Nos. 09-993, 09-1039, and 09-1501

IN THE

# Supreme Court of the United States

PLIVA, INC., ET AL.,

*Petitioners,*

*v.*

GLADYS MENSING,

*Respondent.*

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ACTAVIS ELIZABETH, LLC,

*Petitioner,*

*v.*

GLADYS MENSING,

*Respondent.*

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ACTAVIS INC.,

*Petitioner,*

*v.*

JULIE DEMAHY,

*Respondent.*

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**ON WRITS OF CERTIORARI TO THE UNITED STATES COURTS OF APPEALS FOR THE EIGHTH CIRCUIT AND FOR THE FIFTH CIRCUIT**

## BRIEF FOR MARC T. LAW, JOHN ABRAMSON, JULIE DONOHUE, MICHAEL FISCHER, AND MEREDITH ROSENTHAL AS *AMICI CURIAE* IN SUPPORT OF RESPONDENTS

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## INTEREST OF *AMICI CURIAE*[1]

*Amici* are practitioners and professors who teach and write on various aspects of pharmaceutical regulation and the delivery of healthcare. *Amici* are filing this brief as individuals.

Marc T. Law, Ph.D., is an Associate Professor in the Department of Economics at the University of Vermont and earned his Ph.D. in Economics from Washington University. He has written several papers on the origins and evolution of food and drug regulation and focuses his research generally on the role of asymmetric information about product quality in the rise of the U.S. regulatory state.

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1. The parties have lodged letters with the Court consenting generally to the filing of all briefs by *amicus curiae*. No counsel for any party in the above-captioned cases authored this brief in whole or in part and no person or entity other than *amici* or their counsel has made a monetary contribution to the preparation or submission of this brief.

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## SUMMARY OF ARGUMENT

*Amici* support the view of the respondents and the circuit courts: Congress has not preempted state-law failure-to-warn claims brought against manufacturers of generic drugs.

Generic drugs constitute over three-quarters of the distributed prescription drugs in the United States, typically comprising well over 90% of prescriptions for a pill that has "gone generic." The Drug Price Competition and Patent Term Restoration Act of 1984 ("Hatch-Waxman"),[2] state generic substitution laws, lower reimbursement rates, and other institutional incentives have all combined to propel twenty-five years of generic pharmaceutical industry growth, which now amounts to $60 billion in U.S. sales annually. But the Hatch-Waxman incentives were intended to provide a means to deliver less expensive, *yet equally safe*, drug products. States should not be foreclosed from enforcing failure-to-warn laws that provide needed incentives to generic drug manufacturers to report to the FDA information that manufacturers learn about safety risks or signals concerning these widely used products.

State-law failure-to-warn litigation plays an essential role in promoting drug safety. Significant imbalances in the availability of safety-related information are inherent in the approval of pharmaceutical products, whether through a new drug application ("NDA") to the FDA or an abbreviated one ("ANDA"). While branded

2. Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified at 21 U.S.C. § 355(b), (j), (l); 35 U.S.C. § 156, 271, 282).

manufacturers generally have greater access to their own unpublished drug-specific risk information than do generic manufacturers, the appropriate comparison is not between branded and generic manufacturers but between a product's manufacturer and consumers. Generic manufacturers are not ignorant of the safety risks of their products, and are often in a far better position than patients or physicians to know the accumulating risk information about their particular product. State-law failure-to-warn litigation mitigates this information asymmetry by aligning the incentives of drug manufacturers and consumers. State-law suits serve to: (1) supplement the FDA's inadequate resources to monitor comprehensively the performance of every drug on the market, (2) provide a strong incentive to drug manufacturers to respond to signals of health risks and seek action from the FDA, and (3) provide consumers with recourse in the event that drug manufacturers fail to strengthen or add warnings about their products when appropriate.

Creating significant post-approval incentives for drug manufacturers to report known safety information is especially important for generic manufacturers. Generic drug usage has increased steadily for decades, and it appears that significant institutional efforts will increase that percentage beyond the 75% of U.S. prescriptions currently filled by generic drugs. Within the first year of a drug "going generic," generic substitution laws and institutional formulary requirements typically shift as much as 90% of all prescriptions from the branded to the generic product. Many drugs are available *solely* in generic form: nearly one-third of all drugs have no brand volume at all. Risk information is increasingly sent to

the manufacturers – now generic manufacturers – of the product. In short, the vast majority of prescriptions written after brand exclusivity expires are filled with generic products; to the extent this places the generic manufacturer in a position of acquiring safety risk or signal information, that manufacturer should be incentivized to share such information.

Further, branded drugs are frequently approved after only short-term safety studies have been conducted; the long-term effects of a drug frequently are not reported for many years. The expiration of a drug's statutory exclusivity has nothing to do with when important, long-term safety risk information may become known; it is irrational to link the need for disclosure of such risks to the timing of expiration of exclusivity.

State-law failure-to-warn litigation does not, as the petitioners' *amici* contend, result in generic manufacturers submitting to the FDA risk information that the FDA "neither wants nor needs." The FDA is, after all, in the business of protecting the public's health. Although manufacturers have always faced state-law failure-to-warn liability, history shows that rather than *over*-report risk information for drug products (as a means by which to head off potential, long-term tort liability), manufacturers *under*-report risk information (as a means to maximize short-term profitability). The incentive to under-report is at least as strong for a generic manufacturer and state-law failure-to-warn claims provide counterbalancing incentives to make these important disclosures.

Petitioners' *amici* simply ignore the social and economic benefits of increased reporting of important safety information and the dual realities that (1) drug manufacturers have strong incentives to maximize profits, and (2) these profit-maximizing incentives may be misaligned with public health interests. They assume that the FDA can continuously optimize its regulatory standard throughout a drug's lifecycle and is equipped to address all health risk issues without the aid of reporting incentives on drug manufacturers. But the assumption is incorrect: information asymmetries, budget inadequacies, and regulatory realities limit the FDA's enforcement abilities. The FDA's tools for gathering post-approval information are relatively crude and ineffective. The lack of high-quality information and the limits on FDA enforcement power severely undermine the FDA's ability to effectively regulate what physicians and patients know about a drug once it is on the market. Accordingly, the tort system encourages manufacturers to act reasonably in warning the healthcare community about newly emerging risks and helps ensure that important risk information is provided to the FDA.

Petitioners' *amici* assert, without empirical data or real analysis, that a state-law duty to disclose known health risk or signal information would result in such huge economic costs as to nearly "wipe out" the reduction in drug costs created by the Hatch-Waxman scheme. This assertion is unsupported and dubious. Generic manufacturers are highly sophisticated, heavily-regulated organizations that have sweeping FDA reporting obligations. They persevere through lengthy ANDA application processes to demonstrate product bioequivalency and manufacturing

capabilities to mass-produce products that perform the same as branded products. There is no economic evidence that tort liabilities have (or would ever) cripple the branded pharmaceutical industry; there is similarly no evidence that the prospect of tort liability (tailored to the circumstances of a company marketing a drug product through ANDA approval) does anything other than require effective reporting of known risks.

