MAY 4 - 2010

No. 09-1039

IN THE

Supreme Court of the United States

ACTAVIS ELIZABETH, LLC,
Petitioner,

v.

GLADYS MENSING,
Respondent.

On Petition for a Writ of Certiorari to the United States Court of Appeals for the Eighth Circuit

REPLY BRIEF FOR PETITIONERS

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REPLY BRIEF FOR PETITIONER

This Court should grant review because the Eighth Circuit incorrectly applied this Court's decision in *Wyeth v. Levine*, 129 S. Ct. 1187 (2009). The lockstep adherence of the lower federal courts to the Eighth Circuit's misapplication of *Wyeth* requires this Court's intervention now, before generic drug manufacturers are forced by the threat of liability to abandon their low-cost business model, which provides patients access to drugs at reduced prices as envisioned by Congress when it passed the Hatch-Waxman amendments.

I. THE DECISION BELOW REFLECTS THE LOWER COURTS' CONFUSION ABOUT THE APPROPRIATE APPLICATION OF *WYETH*.

Respondent claims that the decision below was a "straightforward application" of this Court's decision in *Wyeth,* and that the lower courts are not confused about the appropriate application of that case. Opp. at 1, 9-10. In reality, the Eighth Circuit and the lower courts generally have misapplied *Wyeth*, treating it as abrogating federal preemption for all drug product liability claims, even though, in contrast to *Wyeth,* here it is impossible to comply with both federal and state law.

The Court's determination in *Wyeth* that a brand drug manufacturer could comply with federal as well as state law regarding product labeling turned on the "Changes Being Effected" process, which the Court held allows a brand drug manufacturer to change a label on its own, subject to

later FDA approval. *Wyeth*, 129 S.Ct. at 1196-97, 1199. The Eighth Circuit, while relying heavily on *Wyeth,* did not rule on whether the CBE process was available to generic drug manufacturers. Pet. App. 11a-12a. Instead, the Court below thought it was sufficient that a generic drug manufacturer could propose a label change for later FDA approval. *Id.* at 11a-12a, 14a-15a. Nothing in this Court's *Wyeth* opinion, however, suggests that there could be state tort liability for not proposing a change to the FDA. Moreover, unlike a failure to make a label change under the CBE regulation, a generic drug manufacturer's failure to propose a change can cause an injury only if can be shown that the FDA would have approved the change.

The near unanimity among the lower court decisions as to the result of the preemption analysis masks an important divergence in rationale.[1] Unlike the Eighth Circuit, which interpreted *Wyeth* as precluding preemption because a generic drug manufacturer can *request* a labeling change, the Fifth Circuit has concluded that generic drug manufacturers, like brand manufacturers, can unilaterally change the label under the CBE

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[1]In *Gaeta v. Perrigo Pharm.*, 672 F. Supp.2d 1017 (N.D. Cal. 2009), the district court denied a motion for reconsideration based on *Wyeth*, correctly ruling that, in contrast to the brands, generic manufacturers may not change their labels without FDA approval. *Id.* at 1020-21. *Accord Morris v. Wyeth, Inc.*, No. 1:07-CV-176-R, 2009 WL 736200 (W.D. Ky. March 4, 2009), denying reconsideration in light of *Wyeth* of 582 F. Supp.2d 861, 868-69 (W.D. Ky. 2008) (claims against generic but not brand manufacturers preempted). *Morris* and companion cases are before the Sixth Circuit. *See* Pet. 4 n.4; Opp. 7 n.4.

regulation. *See Demahy v. Actavis, Inc.*, 593 F.3d 428, 436 (5th Cir. 2010). As we demonstrate in Section II, the Fifth Circuit's rationale is flatly inconsistent with the applicable statute and regulations. District courts have adopted the incomplete rationale of the Eighth Circuit,[2] the erroneous rationale of the Fifth Circuit,[3] or left the reasoning unclear.[4]

The only other option, according to the Eighth Circuit, is for the generic drug manufacturers to cease selling generic drugs. Pet. App. 18a-19a. But this Court has held in a related context that state laws that prevent companies from engaging in

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[2]*Swicegood v. Pliva, Inc.*, No. 1:07-CV-1671-TWT, 2010 WL 1138455, at *6 (N.D. Ga. March 22, 2010) *Weilbrenner v. Teva Pharmaceuticals USA, Inc.*, No. 7:08-CV-23(HL), 2010 WL 924915, at *7 (M.D. Ga. March 10, 2010); *Vitatoe v. Mylan Pharm., Inc.*, No. 1:08CV85,2010 WL 1008788, at *15 (N.D. W. Va. March 5, 2010); *Fulgenzi v. Wyeth, Inc.*, No. 5:09CV1767, 2010 WL 649349, at *6 (N.D. Ohio Feb. 19, 2010); *Couick v. Wyeth, Inc.*, No. 3:09-cv-210-RJC-DSC, 2009 WL 4644394 at, *3 (W.D.N.C. Dec. 7, 2009).

