DEVELOPMENTS IN US PHARMACEUTICAL LITIGATION: PRE-EMPTION AFTER *WYETH V LEVINE*

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The *New York Times* billed *Wyeth v Levine* as a "blockbuster business case" (see Adam Liptak, 'Justices Weigh Effect of FDA Approval of Drug Labels on Suits in State Courts', 3 November 2008). For the pharmaceutical industry, the long-anticipated decision was expected to shape the future of its product-liability litigation. Specifically, in *Levine*, the US Supreme Court was asked to decide "whether the prescription drug labelling judgments imposed on manufacturers by the [FDA]... pre-empt state-law product liability claims." Thirty amicus curiae briefs were filed, including a brief by the FDA in support of pre-emption. However, on 4 March 2009 the Court issued its ruling, holding that Levine's claims were not pre-empted based on the facts of the case (*Wyeth v Levine*, 129 S. Ct. 1187 (2009)). Now, in the wake of *Levine*, the plaintiffs' bar is seeking to expand the reach of *Levine*, while the defence bar is working hard to limit it. Although the Court ultimately rejected complete pre-emption of state-law claims challenging the sufficiency of FDA-approved warnings, the issue is far from over. This article focuses on current developments relevant to pre-emption and thoughts about what the future may hold.

THE ROOTS OF PRE-EMPTION

The doctrine of pre-emption is rooted in the Supremacy Clause of the US Constitution, which states that the laws of the United States "shall be the supreme Law of the Land; ... any Thing in the Constitution or Law of any State to the Contrary notwithstanding" (Art. VI, Clause 2). Simply put, pre-emption mandates that a "state law that conflicts with federal law is 'without effect'" (*Cipollone v Liggett Group, Inc.*, 505 US 504, 516 (1992)).

Pre-emption may be either express or implied. Express pre-emption arises when specific language evidences an intent to pre-empt any other law dealing with the subject matter of a federal statute. In such situations, a court must decide if the state law is one that Congress intended to pre-empt.

An example of express pre-emption in the context of pharmaceutical and medical device litigation is found in the statutes governing FDA approval of so-called 360k medical devices. Specifically, 21 USC § 360k(a) states that "no State or political subdivision of a State may establish or continue with respect to [a medical device] any requirement... which is different from, or in addition to, any requirement applicable under this Act." The pre-emptive effect of this provision was recently put to the test in *Riegel v Medtronic, Inc.*, 552 US 312 (2008).

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In *Riegel*, the plaintiff alleged injuries due to a defective heart catheter. The heart catheter at issue was a Class III medical device which had been approved by the FDA through the rigorous pre-market approval (PMA) process. Medtronic argued that plaintiff's claims were pre-empted by the express pre-emption clause – § 360k(a) – of the medical device statute. On 20 February 2008, in an 8-1 decision with Justice Ginsberg as the lone dissenter, the US Supreme Court held that state-law tort claims against medical device manufacturers were pre-empted so long as the device was approved by the FDA through the PMA process.

Implied pre-emption, on the other hand, occurs when federal law exclusively occupies an entire field of regulation ("field pre-emption"), or when an implicit conflict exists between a Congressional enactment and a state law ("conflict pre-emption"). For example, in *Buckman Co. v Plaintiffs' Legal Committee*, 531 US 341 (2001), the plaintiffs claimed injuries resulting from defective bone screws. Specifically, the plaintiffs alleged that, were it not for alleged misrepresentations the manufacturer had made to the FDA during the approval process, these injuries would not have occurred. In a unanimous decision, the US Supreme Court held that such fraud-on-the-FDA claims inevitably conflict with the FDA's responsibility to police fraud under the statutory regime. As a result, the plaintiffs' claims were impliedly pre-empted by federal law.

Unlike the express pre-emption provision applicable to 360k medical devices, there is no clear pre-emption provision in the statutes governing FDA's approval of prescription drugs. Accordingly, in *Levine*, Wyeth was left to argue that FDA approval requirements impliedly pre-empt state tort-law claims due to inherently conflicting requirements.

WYETH V LEVINE: FACTUAL AND PROCEDURAL BACKGROUND

In April 2000, Diana Levine was treated for migraines and nausea with the prescription medication, Phenergan, which she first received by intramuscular injection. Ms Levine returned to the doctor as her symptoms continued. She was then given 50mg of Phenergan intravenously by the "IV push" method – twice the recommended dosage. Ms Levine received the entire 50mg dose of Phenergan continuously, despite complaining of pain during the injection. Ms Levine later developed symptoms of arterial exposure. As a result of this error, Ms Levine developed gangrene, ultimately requiring the amputation of her forearm.