Finally, there is no reason to think that Hatch-Waxman was designed, as the generic *amici* contend, to preempt any state-law measure that might impose economic costs on generic manufacturers. Numerous laws in innumerable ways impose costs on businesses; Hatch-Waxman was not intended to give generic manufacturers a free pass through the laws of the states with a single-minded purpose of keeping industry overhead costs reduced. Hatch-Waxman is part of the overall scheme to provide incentives for less expensive, *but equally safe*, medications available to the public.

## ARGUMENT

### I. THE GENERIC PHARMACEUTICAL INDUSTRY IS HIGHLY-REGULATED, SOPHISTICATED, AND PROFITABLE

#### A. Research, Development, and Approval of Generic Drugs Takes Time, Expertise, and Compliance with Multiple Federal Regulations

To obtain approval of a generic drug, a manufacturer must file an abbreviated new drug application ("ANDA"), a procedure defined by the Hatch-Waxman Act.[3] Hatch-Waxman simplified the approval of generic drugs by eliminating the need to prove independently that the generic is safe and effective; rather, generic manufacturers may rely on the scientific finding of safety and effectiveness demonstrated by the NDA so long as the manufacturer can demonstrate that the generic is bioequivalent to the branded product.[4] Where it does, the FDA may approve the ANDA as an AB-rated or bioequivalent generic version of the branded drug.

Branded manufacturers hold their production processes as trade secrets; demonstrating bioequivalence, therefore, is not merely a matter of replicating a recipe or composition.[5] Generic manufacturers must

3. Fed. Food, Drug, & Cosmetic Act, 21 U.S.C. § 355(j); 21 C.F.R. § 314.94 (2011).

4. 21 U.S.C. § 355(j)(2)(A)(iv).

5. 21 C.F.R. § 314.430(g)(1) (manufacturing methods or processes not available for public disclosure by FDA). *See* Current Good Manufacturing Practice in Manufacture, Processing, Packing, or Holding, 43 Fed. Reg. 45,014, 45,024 (Sept. 29, 1978)

use independent expertise to formulate their drugs and conduct both laboratory and clinical testing to ensure that their products are absorbed equally to their branded counterparts. Generic manufacturers must also comply with the same elaborate chemistry, manufacturing, and controls ("CMC") requirements as branded manufacturers.[6] These general statutory quality standards are the same for NDA and ANDA applicants. Different companies satisfy the standards in different ways, often using proprietary methodologies known only to the particular manufacturer. As a result, generic companies develop their own proprietary manufacturing processes.

ANDA requirements ensure that AB-rated generic equivalents perform substantially the same as the branded drug (i.e., they are bioequivalent) – but the generic is rarely *exactly* the same as the branded product.[7]

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(later codified at 21 C.F.R. pts. 210-11) ("many production and control processes are considered by individual firms to be trade secrets").

6. 21 C.F.R. § 314.50(d)(1) (CMC requirements); *id.* at § 314.94(a)(9) (making CMC requirements applicable to ANDAs); for the scope of CMC requirements, *see generally Chemistry, Manufacturing, and Controls (CMC)*, U.S. Food & Drug Admin., http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm064979.htm (last visited Feb. 28, 2011); *Generics*, U.S. Food & Drug Admin., http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm064995.htm (last visited Feb. 28, 2011).

7. A generic is only ever "exactly the same as" the branded when the manufacturer of the branded drug sells the exact same pills it previously sold as the branded drug as a generic equivalent. These identical generics make up a very small percentage of the market for generic drugs.

The composition of the generic may differ from the branded product: generics often use different forms of the active pharmaceutical ingredient (such as a calcium salt formulation instead of a sodium salt formulation) or different inactive ingredients. Generic manufacturers often purchase their active pharmaceutical ingredient from a different supplier. Generics may be manufactured using different processes, in large part because the manufacturing processes of the branded manufacturer may not be publicly disclosed, or may be patent protected. And labels may be different: for example, federal regulations provide for the "carving out" of indications from a generic's label.[8]

The process of seeking and gaining approval of a generic drug in this highly-regulated, highly-involved area is not easy; "[i]n the vast majority of cases, the initial ANDA application is found deficient, requiring the applicant to conduct additional tests or submit additional material."[9] From start to approval, the ANDA process typically takes more than a year and a half, with additional time required before the generic drug can actually be sold.[10] And once approved, generic manufacturers must carefully monitor their products to ensure they are performing equally to the listed reference drug – that

8. 21 C.F.R. § 314.127(a)(7). *See also* Terry Mahn, *Protecting New Investments in Old Drugs*, Update (The Food & Drug L. Inst.), March/April 2009, at 38, 38-44.

9. David Reiffen & Michael R. Ward, *Generic Drug Industry Dynamics*, 87 The Rev. of Econ. & Stat. 37, 38 (2005).

10. *Id.* (observing "In total, the applicant has to anticipate 2 to 3 years elapsing from the time it begins preparing to enter until it can begin selling a generic drug.").

they are, for example, properly manufactured and indeed bioequivalent to the branded pharmaceutical.

In pursuit of FDA approval and post-market follow-up, generic manufacturers spend millions of dollars each year on research and development ("R&D"), gaining substantial information about the active molecules contained in their products. In 2009, petitioners' *amicus* Teva spent $802 million on generic and innovative R&D.[11] The company emphasized that R&D "efforts are integral to all of our operations," and explained that generic R&D "responsibilities include product formulation, chemical and physical (including shelf-life) testing, stability testing, bioequivalence (absorption and extent), blood level testing, clinical testing, registration and approval."[12] In 2003, *amicus* Apotex boasted that it held "the #1 position in Canada for research and development spending in the pharmaceutical industry," devoting $153 million and 20.4% of total revenue to R&D and beating out the top branded manufacturers both in total R&D spend and R&D spend as a percentage of revenue.[13]

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11. Teva Pharm. Indus. Ltd., Annual Report 2009, at 27 (2010), *available at* http://www.tevapharm.com/pdf/Teva20F2009.pdf ("Teva 2009 Annual Report").

12. *Id.*

13. Press Release, Apotex, Generic Company #1 In Canadian Pharmaceutical Industry for Research & Development Spending, (July 15, 2003), *available at* http://www.apotex.com/PressReleases/20030715-01.asp.

### B. Although the Drugs May Differ, Disparities Between Branded and Generic Manufacturers Are Less Stark Than Petitioners and Their *Amici* Suggest

Generic manufacturers share many similarities with their branded counterparts. Indeed, generic manufacturers often enter into agreements with branded manufacturers in the course of launching a generic product and sometimes are even divisions of the same company.

While all must pass FDA muster, generic products come to market in a variety of ways. For example, authorized generics are produced by branded manufacturers and marketed under a private label at generic prices.[14] In other situations, branded and generic manufacturers may enter into agreements allowing the generic to launch with a license from the branded manufacturer, but only after agreeing not to compete for a specified period of time.[15] And some generic products launch in the absence of a

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14. *See*, *e.g.*, Fed. Trade Comm'n., Authorized Generics: An Interim Report, at Exec. Summary (2009), *available at* http://www.ftc.gov/os/2009/06/index.shtm#24.

