial infarctions demonstrated by a meta-analysis, we find the single focus upon fraud on the FDA in each to be sufficiently similar to warrant the application of *Buckman* to this ***94** case. As the *Desiano* court noted, at oral argument in *Buckman,* the pharmaceutical industry stressed the limited nature of the claim presented when it began by stating that the plaintiffs were not alleging a design or manufacturing defect or medical malpractice.

> [T]he plaintiffs' sole claim in this case is the following. They assert that the Federal Food & Drug Administration was deceived into giving regulatory ****276** clearance to these devices, that, absent this deception, these devices would never have been on the market, and that, if the devices had never have been on the market, they wouldn't have been used in their surgeries and they wouldn't have suffered any injuries.

[*Desiano, supra,* 467 *F.*3d at 96.]

This claim closely resembles plaintiffs' position in the present matter that if the complete meta-analysis had been furnished by Merck to the FDA, it would have responded in a different fashion to Merck's supplemental new drug application, approved in April 2002. Because the punitive damages provisions of *N.J.S.A.* 2A:58C-5c impinge upon federal statute and regulation to the same extent that was recognized in *Buckman,* 531 *U.S.* at 349, 121 *S.Ct.* at 1017-18, 148 *L.Ed.*2d at 861-62, we find the principles of implied preemption applied by the Court in *Buckman* to be applicable here.

We thus find McDarby's punitive damage claim to have been preempted and reverse that award.

IX.

Determining that violations of the CFA had occurred that caused ascertainable losses both to John McDarby and to Thomas Cona, the jury awarded damages to each, consisting of the out-of-pocket costs incurred by the two plaintiffs for their purchases of Vioxx.[FN49] The basic award to McDarby was $3968; the award to ***95** Cona was $45. Each was trebled, pursuant to *N.J.S.A.* 56:8-19. Additionally, following trial, the judge also awarded attorneys' fees and costs to plaintiffs as authorized by the same provision of the CFA, granting McDarby an award of $1,615,548 in fees and $162,399 in costs, and granting Cona an award of $2,268,802.80 in fees and $177,870.68 in costs.

> FN49. The jury did not find that Merck committed consumer fraud by using unconscionable commercial practices when marketing Vioxx to prescribing physicians. However, it found that Merck had made misrepresentations that had the capacity to mislead concerning the cardiovascular risk of Vioxx while marketing the drug to prescribing physicians, and that Merck had intentionally suppressed, concealed or omitted material information about an association between Vioxx and an increased risk of cardiovascular events from prescribing physicians.

[21] Merck has appealed from those awards, arguing first that plaintiffs' claims that it misrepresented the safety of Vioxx are not cognizable under the CFA, but only pursuant to the PLA. Additionally, Merck asserts in connection with the award of damages to Cona, whose heart attack was not found to have been causally related to the use of Vioxx and who admitted that he had received symptomatic relief from the administration of the drug, that Cona failed to offer a cognizable theory of ascertainable loss under the CFA and that he had had failed to prove a causal nexus between Merck's alleged fraud and his claimed loss. Merck argues, as well, that the CFA claims of both plaintiffs are preempted by the FDCA and, as a final matter, that the award of attorneys' fees was unreasonable. We agree with Merck's first argument-that the PLA subsumes plaintiffs' CFA claims-and thus find no need to address Merck's additional contentions.

[22] In their brief in opposition to Merck's appeal from judgments entered as the result of alleged violations of the CFA, Cona's attorneys [FN50] admit: "The gravamen ****277** of plaintiffs' consumer fraud claim was that Merck marketed Vioxx fully aware of its cardiovascular risk but made misrepresentations, and intentionally ***96** suppressed, concealed, or omitted material information [and] failed to be truthful while marketing the drug to prescribing physicians." Although asserting what, in essence, is a claim of failure to warn of dangers inherent in Vioxx cognizable under the PLA, *N.J.S.A.* 2A:58C-2 and -4, plaintiffs claim entitlement to an additional damage award for economic loss pursuant to *N.J.S.A.* 56:8-2 as the result of the employment by Merck of an "unconscionable commercial practice, deception, fraud, false pretense, false promise, misrepresentation, or the knowing concealment, suppression, or omission of [a] material fact with intent that others rely upon such concealment, suppression or omission." Merck persuasively argues,

however, that by enacting the PLA, the New Jersey Legislature manifested its intent to replace all pre-existing claims by "one unified, statutorily defined theory of recovery for harm caused by a product." *In re Lead Paint Litig.*, 191 *N.J.* 405, 436, 924 *A.*2d 484 (2007) (quoting William A. Dreier et al., *New Jersey Products Liability & Toxic Torts Law* § 1:2-1 (2007)).

> FN50. Because of the nature of the damage awards, arguments by appellant and respondents with respect to the PLA were set forth in connection with the McDarby appeal, whereas arguments with respect to the CFA were set forth in connection with the Cona appeal. To avoid duplication in these back-to-back appeals, we permitted each party to adopt by reference arguments asserted in either case.

