CASE COMMENT

THE LACK OF PRE-EMPTION FOR PRESCRIPTION DRUGS: HOW JURIES HAVE REPLACED THE FDA AS MEDICAL EXPERTS *MUT. PHARM. CO. v. BARTLETT*, 133 S. CT. 2466 (2012)

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INTRODUCTION

Plaintiff, Karen Bartlett, suffered serious injuries[1] after ingesting a generic form of Clinoril®, sulindac,[2] manufactured by Defendant, Mutual Pharmaceutical.[3] Plaintiff filed suit against Defendant in New Hampshire state court to recover damages for Plaintiff's injuries.[4] Plaintiff filed a design defect claim and a failure to warn claim alleging that the generic drug's label[5] inadequately warned of the risk of developing certain severe skin reactions.[6] Defendant removed the suit to federal court.[7] The District Court dismissed the failure to warn claim.[8]

A jury awarded Plaintiff twenty-one million dollars based on Plaintiff's design defect claim.[9] The First Circuit affirmed, holding that

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1. The patient's physician prescribed the patient the medication to treat shoulder pain. Mut. Pharm. Co. v. Bartlett, 133 S. Ct. 2466, 2472 (2012). After ingesting the medication, the patient developed an acute case of toxic epidermal necrolysis. *Id.* Approximately 60–65% of the surface of the patient's body deteriorated resulting in the surface burning off or turning into an open wound. *Id.* The patient spent months in a medically induced coma, underwent 12 eye surgeries, and was tube-fed for a year. *Id.* The patient currently has a number of physical disabilities and is nearly blind. *Id.*

2. *Id.* Sulindac is a non-steroidal anti-inflammatory prescription drug used to treat shoulder pain. *Sulindac*, CLINICAL PHARMACOLOGY, http://www.clinicalpharmacology-ip.com/Forms/Monograph/monograph.aspx?cpnum=584&sec=mondesc&t=0 (last visited Dec. 4, 2014).

3. *Mut. Pharm. Co.*, 133 S. Ct. at 2466.

4. *Id.*

5. *Id.* at 2472. The generic drug label for sulindac contained a warning that the drug may cause "severe skin reactions," but did not specifically caution against the risk of developing Stevens-Johnson Syndrome or toxic epidermal necrolysis. *Id*. However, the package insert that is given to doctors rather than patients did mention Stevens-Johnson Syndrome and toxic epidermal necrolysis as potential adverse reactions. *Id.*

6. *Id*.

7. *Id.* at 2472.

8. *Id.* The District Court dismissed the failure to warn claim based upon the doctor's admission that the doctor did not read the package insert or box label. *Id.*

9. *Id.*

neither the Food, Drug, and Cosmetic Act (FDCA) nor the Food and Drug Administration's (FDA) regulations pre-empted Plaintiff's design defect claim as Defendant could comply with federal and state law by simply choosing not to make the drug.[10] The U.S. Supreme Court granted certiorari, reversed, and HELD, that design defect claims that turn on the adequacy of a generic drug's warnings are pre-empted by federal law, which expressly prohibits manufacturers of generic drugs from making any unilateral changes to the drug's label.[11]

HISTORY

The FDCA requires manufacturers of brand-name or generic drugs to acquire FDA approval of the drug's safety and effectiveness prior to marketing the drug in interstate commerce.[12] Once approved, brand-name drug manufacturers are generally prohibited from unilaterally making any major changes to a drug's label.[13] Likewise, generic drug manufacturers are required to match the label of the brand-name drug counterpart.[14] In addition, under the Supremacy Clause,[15] state laws that conflict with federal law are without effect and thus pre-empted.[16]

The Supreme Court addressed the doctrine of express pre-emption as it relates to medical devices in *Riegel v. Medtronic, Inc*.[17] In *Riegel*, a patient brought common law claims against a device manufacturer after suffering injuries that resulted from the use of a device that the label for the device specifically cautioned against.[18] An issue in *Riegel* was

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10. *Id.*
11. *Id.* at 2470.
12. 21 U.S.C. § 355 (2012).
13. 21 C.F.R. § 314.70 (2014).
14. 21 C.F.R. § 314.94 (2014); *see also* 21 C.F.R. § 314.150 (2014) (approval of a generic drug may be withdrawn if the generic drug's label is no longer consistent with the label of the brand-name drug).
15. U.S. CONST. art. VI, cl. 2:

> This Constitution, and the Laws of the United States which shall be made in pursuance thereof; and all treaties made, or which shall be made, under the authority of the United States, shall be the supreme law of the land; and the judges in every state shall be bound thereby, anything in the constitution or laws of any state to the contrary notwithstanding.