15. Fed. Trade Comm'n., Pay-for-Delay: How Drug Company Pay-Offs Cost Consumers Billions, Federal Trade Commission Staff Study, at 3 (Jan. 2010), *available at* www.ftc.gov/os/2010/01/100112payfordelayrpt.pdf; *see also*, *e.g.*, Prepared Statement of the Federal Trade Commission Before the United States House of Representatives Committee on the Judiciary Subcommittee: Courts and Competition Policy: Oversight of the Federal Trade Commission Bureau of Competition and the Department of Justice Antitrust Division, at 3 (July 27, 2010), *available at* http://www.ftc.gov/os/testimony/100727antitrustoversight.pdf.

brand name counterpart.[16]

The branded and generic industries overlap. Some of the largest "generic" companies are divisions of branded manufacturers: the third- and fifth-largest generic manufacturers, Sandoz and Greenstone, are divisions of investigative drug companies Novartis and Pfizer, respectively.[17] Further, like branded manufacturers, generic manufacturers regularly seek and obtain patents for their products, protecting them against infringement by competitors. For example, in 2009 petitioner Teva's parent, primarily a generic company, derived $2.66 billion

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In 2008, the Federal Trade Commission analyzed the number and types of settlements and agreements between pharmaceutical companies and found that forty-six such agreements between branded and generic manufacturers filed in fiscal year 2008 involved some restriction on a generic manufacturer's ability to market its product. *See* Fed. Trade Comm'n., Agreements Filed with the Federal Trade Commission under the Medicare Prescription Drug, Improvement, and Modernization Act of 2003: Summary of Agreements Filed in FY 2008, at 2-5, fig. III, *available at* http://www.ftc.gov/bc/healthcare/drug/index.htm.

16. *See*, *e.g.*, 21 U.S.C. § 355(b)(2) (describing "hybrid" applications for drug approval which are neither full NDAs containing safety and efficacy data nor ANDA applications. Products seeking this route of approval use an active pharmaceutical ingredient that the FDA previously has determined is safe and efficacious for its intended use but are modified in some way so that they differ from the original NDA product, *e.g.,* in dosage form, strength, route of administration, changed formulation, dosing regimen, or indication.).

17. Alaric Dearment, *Countdown to 2011: A Big Year for Generics,* Drug Store News, Nov. 14, 2010, *available at* http://www.drugstorenews.com/article/countdown-2011-big-year-generics.

of its $13.9 billion revenue from innovative products.[18]

### C. Institutional and Statutory Constructs Promote the Use of Generic Drugs and the Profitability of the Sector

Since passage of Hatch-Waxman in 1984, United States policy has encouraged use of generic medications. Statutory and institutional factors cause generic medications to quickly capture market share and overtake market shares in areas where they compete with branded drugs. This results in the generic industry's significant revenues and profitability.

In 1983, only 35% of the top-selling drugs with expired patents had generic versions available; by 1998, nearly all did.[19] In 1984, prescription drug revenue for branded and generics totaled $21.6 billion and generic drugs accounted for 18.6% of prescriptions.[20] By 2009, total prescription drug revenue had soared to $300 billion and generic drugs accounted for 75% of prescriptions.[21] Overall prescription drug sales, and the generic share of those sales, have

18. Teva 2009 Annual Report, *supra* n.11, at F-40.

19. Cong. Budget Off., How Increased Competition from Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry, at xii (1998), *available at* http://www.cbo.gov/ftpdocs/6xx/doc655/pharm.pdf ("CBO 1998").

20. *Id.* at 4, 27. The figure of $21.6 billion is apparently adjusted for inflation as of 1998; the point does not depend on a precise figure.

21. Press Release, IMS Health, IMS Health Reports U.S. Prescription Sales Grew 5.1 Percent in 2009, to $300.3 Billion (April 1, 2010), *available at* http://www.imshealth.com/portal/site/imshealth/menuitem.a46c6d4df3db4b3d88f611019418c22a/?vgnextoid=d690a27e9d5b7210VgnVCM100000ed152ca2RCRD&cpsextcurrchannel=1 ("IMS Press Release").

grown considerably in recent years:[22]

| Year | Total U.S. sales - branded and generic (billions)[23] | U.S. Sales - generic only (%)[24] | U.S. Sales - generic only (billions)[25] | Total prescriptions (millions)[26] | Total prescriptions that are generic (%)[27] |
|---|---|---|---|---|---|
| 2003 | $219.6 | 12 | $26.4 | 3,361 | 51 |
| 2004 | $239.9 | 12 | $28.8 | 3,435 | 53 |
| 2005 | $247.3 | 13 | $32.1 | 3,545 | 57 |
| 2006 | $270.3 | 15 | $40.5 | 3,706 | 61 |
| 2007 | $280.5 | 16 | $44.9[28] | 3,805 | 63 |
| 2008 | $285.7 | - | - | 3,842 | - |
| 2009 | $300.3 | 22 | $66.1 | 3,922 | 75 |

22. For 2003-2006: Richard Frank, *The Ongoing Regulation of Generic Drugs*, 357 New Eng. J. Med. 1993, 1993-96 (2007). For 2007 and 2008: *Facts at a Glance*, Generic Pharm. Ass'n, http://www.gphaonline.org/about-gpha/about-generics/facts (last visited Feb. 28, 2011) ("GPhA Facts at a Glance"). For 2009: IMS Press Release, *supra* n.21.

23. For 2003 to 2004: *2007 Top Therapeutic Classes by U.S. Sales*, IMS Health, (2008), http://www.imshealth.com/deployedfiles/imshealth/Global/Content/Document/Top-Line%20Industry%20Data/2007%20Top%20Therapeutic%20Classes%20by%20Sales.pdf. For 2005 to 2009: *Top Therapeutic Classes by U.S. Sales*, IMS Health, (2010), http://www.imshealth.com/deployedfiles/imshealth/Global/Content/StaticFile/Top_Line_Data/Top%20Therapy%20Classes%20by%20U.S.Sales.pdf.

24. For 2003 to 2007: Frank, *supra* n.22, at 1994. For 2009: Natasha Singer, *Deals to Restrain Generic Drugs Face a Ban,* N.Y. Times, Jan. 13, 2010, at B1.

25. Dollar figures for "U.S. Sales - generic only" are calculated by taking the given percentage of "Total U.S. sales - branded and generic."

26. For 2003 to 2004: *2007 Top Therapeutic Classes by U.S. Dispensed Prescriptions*, IMS Health, (2008), http://www.imshealth.com/deployedfiles/imshealth/Global/Content/Document/Top-Line%20Industry%20Data/2007%20Top%20Therapeutic%20Classes%20by%20RXs.pdf. For 2005 to 2009: *Top Therapeutic Classes by U.S. Dispensed Prescription*, IMS Health, (April 6, 2010), http://www.imshealth.com/deployedfiles/imshealth/Global/Content/StaticFile/Top_Line_Data/Top%20Therapy%20Classes%20by%20U.S.RXs.pdf.