[3]*Dorsett v. Sandoz, Inc.*, No. CV 06-7821AHM, 2010 WL 1174204, at *17-18 (C.D. Cal. March 26, 2010) ; *Munroe v. Barr Lab., Inc.*, 670 F. Supp.2d 1299, 1302-03 (N.D. Fl. 2009) ; *Stacel v. Teva Pharm. USA*, 620 F. Supp.2d 899, 907 (N.D. Ill. 2009); *Bartlett v. Mutual Pharm. Co.*, 659 F. Supp.2d 279, 296-305 (D.N.H. 2009).

[4]It is unclear whether the district court considered any argument specific to generic manufacturers in *Schrock v. Wyeth, Inc.*, 601 F. Supp.2d 1262 (W.D. Ok. 2009), which was decided a week after this Court's decision in *Wyeth v. Levine*. The decisions in *Pustejovsky v. Wyeth, Inc.*, No. 4:07-CV-103-Y, 2009 WL 3336032 (N.D. Tex. Sept. 4, 2009), and *Kellogg v. Wyeth*, 612 F. Supp.2d 437 (D. Vt. 2009) are unclear about the rationale for rejecting preemption.

activities expressly authorized by federal law – here the sale of a drug under its FDA-approved label – are preempted. *See Watters v. Wachovia Bank, N.A.*, 550 U.S. 1, 21 (2007) (state law may not interfere with "business of banking" as authorized by the National Banking Act). Forcing companies to go out of business is not an acceptable means of harmonizing federal and state law obligations.

II. GENERIC DRUG MANUFACTURERS CANNOT CHANGE LABELS OR SEND "DEAR DOCTOR" LETTERS WITHOUT FDA APPROVAL.

Respondent claims that generic drug manufacturers have two ways to issue warnings about side effects: a unilateral label change under the CBE regulation or a "Dear Doctor" letter. Opp. at 5. The Eighth Circuit declined to adopt that rationale. Pet App. 11a-12a (declining to decide availability of CBE process), 16a & n.5 (expressing disagreement with the claim that generic drug manufacturers can send Dear Doctor letters without prior FDA approval). Although Respondent's argument is more consistent with the rationale of *Wyeth* than the Eighth Circuit's decision, the decision cannot be defended on that ground. Unlike pioneer drug manufacturers, manufacturers of generic drugs may not change their labels pending FDA approval under the CBE process or unilaterally send information to physicians.

A generic drug is required by law to have the same label as the brand. The Federal Food, Drug and Cosmetic Act states that FDA will approve a generic drug for marketing only upon proof that the drug has,

among other things, the same labeling as the brand drug. 21 U.S.C. § 355(j)(2)(A)(v); *see also* 21 U.S.C. § 355(j)(4)(G); (one of the grounds for not approving a generic drug application is that "information submitted in the application is insufficient to show that the labeling proposed for the drug is the same as the labeling approved for the listed drug"); 21 C.F.R. § 314.94 (generic drug labeling must be identical to brand).[5]

The requirement for identical labeling could not be more straightforward. A generic drug is required to have labeling that is identical to the brand at *all times,* not just at the moment the ANDA is approved. If the brand manufacturer changes the drug label after a generic drug has been on the market, the generic drug manufacturer must revise its label. *See* FDA, Guidance for Industry, Revising ANDA Labeling Following Revision of the RLD Labeling (May 2000). If a generic drug does not maintain the same label as the brand, FDA can remove the generic drug from the market for that reason. 21 C.F.R. § 314.150(b)(10).

Generic drug manufacturers cannot unilaterally issue warning through "Dear Doctor" letters either. FDA's long standing instructions for these mailings are directed to the brand companies, supporting the underlying policy that the brands issue a single letter covering generic and brand products. *Demahy,* 593 F.3d at 444-45. When Congress passed the Food and Drug Administration

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[5]The statute and regulations do permit certain differences in labeling that are not applicable here. *See* 21 U.S.C. § 355(j)(2)(A)(v) and 21 C.F.R. § 314.94.

Amendments Act (FDAAA) of 2007, it directed FDA to send Dear Doctor letters on behalf of generic drug manufacturers. 21 U.S.C. § 355-1(i). The Eighth and Fifth Circuits correctly recognized that FDAAA provides support for the proposition that Congress and FDA never intended that generic drug manufacturers unilaterally send out Dear Doctor letters as respondent suggests. Pet. App. 16 n. 5; *Demahy*, 593 F.3d at 445.

III. THE CONFLICT BETWEEN FEDERAL AND STATE LAW CANNOT BE OVERLOOKED TO PROVIDE COMPENSATION FOR INJURIES.

Respondent accuses generic drug manufacturers of seeking a special immunity that would prevent compensation of patients injured by drug side effects. Opp. at 1, 10-13. To the contrary, the question is whether generic drug manufacturers may be sued under state law for failing to do something they are forbidden to do under federal law – issue warnings that are inconsistent with the pioneer drug's label. Applying federal preemption would limit the potential sources of compensation for a drug-related injury, but that has never dictated the outcome of this Court's preemption cases. *See, e.g., Geier v. American Honda Motor Co.*, 529 U.S. 861 (2000) (holding product liability claim based on lack of air bags preempted).