16. Maryland v. Louisiana, 101 S. Ct. 2114, 2129 (1981).
17. Riegel v. Medtronic, Inc., 552 U.S. 312, 315 (2008).
18. *Id*. The patient underwent an angioplasty after suffering a myocardial infarction. *Id.* The doctor decided to use the manufacturer's balloon catheter during the procedure in order to dilate the patient's artery. *Id.* The catheter's label warned that the catheter should not be inflated above the rated burst pressure of eight atmospheres. *Id.* During the procedure, the doctor inflated the catheter to a pressure of ten atmospheres. *Id.* In addition, the catheter's label contained a

whether a patient's common law claims[19] were pre-empted by the pre-emption clause in the Medical Device Amendments of 1976 (MDA)[20] that challenged the safety and effectiveness of a medical device that received pre-market approval.[21] More specifically, the Supreme Court considered whether common law claims were considered different or additional requirements to the federal requirements of a pre-market approval and thus expressly pre-empted by the MDA.[22]

The Supreme Court held that the MDA expressly pre-empted the patient's common law claims, determining that the state common law duties were requirements that were "different from, or in addition to," the federal requirements.[23] The Supreme Court further determined that pre-market approvals of medical devices served as a specific safety and effectiveness review of that particular device.[24] Because the pre-market approval of a device served as a federal safety and effectiveness review, and the state common law duties were in addition to the federal requirements of a safety and effectiveness approval, the Supreme Court held that the pre-emption clause of the MDA pre-empted the common law claims.[25]

In *Wyeth v. Levine*, the Supreme Court considered whether the FDA approval of a brand-name drug's label pre-empted a patient's failure to warn claim against the brand-name drug manufacturer.[26] The patient suffered serious injuries following the intravenous (IV)-push administration of Wyeth's brand-name drug.[27] The drug label cautioned

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contraindication in which the catheter should not be used in patients with diffuse or calcified stenosis. *Id.* at 315. The patient in this case had a right coronary artery that was diffusely diseased and heavily calcified, but the doctor used the catheter despite this contraindication. *Id.* The catheter subsequently ruptured and the patient developed heart block. *Id.* The patient then underwent emergency coronary bypass surgery as a result of the heart block. *Id.*

19. The patient brought claims of strict liability, breach of implied warranty, and negligence in the design, testing, inspection, distribution, labeling, marketing, and sale of a catheter following injuries after the doctor's misuse of the manufacturer's balloon catheter. *Id.*

20. 21 U.S.C. § 360k (2012):

> Except as provided in subsection (b) of this section, no State or political subdivision of a 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.

21. *Riegel*, 552 U.S. at 322–23.
22. *Id.*
23. *Id.* at 330.
24. *Id.* at 323.
25. *Id.* at 330.
26. Wyeth v. Levine, 555 U.S. 555, 558 (2009).
27. *Id.* The patient received IV-push administration of the drug manufacturer's brand name

the higher risk of the drug escaping a patient's vein associated with the IV-push method as compared to the IV-drip method.[28] The patient filed a failure to warn claim stating that the warning inadequately cautioned against the risk of using the IV-push method.[29] The brand-name drug manufacturer argued that the FDCA's regulations concerning alterations to the drug label pre-empted the failure to warn claim because the state common law duties made it impossible for the brand-name drug manufacturer to comply with both the FDCA's regulations and the state common law duties.[30] Furthermore, the brand-name drug manufacturer argued that it could not change the label using the "changes being effected" (CBE)[31] regulation because it did not have any newly acquired information.[32]