27. For 2003 to 2007: Frank, *supra* n.22. For 2009: IMS Press Release, *supra* n.21.

28. Our calculated figure may be low; other reports put generic industry revenue in 2007 at $58.5 billion. GPhA Facts at a Glance, *supra* n.22.

Indeed, just since 2003, the share of total prescriptions filled by generic manufacturers has grown from 51% to 75%, with generic sales expanding from $26.4 billion to $66.1 billion. Generic drug sales in some years fully account for the growth in medication spending: "[t]he total number of generic prescriptions dispensed increased 5.9 percent in 2009, while the number of branded prescriptions dispensed *declined* 7.6 percent."[29] And the generic industry will likely continue to grow as the United States seeks to limit medication costs.[30]

Where they do compete with branded drugs, generic drugs quickly capture the majority of sales. More than 90% of prescriptions for "multiple-source" drugs (meaning they are available in branded and generic forms) are filled by generics.[31] The speed of market share capture by generic drugs appears to be increasing: in a sample of drugs losing patent protection between 1991 and 1993, generics on average held a 44% market share after one year;[32] by 2008, generic versions could capture "as much as 86 to 97 percent of the market within the first month."[33]

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29. IMS Press Release, *supra* n.21 (emphasis added).

30. *See generally*, *e.g.*, U.S. Dep't Health & Hum. Serv., ASPE Issue Brief, Expanding Use of Generic Drugs (Dec. 1, 2010), *available at* http://aspe.hhs.gov/sp/reports/2010/GenericDrugs/ib.pdf ("ASPE Issue Brief").

31. Cong. Budget Off., Effects of Using Generic Drugs on Medicare's Prescription Drug Spending, at 7 (2010), *available at* http://www.cbo.gov/ftpdocs/118xx/doc11838/09-15-PrescriptionDrugs.pdf.

32. CBO 1998, *supra* n.19, at 28.

33. Protecting Consumer Access to Generic Drugs Act of 2009: Hearing on H.R. 1706 Before the U.S. House of Representatives

As a result of this generic competition, branded manufacturers often cease production of out-of-patent drugs entirely. In 2009, out of a universe of 4,318 unique drug molecules with active sales volume tracked by IMS Health, a leading aggregator of pharmaceutical sales and prescription data, 32% were sold solely as generics.[34] Our own analysis of FDA data indicates that out of 4,653 approved drugs with distinct ingredients, delivery routes, and strengths, more than half – 2,438 – are available in generic form. Of those, 1,062 are available *solely* in generic form; the only available versions of the drug received ANDA approval.[35]

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Subcommittee on Commerce, Trade and Consumer Protection, of the Committee on Energy and Commerce 8 (March 31, 2009) (prepared statement of Diane E. Bieri, Exec. VP and Gen. Coun., Pharm. Research & Mfrs. of Am.).

34. Generic Pharm. Ass'n, Savings Achieved Through the Use of Generic Pharmaceuticals 2000-2009, at 7 (2010), *available at* http://www.gphaonline.org/sites/default/files/GPhA%20Savings%20Study%20Book%20Updated%20Web%20FINAL%20Jul23%2010_0.pdf ("GPhA, Savings Achieved 2000-2009").

35. We base this analysis on the FDA's "Orange Book" database. The FDA's Orange Book lists approved drug products with therapeutic equivalence evaluations, all of which have been approved under Section 505 of the Federal Food, Drug, and Cosmetic Act. *Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations*, U.S. Food & Drug Admin., http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm (last visited Feb. 26, 2011). We filtered the database to include only prescription medications; grouped individual products having a unique combination of ingredients, delivery routes, and strengths; and counted what portion of the groups contained NDA products, ANDA products, or both. *Electronic Orange Book (EOB) Query Data Files,* U.S. Food & Drug Admin., http://www.fda.gov/Drugs/InformationOnDrugs/ucm129689.htm (last visited Jan. 11, 2011).

Several factors influence generic manufacturers' ability to capture market share. Since passage of Hatch-Waxman, every state has adopted substitution laws that either require or permit pharmacies to substitute generic equivalents for branded prescriptions unless the prescribing physician has specifically ordered otherwise.[36] Even beyond this, pharmacies have an incentive to substitute generic drugs if possible. When a drug becomes newly available as a generic, federal reimbursement rules and the industry pricing structure typically mean pharmacies can earn a higher markup on the generic option than the branded one.[37] In the private market, insurers may offer direct incentives to pharmacies to substitute cheaper generic products for more expensive branded ones.[38] As a result of these incentives, one recent study found no significant difference in substitution rates between "permissive" and "mandatory" substitution states.[39]

Consumers are also incentivized to select generic medications. Many insurers require lower consumer

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36. *See* Judith K. Hellerstein, *The Importance of the Physician in the Generic versus Trade-Name Prescription Decision*, 29 RAND J. Econ. 108, 109 (1998); ASPE Issue Brief, *supra* n.30, 7-8.

37. *See* Cong. Budget Office, Medicaid's Reimbursements to Pharmacies for Prescription Drugs, at 4 (2004), *available at* http://www.cbo.gov/ftpdocs/60xx/doc6038/12-16-Medicaid.pdf.

38. Helene L. Lipton et al., *Pharmacy Benefit Management Companies: Dimensions of Performance*, 20 Ann. Rev. Pub. Health 361 (1999).

39. ASPE Issue Brief, *supra* n.30, at 8 (citing William H. Shrank et al., *State Generic Substitution Laws Can Lower Drug Outlays Under Medicaid*, 29 Health Affairs 1383 (2010)).

copayments for generics than branded drugs to encourage consumers to request a generic option.[40] Federal agencies routinely investigate ways to encourage consumer adoption of generic medication.[41] And according to petitioners' *amicus* Generic Pharmaceutical Association ("GPhA"), both the FDA itself and the generic industry spend millions of dollars each year encouraging customers to trust generic drugs in place of their branded counterparts.[42]

All of this combines to help many generic manufacturers earn above-average profit margins. Profit margins for the top fifty industries averaged 4.9% in 2008;[43] concurrently, petitioners and their *amici* saw profits of 12-25%, some of which even topped the pharmaceutical industry's 19.3% profit margin without incurring the risk undertaken by branded manufacturers in researching potential new drugs that may never come to market:

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40. *See* Geoffrey F. Joyce et al., *Employer Drug Benefit Plans and Spending on Prescription Drugs*, 288 J. Am. Med. Ass'n 1733, 1733-34 (2002); Haiden A. Huskamp et al., *The Effect of Incentive-based Formularies on Prescription-Drug Utilization and Spending*, 349 New Eng. J. Med. 2224, 2225 (2003).

41. *See generally* ASPE Issue Brief, *supra* n.30.