It is also not clear that allowing lawsuits against generic drug manufacturers is necessary to compensate patients injured by generic drugs. In prescribing metcoclopramide for four years, Mensing's physicians disregarded the labeling

limiting the approved use of the drug to 12 weeks in light of the increased risk of side effects, and subjected themselves to potential liability for misprescibing the drug.

In her complaint, Mensing also sought damages from the makers of the pioneer drug (sold as Reglan) for promoting prolonged, off-label, use and misleading doctors about the risks by failing to modify its label. CA App. 25a. The Eighth Circuit ruled that Mensing could not pursue such claims as a matter of state law. Pet. App. 21a-24a. Courts applying state law have generally rejected such claims, holding that the pioneer drug manufacturers have no duty towards purchasers of the generic drug. However, the absence of compensation for injuries in such cases results from state product liability rules, not federal preemption.

IV. THIS COURT SHOULD NOT AWAIT A CIRCUIT SPLIT.

This case is an appropriate vehicle to decide a question of national importance that should be settled by this Court, as the Court did with respect to branded drugs in *Wyeth*. Although a division among the Circuits would be an additional reason to grant review, this Court should not wait for the outcome of the appeals now pending before the Sixth and Ninth Circuits. *See* Opp. at 7 n.4.[6]

Low-priced generic drugs now account for nearly 70% of prescription drugs sold in this country,

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[6]*Smith v. Wyeth, Inc.*, No. 09-5460 (6th Cir.) is scheduled for argument on June 9, 2010.

and are an important component of efforts to control healthcare costs.[7] The Eighth Circuit decision, however, threatens to undercut this success by imposing on the generic drug industry some of the very burdensome and duplicative requirements that the Hatch Waxman Act sought to eliminate.

As explained in the *amicus curiae* brief filed by the Generic Pharmaceutical Association, pp. 5-8, Congress designed a bifurcated regime for the manufacture of pharmaceuticals. Companies that manufacture branded "pioneer" drugs are responsible for testing the safety and effectiveness of their products through clinical trials. Generic drug manufacturers, in contrast to their brand counterparts, do not compile pre-approval safety data and they are not required to conduct pre-approval clinical trials. These companies, which manufacture generic drugs after the pioneer drug's patent protection has expired, are not even in possession of any of the brand manufacturer's pre-approval data. Nor are they in possession of any post-marketing data generated before approval of the generic.

Generic drug companies are required to report adverse events involving their products to the FDA, but they are not required to conduct any post-approval safety analyses. In fact, even after a generic

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[7] IMS Health and the Generic Pharmaceutical Association, *Economic Analysis, Generic Pharmaceuticals 1999-2008: $734 Billion in Health Care Savings* (May 2009), *available at* http://gphaonline.org/about-gpha/about-generics/case/generics-providing-savings-americans (generic medicines saved the American health care system more than $734 billion between 1999 and 2008 with approximately $121 billion in savings in 2008 alone).

drug is approved, the vast majority of adverse event reports go directly to FDA or the branded drug manufacturer. *See* FDA, Manual of Policies and Procedures, CDER, Office of Generic Drugs, Handling of Adverse Experience Reports and Other Generic Drug Postmarketing Reports, MAPP 5240.8 (November 1, 2005). Thus, even after generic drug competition has begun, the FDA will not permit a generic drug manufacturer to make a label change until the brand name does and then only to parallel a change made by the brand manufacturer. It is fair that the brand should bear the responsibility for monitoring new information about its drug since it has already reaped the benefits of patents that were extended in exchange for streamlining the requirements applicable to generic drug competitors. *See Abbott Labs, Inc. v. Young,* 920 F.2d 984, 985 (D.C. Cir. 1990).

The parade of district courts that have already followed the Fifth and Eighth Circuits into error threatens to force a restructuring of the drug industry from one in which development and monitoring expenses are borne by pioneer drug manufacturers who are compensated with an extended patent monopoly, to one in which generic drug manufacturers must develop their own analytical capabilities or must exit the business under threat of state tort liability. Generic drug manufacturers will be required to invest the substantial sums of money and time needed to analyze the underlying safety data and to collect and evaluate new data. Such an outcome would undermine the ability of generic drug companies to continue to sell their products at the substantially

reduced prices currently charged, as Congress intended.

The decisions of the lower courts create tremendous uncertainty which should be resolved by this Court so that the industry will know with clarity whether its companies are required to change their entire business model. The financial impact on this industry, which is so vital to patient care and efforts to control national health care costs, is by itself a sufficient reason to grant certiorari.

CONCLUSION

The petition for certiorari should be granted.

Respectfully submitted,

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