The *Wyeth* Court held that federal law did not pre-empt the failure to warn claim because of the CBE regulation.[33] The 2008 amendment to the CBE regulation allowed manufacturers to unilaterally change the label upon obtaining "newly acquired information."[34] In determining that federal law did not pre-empt the failure to warn claim, the Supreme Court found that "newly acquired information" includes both new data as well as a reanalysis of previously submitted data.[35] The dissent notably focused on federal law's reliance on an FDA approval of a prescription drug and thus conflict pre-emption should have prevented the failure to

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drug Phenergan®, used to treat nausea. *Id.* The patient developed gangrene and the patient's entire left forearm had to be amputated as a result of the gangrene. *Id.*

28. *Id.* If a drug is administered via the IV-push method, the drug is injected directly into the patient's vein. *Id.* If a drug is administered via the IV-drip method, the drug is injected into a saline solution in a hanging intravenous bag. *Id.* Once the drug is placed in the hanging bag, the drug slowly descends into a catheter inserted into the patient's vein. *Id.* When a drug is injected into a patient's vein by either method, the drug can escape the patient's veins by one of two ways. *Id.* First, the drug can escape the patient's vein if the needle used to inject the drug penetrates the vein. *Id.* Second, the drug can escape through a phenomenon known as perivascular extravasation, in which the drug escapes the vein into surrounding tissue. *Id.* Using the IV-push method creates a higher risk of the drug escaping the patient's vein since it is injected directly into the vein. *Id.* If Phenergan® escapes a patient's artery, the patient may develop irreversible gangrene due to the corrosiveness of the drug. *Id.*

29. *Id.* at 559. The patient argued that the warning should have instructed clinicians to use the IV-drip method rather than the IV-push method. *Id*.

30. *Id.* at 568.

31. 21 C.F.R. § 314.70 (2014). The CBE regulation allowed manufacturers to unilaterally change the drug label without FDA approval upon filing a supplemental application only if the manufacturer is changing the label to "add or strengthen a contraindication, warning, precaution, or adverse reaction" or to "add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product." *Id.*

32. *Wyeth*, 555 U.S. at 568.

33. *Id.* at 573.

34. *Id.* at 568.

35. *Id.* at 569.

warn claim.[36]

The Supreme Court subsequently addressed the issue of pre-emption as it relates to a generic drug manufacturer's responsibility for the contents of its generic drug's label.[37] In *PLIVA, Inc. v. Mensing*, a patient brought a failure to warn claim against a generic drug manufacturer[38] that produced the drug metoclopramide.[39] The patient alleged that the manufacturer's label inadequately warned of the risk of developing tardive dyskinesia[40] associated with the long-term use of metoclopramide.[41] The manufacturer argued that federal laws regarding the labels of generic drugs pre-empted the failure to warn claim because the state common law duties made it impossible for the generic drug manufacturer to comply with both federal and state law.[42]

The Supreme Court held that federal law pre-empted state laws that imposed a duty on generic drug manufacturers to change a generic drug's label.[43] The Supreme Court distinguished *PLIVA* from *Wyeth* due to the fact that brand-name manufacturers had the possibility of changing the label through the CBE regulation.[44] However, generic drug manufacturers did not have that same option as generic drug manufacturers must match the labels of their generic drugs to the labels of the corresponding brand-name drugs.[45] Accordingly, the Supreme Court determined that federal law pre-empted the failure to warn claim as complying with the state imposed duty would directly violate federal law.[46]

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36. *Id.* at 606 (Alito, J., dissenting).

37. PLIVA, Inc. v. Mensing, 131 S. Ct. 2567, 2572 (2011).

38. *Id.*

39. *Id.* Metoclopramide is the generic form of the brand-name drug Reglan®. *Metoclopramide*, CLINICAL PHARMACOLOGY, http://www.clinicalpharmacology-ip.com/Forms/Monograph/monograph.aspx?cpnum=757&sec=mondesc&t=0 (last visited Dec. 4, 2014). Metoclopramide is a prokinetic and antiemetic drug used to treat nausea and several digestive tract problems. *Id.*

40. *PLIVA*, *Inc.*, 131 S. Ct. at 2573. Tardive dyskinesia is a side effect associated with the long-term use of metoclopramide. *Metoclopramide*, *supra* note 39. Tardive dyskinesia consists of involuntary, repetitive tic-like movements primarily in the facial muscles but may also occur in limbs, fingers, and toes. *Id.* Tardive dyskinesia associated with metoclopramide use is most often permanent and difficult to treat. *Id.*

41. *PLIVA*, *Inc.*, 131 S. Ct. at 2573.