42. Brief of the Generic Pharm. Ass'n as Amicus Curiae in Support of Petitioners at 2-3, *Pliva, Inc., et al. v. Mensing* (No. 09-993) ("GPhA Brief").

43. *Top Industries: Most Profitable*, Fortune (May 4, 2009), http://money.cnn.com/magazines/fortune/fortune500/2009/performers/industries/profits/.

| Company | Last Available Year | Revenue | Net Income | Calculated Profit Margin |
|---|---|---|---|---|
| PLIVA, Inc.[44] | 2007 | 6,061,978 HRK (Croatian Kuna) | 731,934 HRK | 12.1% |
| Teva Pharmaceuticals Industries Ltd.[45] | 2009 | $13.9 billion | $2 billion | 14.4% |
| Actavis[46] | 2009 | 1.7 billion euros | 300 million euros (estimated earnings before interest, tax, depreciation and amortisation) | 17.6% |
| Morton Grove Pharmaceuticals Inc.[47] | 2009 | 2,959.41 million rupees | 751.20 million rupees | 25.4% |

44. PLIVA, Annual Report 2007, at 4 (2008), *available at* http://www.pliva.com/newsattach/2246/2007%20Annual%20Report%20EN%20FINAL.pdf.

45. Teva 2009 Annual Report, *supra* n.11, at 2.

46. Ben Hirschler &Quentin Webb, *Actavis Sees Record Year, No Rush to Sell,* Reuters, Sept. 30, 2010, *available at* http://www.forexpros.com/news/financial-news/interview-update-1-actavis-sees-record-year,-no-rush-to-sell-163724 (last visited Feb. 28, 2011). Because Actavis is not publicly traded, public estimates of its profit margin are approximate.

47. Wockhardt Unlimited, Annual Report 2009-10, at 73 (2010), *available at* http://www.wockhardt.com/pdf/investor/annual/NotestoAccounts_2009.pdf.

In sum, generic manufacturers have enjoyed considerable recent growth in revenue and profit as regulatory and institutional factors grant them an increasing share of the prescription medication market.

## II. GENERIC MANUFACTURERS OFTEN LEARN OF SAFETY RISKS BEFORE THE FDA OR OTHER HEALTHCARE STAKEHOLDERS

### A. Generic Manufacturers Must Investigate and Report Safety Risks

"[I]t has remained a central premise of federal drug regulation that the manufacturer bears responsibility for… ensuring that its warnings remain adequate as long as the drug is on the market."[48] In large part, this responsibility derives from the fact that pharmaceutical manufacturers, whether branded or generic, are often better positioned than the FDA or consumers to learn of, and warn about, such risks.

While not identical to the post-approval requirements imposed on NDA holders, generic manufacturers marketing under an approved ANDA also face post-approval reporting requirements regarding the safety of their products and the need to monitor ongoing bioequivalency. These manufacturers must "develop written procedures for the surveillance, receipt, evaluation, and reporting of postmarketing adverse drug experiences ["ADEs"] to FDA."[49] Generic manufacturers must report all ADEs to the FDA, either in periodic reports or, in the

48. *Wyeth v. Levine*, 129 S. Ct. 1187, 1197-98 (U.S. 2009).

49. 21 C.F.R. § 314.80(b) (made applicable to generic companies by 21 C.F.R. § 314.98).

case of "serious and unexpected" ADEs, within fifteen days of learning of them.[50] "Serious and unexpected" ADEs that "may jeopardize the patient or subject" require "prompt[] investigat[ion]" and submission of follow-up reports to the FDA by the generic manufacturer.[51]

By 1998, approximately 90% of ADE reports came from manufacturers;[52] these reports are more valuable than ones filed directly with the FDA, because they "leverage[] the firm's resources in identifying, assessing, and following up on reports of drug injury."[53] Follow-up from ADEs can lead to the dissemination of important safety information. For example, *amicus* Teva engaged in a nationwide recall of its anesthesia product propofol in 2009 after receiving and investigating information from ADEs.[54]

Put differently, generic manufacturers already face post-reporting requirements. The imposition of potential

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50. *Id.* at § 314.80(c)(1)(i), (c)(2).

51. *Id.* at § 314.80(a), (c)(1)(ii).

52. *See* Vaccine Adverse Event Reporting System: Hearing Before the House Com. on Gov't Reform, (May 27, 1999) (prepared statement by Joseph A. Levitt, Dir., Ctr. for Food Safety and Applied Nutrition, Food & Drug Admin.), *available at* http://www.fda.gov/NewsEvents/Testimony/ucm115054.htm.

53. *Id.*

54. Press Release, Teva, Teva Pharmaceuticals USA Issues a Voluntary User-Level Nationwide Recall of Propofol Injectable Emulsion 10 mg/mL 100 mL Vials, Lot Numbers 31305429B and 31305430B (July 16, 2009), *available at* http://www.fda.gov/Safety/Recalls/ArchiveRecalls/2009/ucm172474.htm.

liability through state-law failure-to-warn suits simply provides added incentive to fulfill these obligations.

### B. The FDA Cannot Track Safety Data for All Approved Drugs

Writing in the context of litigation against a branded pharmaceutical manufacturer, this Court observed in *Wyeth v. Levine* that "[t]he FDA has limited resources to monitor the 11,000 drugs on the market, and manufacturers have superior access to information about their drugs, especially in the postmarketing phase as new risks emerge."[55] A similar imbalance in resources and knowledge of post-approval risk information exists between the FDA and a generic manufacturer; state law should be allowed to impose a duty on generic manufacturers to disclose known risk information.

The FDA possesses a limited ability to monitor generic medications for emerging safety problems. The universe of approved drugs that must be monitored by the FDA's limited resources is large and grows daily; as this Court noted, there are more than 11,000 currently-approved prescription medications,[56] of which 4,318 separate molecules have active sales volume.[57] New medications are typically approved based on a small number of studies in a modest number of subjects. Such limited testing permits important new products to come to

55. 129 S. Ct. at 1202 (internal citation omitted).

56. *See id.*

57. *See* GPhA, Savings Achieved 2000-2009, *supra* n.34, at 7.

market relatively quickly[58] but also means that when the FDA approves a drug, it "cannot fully certify its ongoing safety."[59] Instead, the FDA relies on postmarketing data from manufacturers to refine the safety profile of a drug.

But the FDA has long-acknowledged deficiencies in its ability to acquire post-approval drug risk information. The FDA had no more that 211 employees in 2009 in its Office of Surveillance and Epidemiology, which is responsible for evaluating and monitoring ongoing risks for all drugs,[60] and total FDA funding for postmarketing drug safety reached only $139 million in fiscal year 2008.[61] In fact, the Government Accountability Office placed the FDA's drug safety program on its watchlist of high-risk areas requiring attention by Congress and the executive branch, stating in February 2011:

> Although improvements have been made, long-standing concerns remain regarding the

58. Should FDA Drug and Medical Device Regulation Bar State Liability Claims?: Hearing Before H. Comm., on Oversight and Government Reform, 110th Cong., Ser. No. 110-212, at 30 (May 14, 2008) (statement of Aaron S. Kesselheim, Harvard Med. Sch.).