At the time Ms Levine received

Phenergan, the product labelling included several warnings about improper administration, the risk of arterial exposure and the resulting risk of gangrene. The label, however, did not explicitly contraindicate the "IV push" method. The Phenergan label had been reviewed a number of times by the FDA as well as by an expert advisory committee. The plaintiff argued that Wyeth should have specifically contraindicated the "IV push" method; Wyeth, on the other hand, argued that it could not change the FDA-approved labelling without violating federal law.

The plaintiff sued Wyeth in a Vermont trial court claiming that the Phenergan labelling and warnings were inadequate. In dispositive motions, Wyeth argued that the plaintiff's claims were pre-empted, but the motions were denied by the trial court. The jury returned a verdict for the plaintiff in the amount of $6.7 million. On appeal, the Vermont Supreme Court affirmed the trial court's decision. The US Supreme Court granted certiorari in January 2008, and oral argument was held on 3 November 2008.

On 4 March 2009 the Court issued its 6-3 opinion in favour of Levine. Justice Stevens delivered the Court's majority opinion, joined by Justices Kennedy, Souter and Ginsberg. Justices Breyer and Thomas concurred in the judgment. Justice Alito wrote a dissenting opinion in which Chief Justice Roberts and Justice Scalia joined.

The Court's decision sets two "cornerstones" of pre-emption jurisprudence. First, the "purpose of Congress" is the ultimate touchstone in every pre-emption case. And second, in all pre-emption cases, the Court starts with the assumption that the historic police powers of the States were not to be superseded by a federal act unless that was the "clear and manifest purpose" of Congress.

The Court summarised the two main arguments advanced by Wyeth in favour of pre-emption. First, Wyeth argued that the plaintiff's state law claims were pre-empted because it was impossible for Wyeth to comply with both the state law warning duties and its duties to comply with the FDA approval requirements. The Court disagreed. It found that while federal law requires that every prescription drug label be approved by FDA, the "changes being effected" (CBE) regulation permits certain pre-approval changes to strengthen a drug's warnings and improve safety. Absent clear evidence that the FDA would not have approved the specific label change at issue, the Court would not agree that it was impossible for Wyeth to comply with both the federal and state requirements.

Second, Wyeth argued that requiring it to comply with a state law duty to provide a stronger warning would obstruct the purposes and objectives of federal drug labelling regulation. In other words, because Congress has entrusted an expert agency (the FDA) to make drug labelling decisions, states should not be permitted to allow lay juries to undermine those decisions. The Court rejected this argument as well, finding that if Congress was concerned that state-law suits posed an obstacle to its objectives, it would have enacted an express pre-emption provision – as it did for 360k medical devices.

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In sum, the Court held that the "manufacturer bears responsibility for the content of its label at all times ... [and] is charged both with crafting an adequate label and with ensuring that its warnings remain adequate as long as the drug is on the market." The Court noted that with over 11,000 approved drugs on the market, the manufacturer – not the FDA – is in the best position to monitor a drug's safety in light of new and existing information.

WHAT DOES THE HOLDING IN *LEVINE* MEAN?

Two lessons can be gleaned from the Court's opinion in *Levine*. First, while the US Supreme Court clearly rejected the application of pre-emption to the facts of *Levine*, its opinion did not close the door on pre-emption altogether. In fact, the Court's analysis recognises that there could be situations where it is impossible for a drug manufacturer to comply with both state law warning duties and FDA approval requirements. This point was conceded during oral argument by Levine's counsel. In response to a question about a circumstance where the FDA considered and rejected the specific warning at issue, Levine's counsel replied: "That'd be pre-empted. And the reason it would be pre-empted is because the FDA would have considered and rejected on the basis of the same information or similar information the very duty that underlies the State claim." The Court echoed this sentiment in its ruling, indicating that where a manufacturer can provide clear evidence that the FDA would not have approved the specific label change at issue, federal pre-emption is still a valid defence.

However, the Court noted that "impossibility pre-emption is a demanding defence" and made it clear that, if the manufacturer and FDA gave nothing more than "passing attention" to the health risk at issue, such evidence will not be enough to establish impossibility pre-emption. Drug manufacturers should be mindful of this caveat and structure their communications to the FDA in a manner that makes clear what health risks and what underlying information were considered and rejected by the FDA for inclusion in the product labelling.