42. *Id.*

43. *Id.* at 2581.

44. *Id.*

45. *Id.* at 2575.

46. *Id. at* 2582.

INSTANT CASE

The instant case required an application and expansion of *PLIVA*. The First Circuit avoided the pre-emption issue by arguing that generic manufacturers can comply with state and federal law by simply not marketing the product in that particular state.[47] The Supreme Court flatly rejected this notion[48] and determined that, similar to *PLIVA*, the design defect claim turned on whether a generic drug manufacturer may unilaterally strengthen a warning.[49] As the Supreme Court found that federal law pre-empted the design defect claim,[50] the instant case expands the field of pre-emption for generic drug manufacturers to include not only failure to warn claims, but also design defect claims that turn on the adequacy of the drug's warning.[51]

In the instant case, New Hampshire design defect claims imposed affirmative duties on manufacturers to design products to be reasonably safe.[52] In assessing whether a drug is unreasonably dangerous, New Hampshire employed a risk-utility approach looking at three factors: (1) the usefulness of the product; (2) whether the risk of the danger could be reduced without significantly affecting the cost and effectiveness of the product; and (3) the presence and adequacy of a warning.[53] The Supreme Court found that the first two factors required the manufacturer to alter the product's design—which was not possible and thus not at issue.[54] Therefore, the manufacturer could only ameliorate the risk-utility analysis by altering the warning.[55]

As *PLIVA* made clear, federal law prevented generic drug manufactures from unilaterally changing the label.[56] Therefore, the manufacturer could not take remedial action to avoid liability under state law.[57] Since the manufacturer could not possibly comply with both state and federal law, the Supreme Court determined that federal law pre-empted the design defect claim.[58]

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47. Mut. Pharm. Co. v. Bartlett, 133 S. Ct. 2466, 2472 (2012).
48. *Id.* at 2470.
49. *Id.* at 2475.
50. *Id*. at 2470.
51. *Id.*
52. *Id.* at 2474.
53. *Id.* at 2475.
54. *Id*.; *see also* 21 U.S.C. §§ 355(j)(2)(A)(ii-v) (2012) (the generic drug must have the same active ingredient, dosage form, strength, route of administration, and rate and extent of absorption as the brand-name counterpart).
55. *Mut. Pharm. Co.*, 133 S. Ct. at 2475.
56. PLIVA, Inc. v. Mensing, 131 S. Ct. 2567, 2581 (2011).
57. *Id.*
58. *Mut. Pharm. Co.*, 133 S. Ct. at 2470.

ANALYSIS

Since generic drugs have entered the market, the FDA has ensured generic drugs contain the same active ingredients, dosage form, strength, and other bioequivalency standards.[59] In addition, generic drugs are generally eighty to eighty-five percent cheaper than the brand-name counterpart.[60] Thus, when a consumer is provided the option to purchase a generic or brand-name drug, the generic is chosen most often. Because of these considerations, generic drugs account for approximately eighty percent of the prescription drugs consumed in America.[61]

As greater numbers of consumers purchase generic drugs, they often do not realize they will be without legal recourse if they suffer an injury from the generic drug.[62] In affirming and expanding *PLIVA*, the instant case held that generic drug state design defect claims are pre-empted under federal law.[63] Therefore, generic drug manufacturers are protected against liability while the brand-name drug manufacturers are still liable for design defect and failure to warn claims.[64] Consumers are essentially choosing to pay less up front for generic drugs, but they may have to pay far more if they are injured as a result of taking those drugs.