59. *Id. See, e.g.*, *A Guide to Drug Safety Terms at FDA*, U.S. Food & Drug Admin., (Feb. 28, 2011), http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm107970.htm ("[E]ven with a rigorous evaluation process, some safety problems surface only after a drug has been on the market and has been used in a broader population,").

60. U.S. Gov't Accountability Off., GAO-10-68, Drug Safety: FDA Has Begun Efforts to Enhance Postmarket Safety, but Additional Actions Are Needed, at 1, n.75 (2009) ("GAO-10-68").

61. *Id.* at 14.

> effectiveness of FDA's postmarket oversight. FDA staff have expressed concern about their ability to meet a growing postmarket workload, with some maintaining that their premarket responsibilities are considered a higher priority. FDA is also encountering technological and staffing issues that limit its capacity to conduct drug safety studies.[62]

Problems with the FDA's postmarketing drug safety monitoring have been reported for over thirty years.[63] In a 2006 report, the GAO observed that the "FDA's postmarket drug safety decision-making process has been limited by a lack of clarity, insufficient oversight by management, and data constraints."[64] Fiscal constraints are another important limitation, with a large majority of the FDA's drug safety budget earmarked for premarketing rather than postmarketing efforts, and a majority of FDA doctors and scientists believing that the agency lacks sufficient funds to do its job.[65] Congress expanded the FDA's postmarketing budget in 2007 but simultaneously expanded the Agency's post-approval surveillance duties as well,

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62. U.S. Gov't. Accountability Off., GAO-11-278, High-Risk Series: An Update 116-17 (February 2011).

63. GAO-10-68, *supra* n.60, at 39.

64. U.S. Gov't. Accountability Off., GAO-06-402, Drug Safety: Improvement Needed in FDA's Postmarket Decision-making and Oversight Process 18 (2006).

65. David A. Kessler & David C. Vladeck, *A Critical Examination of the FDA's Efforts To Preempt Failure-To-Warn Claims*, 96 Geo. L.J. 461, 484-85 (2008). *See also* GAO-10-68, *supra* n.60, at 2, 31-34.

leaving unchanged the problem of inadequate funding.[66] Following the increase in funding and postmarketing duties, the GAO opined in 2009 that "it is not yet clear if or when FDA's decision-making process will be substantially improved as a result of its efforts."[67]

### C. Many Risks Do Not Emerge Until After Patent Expiration for the Branded Drug

Under the system proposed by petitioners' *amici*, branded manufacturers and the FDA are solely responsible for developing drugs, monitoring them for emerging safety concerns, reporting safety signals, and proposing label changes; generic manufacturers need only follow their directions. But (1) an increasing number of drugs have no branded company to monitor them; (2) many long-term risks do not emerge until after a drug goes generic; and (3) some risks arise spontaneously when a product is manufactured by a generic company, including contamination and other manufacturing problems as well as safety concerns resulting from differences between the branded and generic products.

Petitioners' *amici* suggest that the safety of all drugs will be maintained through monitoring and reporting required of NDA holders:

> Each applicant having an approved application under § 314.50 or, in the case of a 505(b)(2) application, an effective approved application,

66. Kessler & Vladeck, *supra*, at 485-86; *see* GAO-10-68, *supra* n.60, at 13.

67. GAO-10-68, *supra* n.60, at 39.

> shall promptly review all adverse drug experience information obtained or otherwise received by the applicant from any source, foreign or domestic, including information derived from commercial marketing experience, postmarketing clinical investigations, postmarketing epidemiological/surveillance studies, reports in the scientific literature, and unpublished scientific papers.[68]

Whatever optimistic view one might hold for branded manufacturer compliance with existing regulations, the plain economic fact is that a growing number of drug products distributed in the U.S. have no corresponding approved application under § 314.50: out of 2,438 distinct drugs available as generics through ANDA applications, nearly half are available solely in that form—any approved applications under § 314.50 have been withdrawn.[69] Petitioners and their *amici* would leave an entire segment of distributed drug products without any surveillance.

Further, branded drugs are frequently approved after only short-term safety studies have been conducted and the long-term effects of a drug typically are not known or reported for many years. Ongoing monitoring for emerging side effects is thus an important tool to ensure drug safety, even in drugs that have lost patent protection. For example, Neurontin, approved for use in treating epilepsy, entered the market in 1996 and lost patent protection in 2004. During that time, Neurontin sales exceeded $10 billion and in 2003, Neurontin was one

68. 21 C.F.R. § 314.80(b).

69. *Supra* n.35 and accompanying text.

of the most-prescribed drugs in the United States. Risks of suicidal ideation associated with Neurontin and generic versions of the drug emerged late in the day and led to a label change, warning of suicidality, in 2009, five years after generics entered the market.

Metoclopramide, a drug at issue here, is another example. First marketed as Reglan in 1979, the drug was available in generic form by the mid-1980s. New risk information continued to emerge, causing significant label changes for safety issues in 2004 and 2009, more than twenty-five years after its launch.

Recent news about the analgesic Darvon is apt. Darvon, known generically as propoxyphene, was approved for use in 1957 for use in treating mild to moderate pain. In November 2010, more than forty years after approval, the FDA requested that all manufacturers of propoxyphene remove the drug from market after determining the risks of severe cardiac side effects outweighed the benefits of the drug.[70]

"Off-label" uses of a drug increase the possibility of new side effects. For example, in 1981, the FDA approved the antidepressant trazadone hydrochloride for the treatment of depression under the brand name Desyrel.[71]

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70. *See, e.g.*, Duff Wilson, *Darvon Pulled From Market by F.D.A.*, N.Y. Times, (Nov. 19, 2010), http://prescriptions.blogs.nytimes.com/2010/11/19/darvon-pulled-from-market-by-f-d-a/ (last visited Feb. 28, 2011).

71. *See Label and Approval History for Desyrel*, Drugs @ FDA, U.S. Food & Drug Admin., http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Label_ApprovalHistory#apphist (last visited Feb. 28, 2011).

Desyrel lost patent protection in the mid 1980s. By the late 1980s, physicians prescribed trazodone off-label with increasing frequency to treat insomnia. As off-label use of trazodone increased, new side effects emerged, including the risk of excessive sedation when used for insomnia with fluoxetine, a selective serotonin reuptake inhibitor (such as Prozac).[72]

Some risks can arise as a result of differences between the branded and generic versions of a drug. In 2006, the FDA approved *amicus* Teva's ANDA for Budeprion XL, a generic version of the antidepressant Wellbutrin XL. Scores of patients reported loss of effect and new onset or worsening of side effects when switching from branded Wellbutrin XL to generic Budeprion XL, leading to an investigation by the FDA into whether differences between the drugs in the manufacturing and rate of chemical release and absorption caused safety risks for Budeprion XL not seen in Wellbutrin XL.[73]

The regime proposed by the petitioners is therefore one in which, for nearly half the drugs they produce, the FDA is solely responsible for monitoring the medical literature and ADEs for emerging safety concerns. Under this scheme, neither generic manufacturers nor any other private party has a duty to evaluate the ongoing safety of

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72. Alan Metz and Richard I. Shader, *Adverse Interactions Encountered When Using Trazodone to Treat Insomnia Associated with Fluoxetine*, 5 Int'l. Clinical Psychopharmacology 191 (1990).