In its *Lead Paint* decision, the Court discussed at some length the scope of the PLA when affirming the dismissal on the pleadings of a public nuisance action by municipalities and other jurisdictions against manufacturers of lead paint that sought recovery of costs of detecting and removing such paint from homes and buildings, providing medical care to residents afflicted with lead poisoning, and developing educational programs about the paint's dangers. The Court's determination that plaintiffs' public nuisance theory was non-cognizable was based in part on its recognition of the "expansive and inclusive," *id.* at 436, 924 *A.*2d 484, language adopted by the Legislature in defining "product liability action" to include "any claim or action brought by a claimant for harm caused by a product, irrespective of the theory underlying the claim, except actions for harm caused by breach of an express warranty," *N.J.S.A.* 2A:58C-1(b)(3)-language that the Court characterized as "encompassing virtually all possible causes of action relating to harms caused by consumer and other products." *Lead Paint, supra*, 191 *N.J.* at 436-37, 924 *A.*2d 484. The Court then found that the language of the PLA embraced both the ***97** product at issue and the economic harms attributed by plaintiffs to the product. *Id.* at 437, 924 *A.*2d 484. "Were there any doubt," the Court concluded that a careful reading of the claims in plaintiffs' complaint would demonstrate that they sounded in product liability. *Ibid.* In that regard, the Court noted: "The central focus of plaintiffs' complaints is that defendants were aware of dangers associated with lead-and by extension, with the dangers of including it in paint intended to be used in homes and businesses-and failed to warn of those dangers." *Ibid.* The Court found that "this classic articulation of tort law duties, that is, to warn of or to make safe, is squarely within the theories included in the PLA." *Ibid.* (citing *N.J.S.A.* 2A:58C-2).

> In light of the clear intention of our Legislature to include all such claims within the scope of the PLA, we find no ground on which to conclude that the claims being raised by plaintiffs, regarding an ordinary household product used ****278** by consumers, were excluded from the scope of that Act.
>
> [*Ibid.*]

Although the cause of action under the CFA asserted by plaintiffs in the present matter differs from the public nuisance theory espoused by the plaintiffs in the *Lead Paint* litigation, we can discern no reason to distinguish the two actions on that ground. As in *Lead Paint*, plaintiffs' own arguments make it clear that what they are asserting is, at its core, that Merck failed to warn of dangers from a product of which it had knowledge, resulting in alleged economic harm to them. Further, the economic "harm" upon which their claims are based, consisting of a loss "deriving from" personal physical illness, injury or death, pain and suffering, mental anguish or emotional harm, and loss of consortium is, as in *Lead Paint*, encompassed within the definition of harm set forth in the PLA. *See N.J.S.A.* 2A:58C-1(b)(2).

> [23] As the Court stated in *Zaza v. Marquess & Nell, Inc.*:
>
> The Legislature passed the [PLA] as "remedial legislation to establish clear rules [in] ... actions for damages for harm caused by products, including certain principles under which liability is imposed." *N.J.S.A.* 2A:58C-1. The Act has been interpreted as evincing a legislative policy "to limit the expansion of products-liability law." *Roberts v. Rich Foods, Inc.*, 139 *N.J.* 365, 374, 654 *A.*2d 1365 (1995) (quoting *Shackil v. Lederle Labs.*, 116 *N.J.* 155, 187, 561 *A.*2d 511 (1989)). The ***98** Legislature intended for the Act to limit the liability of manufacturers so as to "balance[ ] the interests of the public and the individual with a view towards economic reality." *Shackil, supra*, 116 *N.J.* at 188, 561 *A.*2d 511 (quoting *Shackil v. Lederle Labs.*, 219 *N.J.Super.* 601, 643, 530 *A.*2d 1287 (1987) (Shebell, J.A.D., dissenting), *rev'd.*, 116 *N.J.* 155, 561 *A.*2d 511 (1989)). *See also DePrimo v. Lehn & Fink Prods. Co.*, 223 *N.J.Super.* 265, 273, 538 *A.*2d 461 (Law Div.1987) (finding that in interpreting the Act, courts should "as a matter of sound judicial policy, ... apply this conservative legislative policy").
>
> [144 *N.J.* 34, 47-48, 675 *A.*2d 620 (1996).]

With these precepts in mind, we find no basis, in legislative history, statutory language or Court decisions, to conclude that plaintiffs can maintain separate causes of action under the PLA and the CFA in this case. As Merck notes, to permit such an expanded form of relief would be to destroy the balance established between the interests of manufacturers, the public and individuals established by the Legislature in enacting the PLA by introducing an otherwise unavailable treble-damage remedy for harms resulting

from a failure to warn. *See Rowe, supra, 189 N.J. at 623-24, 917 A.2d 767* (discussing the balance in favor of manufacturers established by the PLA). Additionally, the essential effect of recognition of a cause of action for the fraudulent withholding of safety information such as that espoused by plaintiffs pursuant to the CFA-a cause of action that likely would be available to most product liability plaintiffs claiming a failure to warn-would be to permit an award of attorneys fees in the majority of product liability actions without Legislative authorization for such relief. We find no warrant for such action.[FN51] Plaintiffs' verdicts based ****279** upon Merck's alleged violation of the CFA are thus reversed, and the awards of attorneys' fees and costs are vacated.

> FN51. While finding no need to directly address the issue of federal preemption, we note our concern that a cause of action pursuant to the CFA could be deemed preempted under the principles established in *Buckman* that we discussed in connection with McDarby's punitive damage claim.

In summary, we affirm the award of compensatory damages to McDarby pursuant to the PLA, determining that the cause of action asserted under that statute is not preempted and that no ***99** reversible error occurred in connection with that claim. We reverse the award of punitive damages pursuant to the PLA as preempted by the FDCA, and we reverse the awards of damages to McDarby and Cona and the awards of attorneys' fees pursuant to the CFA, determining that plaintiffs' CFA claims are subsumed within the PLA.

Affirmed in part and reversed in part.

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