However, in November 2013, the FDA proposed a new rule that would provide a CBE regulation for generic drug manufacturers.[65] If the generic drug formulation of the CBE is interpreted in the same manner as the CBE regulation for brand-name drugs, then consumers of generic drugs will not be without legal recourse. But would this result prove beneficial? And, considering that FDA review teams consist of medical doctors, chemists, statisticians, microbiologists, pharmacologists, and other experts, should state tort juries, rather than the FDA, regulate the warning labels of prescription drugs?[66]

An alternative analysis of the pre-emption field of prescription drug products as a whole traces back to the dissent in *Wyeth*. In *Wyeth*, the dissent focused on the federal law's reliance on the FDA's determination

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59. *Facts About Generic Drugs*, U.S. FOOD & DRUG ADMIN., *available at* http://www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/understandinggenericdrugs/ucm167991.htm.

60. *Id.*

61. *Id*.

62. Marie Boyd, *Unequal Protection Under the Law: Why FDA Should Use Negotiated Rulemaking to Reform the Regulation of Generic Drugs*, 35 CARDOZO L. REV. 1525, 1527 (2014).

63. *Mut. Pharm. Co.*, 133 S. Ct. at 2470.

64. Boyd, *supra* note 62, at 1527.

65. Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, 78 Fed. Reg. 67985 (proposed Nov. 13, 2013) (to be codified at 21 C.F.R. pts. 314 and 601).

66. Mary K. Olson, *PDUFA and Initial U.S. Drug Launches*, 15 MICH. TELECOMM. & TECH. L. REV. 393, 396 (2009).

that a drug product is safe and effective.[67] The FDA approval of a drug is quite rigorous, as it generally demands at least three phases of clinical trials to determine safety and effectiveness.[68] In addition, the FDA thoroughly examines the drug's label to further assess the safety and effectiveness of the drug.[69] The FDA will only approve the drug if the drug is safe under the suggested uses on the label, there is evidence that the drug will have the effect described on the label, and the label is not false or misleading.[70]

Considering what it takes to obtain FDA approval, the dissent in *Wyeth* turned to the doctrine of conflict pre-emption.[71] The principles of conflict pre-emption turn on whether a state has upset the regulatory balance struck by the federal agency.[72] In *Wyeth*, the dissent determined that the FDA approval of the drug's label pre-empted the tort suit, even though the CBE regulation was in effect.[73] More specifically, the dissent found that the FDA and drug manufacturer strengthened and altered the drug's label multiple times for a period of thirty-four years when assessing the adequacy of the warning.[74] Since the FDA approved the strengthened warnings, the dissent believed that the state tort suit challenging the adequacy of the warning would upset the regulatory balance struck by the FDA regarding drug labels.[75]

Consistent with the dissent in *Wyeth*, other fields in medical technology provide guidance on whether an FDA approval should pre-empt state tort claims.[76] A prescription drug product's FDA approval is as rigorous, if not more rigorous, than a medical device's pre-market approval.[77] Likewise, an FDA approval of a medical device and prescription drug consists of a federal review of the device or drug's safety and effectiveness.[78] However, medical devices that receive pre-

67. Wyeth v. Levine, 555 U.S. 555, 606 (2009) (Alito, J., dissenting).

68. 21 C.F.R. § 312.21 (2014).

69. 21 U.S.C. § 355(b)(1) (2012).

70. 21 U.S.C. § 355(d) (2012).

71. *Wyeth*, 555 U.S. at 610 (Alito, J., dissenting).

72. Geier v. Am. Honda Motor Co., 529 U.S. 861, 865–68 (2000).

73. *Wyeth*, 555 U.S. at 610 (Alito, J., dissenting).

74. *Id.* at 612–19. The patient in *Wyeth* was injured in 2000. *Id.* at 559. As of 2000, the label consisted of several warnings including, but not limited to: a full page discussing the use of the Tubex system that is used only for IV-push administration; cautioning against the use of plungers with rigid needles to protect against puncturing a vein; the warning that "INADVERTENT INTRA–ARTERIAL INJECTION CAN RESULT IN GANGRENE OF THE AFFECTED EXTREMITY" in bold letters; directing medical professionals to choose veins wisely when using the IV-push method; and a warning against the risk of aspiration that is only associated with the use of the IV-push method. *Id.* at 612–19.

75. *Id.* at 621.