73. *E.g.*, *Review of Therapeutic Equivalence Generic Buproprion XL 300mg and Wellbutrin XL 300mg*, U.S. Food & Drug Admin., http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm153270.htm (last visited Feb. 27, 2011).

their products or report known risks, and patients have no recourse if the generic manufacturers unreasonably ignore information that could have prevented personal injury. Such a reading of federal law and regulation is not one that Congress or the FDA would likely have selected, or one that should be adopted lightly.

## III. GENERIC MANUFACTURERS PRESENT NO EVIDENCE THAT A DUTY TO WARN CONFLICTS WITH, OR WILL CRIPPLE, THE HATCH-WAXMAN SCHEME

Petitioners and their *amici* argue that compliance with duties to report safety information would undo all of the benefits generated by Hatch-Waxman. To the contrary, failure to hold generic manufacturers accountable for non-disclosure of known risks associated with their products would create important differences between branded and generic drugs that are likely to be exploited in marketing campaigns and that may result in a turning away from generic drugs by physicians and consumers, not to mention a rethinking of state generic substitution laws.

Petitioners' *amici* suggest that requiring generic manufacturers to monitor the safety of their products will "wipe out" more than $100 billion per year in savings under the Hatch-Waxman scheme.[74] They make no attempt to estimate the actual costs to generic manufacturers of reporting known health risks, or of monitoring widely-available public information about a generic drug. Nor do they explain why doing so would be so costly as to seriously undermine the savings from the use of generic rather than branded drugs.

74. *See* GPhA Brief, *supra* n.42, at 3.

This case, and others like it, seeks to impose on generic manufacturers only the most minimal duties of surveillance and disclosure of risk information. No one questions the reasonableness of adopting the labels used by branded companies, approved by the FDA, and consistent with medical literature at the time a drug loses patent protection. But to comply with their ongoing duties, generic manufacturers must act on information that becomes reasonably available to them – ADEs and published medical literature – to ensure that their product labels provide adequate notice of safety requirements.

Petitioners' assertion boils down to this: because Congress intended their products to be affordable, it must have intended to exempt generic manufacturers from all economic burdens associated with the manufacture and distribution of generic drugs, including the cost of reporting available information about their products to ensure that product use remains safe and labels are kept up to date. This is not so. The generic industry remains subject to a wide range of laws that impose costs of doing business, including state wage and hour laws, state discrimination laws, and state torts for negligent manufacture. It has achieved success without exemption from those laws, and has demonstrated no real need for exemption from the claims at issue here.

Economics teaches us that the cost of accidents is lessened where society imposes such costs on "the 'cheapest cost avoider' or [the actor] who is in the best position to make the cost-benefit analysis between accident costs and accident avoidance costs and to act

on that decision once it is made."[75] This Court's finding in *Wyeth v. Levine* recognized and upheld this teaching, finding manufacturers of pharmaceuticals "have superior access to information about their drugs, especially in the postmarketing phase as new risks emerge,"[76] and that "state-law remedies further consumer protection by motivating manufacturers to produce safe and effective drugs and to give adequate warnings."[77] Petitioners and their *amici* ask this Court to reject this notion only two years later, setting up an entirely different standard for generic manufacturers than their branded counterparts.

The decision to hold generic manufacturers to the same state law standard as branded manufacturers directly serves Congress's intent to create a market of generic drugs equivalent in value to their branded counterparts. For the generic market to succeed, generic drugs must have equal value to branded drugs; in economic terms, they must be "perfect substitutes," and in safety terms, the requirements for disclosure of risk must be equal to that applied to branded drugs A holding that product liability claims are preempted against generic manufacturers but not against branded manufacturers undercuts these goals.

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75. *Beshada v. Johns-Manville Prods. Corp.*, 447 A.2d 539, 548 (N.J. 1982) (*citing* Guido Calabresi & Jon T. Hirschoff, *Toward a Test for Strict Liability in Torts*, 81 Yale L.J. 1055 (1972)); *see generally* Robert L. Rabin, *Reassessing Regulatory Compliance*, 88 Geo. L.J. 2049, 2071 (2000).

76. 129 S. Ct. at 1202.

77. *Id.* at 1200.

In the marketplace, critical to the value equation for any product is the consumer's recourse in the event a product is defective. A product sold "as is" is less valuable than one sold with the implied warranties of fitness and merchantability. A product sold without waiver of personal injury claims resulting from any defect is more valuable than one sold with waiver. Similarly, a product sold without preemption of state tort claims is more valuable than one sold with preemption. Taking the case at hand as an example, patients whose prescriptions were filled with name-brand Reglan may be able to recover under state law if they suffer tardive dyskinesia because their medication was defectively labeled. Patients whose prescriptions were filled with identically labeled generic metoclopramide will not have recourse to any recovery.

The fact that a broad class of patients suffered the misfortune of having prescriptions filled with generics, as encouraged or often required by state substitution laws, would not go unnoticed in the marketplace – if for no other reason than because branded manufacturers would have a strong incentive to publicize that information. The bifurcated scheme proposed by petitioners and their *amici* will create a hierarchical distinction between branded drugs and generic therapeutic substitutions by mandating substantially greater safety monitoring for branded drugs and, from a safety point of view, an inferior class of solely generic drugs. A doctor choosing between therapeutic substitutes will therefore have a practical incentive to select the branded drug knowing its patent holder will actively monitor it for health risks (and that if there is a failure to do so, the patient will have recourse), thereby undercutting Congress's goal to promote substitution of generic equivalents. This Court recently determined

state-law failure-to-warn suits concerning branded drugs are not preempted; finding preemption for similar suits concerning generic drugs places actually places generic drugs at a competitive disadvantage in the healthcare marketplace.

In sum, petitioners and their *amici* present no evidence that state tort claims must be preempted to preserve the viability of the generic market. A finding of preemption would in fact undercut the purposes of Hatch-Waxman, as well as the confidence physicians and consumers have in generic products, by creating a meaningful difference in the value of generic and branded drugs where previously none existed.

## IV. STATE TORT LIABILITY ENSURES THE INCENTIVES OF GENERIC MANUFACTURERS, LIKE THEIR BRANDED COUNTERPARTS, ARE ALIGNED WITH CONSUMERS

The contributions of tort law to product safety were recognized early on by leading thinkers of the law and economics movement. The safety and efficiency benefits of state-law failure-to-warn suits are precipitated by a nuanced array of economic and structural forces, but all those forces are tied together by two fundamental concepts: incentives and information. The recourse provided by state failure to-warn suits helps align producer incentives with consumer safety concerns and ensure that consumers have optimal information so that market transactions are more apt to be based on mutually beneficial exchanges between consumers and producers.

### A. Failure-to-Warn Litigation Promotes Safety by Encouraging Drug Manufacturers to Respond to Risks

Both branded and generic manufacturers share the need to be incentivized beyond the federal regulatory machinery to report known safety risks or signals of their products. State tort suits provide the incentives that complement the FDA, a deterrence mechanism that federal agencies like the FDA cannot replicate. The availability of state failure-to-warn litigation helps protect consumers when harmful consequences become apparent regarding drugs that have already been approved by the FDA. When such information becomes apparent to manufacturers and not the FDA, as is usual, manufacturers may not act appropriately with that information.

Manufacturers often continue to distribute their products for many years while denying serious safety risks or downplaying emerging safety concerns.[78] That conduct occurs because providing new safety information quickly and accurately to the FDA may cause the Agency to recommend adding new warnings to the label, or to remove the drug from the market altogether, reducing (or eliminating) use of the product as well as manufacturer profits. Even under the current system, there is evidence

78. *See* Bruce M. Psaty & Richard A. Konmal, *Reporting Mortality Findings in Trials of Rofecoxib for Alzheimer Disease or Cognitive Impairment: A Case Study Based on Documents from Rofecoxib Litigation*, 299 J. Am. Med. Ass'n 1813, 1813-17 (2008); Bruce M. Psaty et al., *Potential for Conflict of Interest in the Evaluation of Suspected Adverse Drug Reactions: Use of Cerivastatin and Risk of Rhabdomyolysis*, 292 J. Am. Med. Ass'n 2622, 2626-30 (2004).

that some drug manufacturers have attempted to hide information from the FDA to get approval to market their drugs.[79]

State failure-to-warn litigation provides substantial penalties for manufacturers' decisions to hide or downplay reports of safety issues that emerge after a product reaches the market. Potential damage awards provide drug manufacturers with a strong incentive to expeditiously provide full and clear information to physicians and the FDA that otherwise may not come to light. Without such litigation, drug manufacturers would have a stronger incentive to act in their immediate financial interest and be less forthcoming in providing emerging safety-related data and the vast majority of consumers would have no remedy or recourse in the face of injury as a result of drug manufacturers' failure to disclose known risk information.

Further, state failure-to-warn suits encourage drug manufacturers to work with the FDA to ensure that labels accurately reflect the risks associated with a given treatment. The overwhelming incentive in the absence of state tort liability would be to refrain from proposing label changes under FDA regulations, even though they have the right and duty to propose such changes and even if they have a clear understanding that such changes are necessary to protect patient health.

Reducing the potential cost of concealing information (which would occur if state tort liability were removed)

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79. *See, e.g.*, *In re Baycol Prods. Litig.*, 218 F.R.D. 197, 201-02 (D. Minn. 2003); *In re W. Va. Rezulin Litig.*, 585 S.E.2d 52, 58-59 (W. Va. 2003).

would encourage drug manufacturers to withhold critical safety information more often. Failure-to-warn litigation thus encourages manufacturers to market their products accurately and fairly. The net effect of this complementary arrangement is the promotion of full and accurate knowledge about drug risks and the minimization of misstatements or error in drug labeling. A significant literature chronicles the social welfare benefits of dual regulation of risky technologies,[80] noting, for example, that "[t]he common law system's independence and private incentives to challenge the status quo are particularly valuable antidotes to complacency and ineffective regulation."[81] Accordingly, state-law failure-to-warn litigation serves as a valuable complement to FDA regulation.

### B. Harnessing the Forces of Decentralization, Failure-to-Warn Litigation Expedites the Diffusion of New and Potentially Vital Information on Emerging Drug Risks

State tort liability suits serve an essential role in facilitating the rapid transmission of information about drugs' properties. Given the decentralized nature of

80. *See generally* C.F.Larry Heimann, *Acceptable Risks: Politics, Policy, and Risky Technologies* (1997); Jonathan Bendor, *Parallel Systems: Redundancy in Government* (1985); Michael M. Ting, *A Strategic Theory of Bureaucratic Redundancy*, 47 Am. J. Pol. Sci. 274 (2003); Martin Landau, *Redundancy, Rationality, and the Problem of Duplication and Overlap*, 29 Pub. Rev. 346 (1969).

81. William W. Buzbee, *Asymmetrical Regulation: Risk, Preemption, and the Floor/Ceiling Distinction*, 82 N.Y.U. L. Rev. 1547, 1556 (2007).

the court system, civil tort trials can help reveal the unexpected effects of drugs after they have been approved by the FDA, and even after the branded manufacturer has left the market, by providing individuals with local recourse. Litigation brought by individual patients can help uncover previously unavailable data on adverse effects, questionable practices by manufacturers, and flaws in regulatory systems.[82]

Forcing generic manufacturers to report known safety risk or signal information places drug-wide labeling issues under the microscope of the adversarial system and at the FDA. The immense value of the adversarial system in gathering information that even a centralized body of experts might miss is a philosophical pillar of the U.S. court system.[83]

The court system harnesses the power of market forces to catalyze the dissemination of information. Failure-to-warn suits give lawyers an economic incentive to gather information about safety risks or signals which might be known to drug manufacturers but which have not yet been acted upon by national regulatory bodies. Conversely, the nontrivial costs of bringing a failure-to-warn suit acts as an additional filter on the legitimacy of the cases brought before the court: plaintiffs' attorneys will not recoup their investment if they undertake cases

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82. Aaron S. Kesselheim & Jerry Avorn, *The Role of Litigation in Defining Drug Risks*, 297 J. Am. Med. Ass'n 308, 308-11 (2007).

83. *See, e.g.*, David Bernstein, *Expert Witnesses, Adversarial Bias, and the (Partial) Failure of the Daubert Revolution*, 93 Iowa L. Rev. 451, 457 n.28 (2008).

without a reasonable hope of success. Similarly, FDA decisions and pronouncements can also play a significant role in juries' evaluation of failure-to-warn cases.[84]

84. Kessler & Vladeck, *supra* n.65, at 477 (noting that a "drug company would have a powerful defense" when it is "able to argue to the jury that it complied with applicable FDA requirements and that the plaintiff is complaining about the absence of a warning the FDA had rejected").

## CONCLUSION

Given the potential ambiguity and bias inherent in drug risk assessment, the well-documented problems with manufacturers' reporting of adverse events to the FDA, and the Agency's limited capacity to analyze the safety data it receives, state failure-to-warn suits are necessary to supplement the FDA's regulatory mission. Generic manufacturers have ample scientific and financial resources with which to fulfill the reasonable demands of product liability in state court. Continued tort liability is essential to preserve the alignment of manufacturers' and consumers' interest in full disclosure of evolving risk information. For these reasons and those in the respondents' brief, the Court should affirm the judgment of the lower courts.

Respectfully submitted,

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