76. *See, e.g.*, Riegel v. Medtronic, Inc., 552 U.S. 312, 330 (2008).

77. *Wyeth*, 555 US at 607–08 (Alito, J., dissenting).

78. *See id.*

market approval are protected from state common law duties[79] by an express pre-emption clause within the MDA,[80] while prescription drugs are not.[81]

The MDA prevents states from establishing any requirement in addition to the requirements of the MDA that relates to the safety and effectiveness of the device.[82] The Supreme Court held that state common law duties were additional requirements under the MDA, and thus common law claims were pre-empted by federal law.[83] On the other hand, the FDCA does not contain any language similar to that effect, hence express pre-emption is not applicable for prescription drug products.[84] However, as discussed earlier, the dissent in *Wyeth* believed that conflict pre-emption should still prevent a common law claim.[85] Therefore, similar to a pre-market approval of a medical device, the FDA's approval of a prescription drug should pre-empt state common law claims challenging the safety and effectiveness of the drug based upon the doctrine of conflict pre-emption.[86]

This alternative approach to the pre-emption field for prescription drug products could lead to harsh results for some patients. However, drug manufacturers spend billions of dollars and years of scientific research to obtain FDA approval for a prescription drug product.[87] Likewise, FDA approval consists of three phases of clinical trials and a review of the manufacturing process, packaging, and labeling of the prescription drug.[88] In the end, the FDA approval is a cost-benefit analysis that balances the drug's safety, quality, and efficacy.[89]

In contrast to the FDA's analysis, juries see only the cost of expensive improvements or changes—not the benefits of those changes.[90] Juries also do not see the patients that benefitted from the FDA approved drug.[91] Rather, jury members see only an injured party and do not apply cost-

79. *Riegel*, 552 U.S. at 330.
80. 21 U.S.C. § 360k (2012).
81. *Wyeth*, 555 U.S. at 609 (Alito, J., dissenting).
82. 21 U.S.C. § 360k (2012).
83. *Riegel*, 552 S. Ct. at 330.
84. *Wyeth*, 555 U.S. at 609 (Alito, J., dissenting).
85. *Id.*; *see supra* text accompanying notes 71–75.
86. Geier v. Am. Honda Motor Co., 529 U.S. 861, 869–70 (2000) (holding that the absence of an express pre-emption clause does not bar the ordinary working of conflict pre-emption principles).
87. Stuart R. Cohn & Erin M. Swick, *The Sitting Ducks of Securities Class Action Litigation: Bio-Pharmas and the Need for Improved Evaluation of Scientific Data*, 35 DEL. J. CORP. L. 911, 916 (2010).
88. *Id.* at 917–18.
89. *Id.* at 919.
90. Riegel v. Medtronic, Inc., 552 U.S. 312, 325 (2008).
91. *Id.*

benefit analyses.[92] If juries continuously increase the liability of prescription drug manufacturers, these manufacturers would cover the costs of liability by increasing the price of prescription drugs. As a result, overall healthcare costs would continue to increase.

CONCLUSION

Although the Supreme Court reached the correct judgment in the instant case, the rationale of the decision is imperfect as is the rationale of previous cases addressing pre-emption in the prescription drug arena. The dissent in *Wyeth* reached the correct conclusion in which the expertise of an FDA drug panel consisting of medical doctors, chemists, statisticians, microbiologists, pharmacologists, and other experts should control the labeling of prescription drugs, not state tort juries.[93] Although there is no express pre-emption clause in the FDCA, the doctrine of conflict pre-emption should prevent additional state requirements to the safety and effectiveness of prescription drugs.

Once the new CBE regulation for generic drug manufacturers is passed, the decisions in *PLIVA* and the instant case will essentially be nullified as both cases were premised on the absence of a CBE regulation for generic drug manufacturers. Therefore, all drug manufacturers will now be susceptible to additional safety and effectiveness requirements arising from state tort duties. Is this the appropriate course of action? If so, drug manufacturers will respond by increasing the price of prescription drug products, thus increasing the overall healthcare costs. Moreover, the associated costs of liability may dissuade manufacturers from developing new products that could benefit many patients.

92. *Id.*
93. *Id.*