Second, reading *Levine* in conjunction with *Riegel* indicates that the future of pre-emption, as applied to the FDA approval process, likely rests more in the make-up of Congress than in the make-up of the US Supreme Court. Indeed, the presence of a statutory pre-emption provision was the key difference between an 8-1 decision in favour of pre-emption as to medical devices and a 6-3 decision rejecting pre-emption as to prescription drugs. As the *Levine* court noted,

the "purpose of Congress" is the ultimate touchstone in every pre-emption case.

Amendments to add or remove pre-emption clauses from the current statutes could immediately abrogate *Riegel* or *Levine*. Shortly after the Court handed down its decision in *Riegel*, groups in both Houses of Congress began working on proposed changes that would eliminate any pre-emptive intent. Specifically, Rep. Frank Pallone, Jr. proposed HR 6381 – entitled the "Medical Device Safety Act of 2008"– which would add a provision stating that the Food, Drug, and Cosmetic Act would have no effect on liability under state law. Rep. Bruce Braley stated that such legislation would address the Supreme Court's "flawed decision in *Riegel v Medtronic*." In light of the current make-up of Congress, it is unlikely that any legislation in favour of pre-emption will become law. This outlook could change if there is a shift in the Congressional majority after the next election.

THE IMMEDIATE AFTERMATH OF *LEVINE*

Immediately following *Levine*, there was a judicial "backlash" against pre-emption in prescription drug cases. District courts that had granted temporary stays pending the outcome of *Levine* took up the issue and uniformly ruled against pre-emption. Moreover, less than a week after handing down its opinion in *Levine*, the US Supreme Court granted certiorari in *Pa. Employee Benefit Trust Fund v Zeneca, Inc.*, 499 F.3d 239 (3rd Cir. 2007) and *Colacicco v Apotex, Inc.*, 521 F.3d 253 (3rd Cir. 2008) – two Third Circuit cases that had specifically upheld the implied pre-emption defence. The Supreme Court immediately vacated the judgment in both cases and remanded them to the Third Circuit for further consideration in light of the *Levine* decision. The Third Circuit, in turn, reversed and remanded both cases to the district courts for further proceedings consistent with *Levine*.

Some lower courts, at the urging of the plaintiffs' bar, have also undertaken to expand the Supreme Court's holding in *Levine* beyond name-brand manufacturers. For example, on 27 November 2009, the Eighth Circuit became the first to apply *Levine* to failure-to-warn claims against generic drug manufacturers. In *Mensing v Wyeth, Inc.*, 588 F.3d 603 (8th Cir. 2009), the plaintiff sued both name-brand and generic drug manufacturers for alleged injuries resulting from ingestion of her prescription diabetes medication. The generic drug manufacturers sought summary judgment on grounds that, because the FDA requires generic drug manufacturers to use precisely the same label as the name-brand drug, it was impossible for them to comply with both state law and FDA requirements.

Pre-emption still remains a potential defence under limited factual circumstances

The court denied the motion, holding that, at most, the generic drug manufacturers established that it would be difficult but not impossible to comply with both requirements. The court stated that the regulatory framework governing generic drugs makes it clear that generic drug manufacturers must take steps to warn customers when it learns it may be marketing an unsafe drug. The generic manufacturers have filed Petitions for Writ of Certiorari in the US Supreme Court.

Soon thereafter, the Fifth Circuit Court of Appeals held that *Levine* applied to failure-to-warn claims against generic drug manufacturers. In *Demahy v Actavis*, Inc., 593 F.3d 428 (5th Cir. 2010), the court held that, while the statutes require the generic drug manufacturer to use the name-brand drug's label initially, there is nothing preventing it from modifying the label following initial approval.

At least one district court, however, has declined to extend *Levine* to claims against generic drug manufacturers. In *Gaeta v Perrigo Pharmaceuticals Co.*, 672 F. Supp. 2d 1017 (ND Cal. 2009), the US District Court for the Northern District of California was asked to reconsider its grant of summary judgment in favour of the generic drug manufacturer in light of *Levine*. The court declined, holding that the *Levine* court was not faced with the question of whether the CBE regulations allow generic drug manufacturers to make changes to their label without FDA approval. The court recognised that the underlying statutory framework governing labelling of name-brand drugs differs substantially from the one governing generic drugs.

The issue of generic drug pre-emption will continue to be on the "front burner" in the days ahead. Just recently, on 24 May 2010, the US Supreme Court issued an order in *Mensing*, inviting the Solicitor General to file briefs expressing the view of the United States on generic drug pre-emption. This unusual order, which came in the context of Petitions for Writ of Certiorari, indicates that the Court is well aware of the significance of this issue and its potential impact on the generic drug industry.

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While the US Supreme Court's ruling in *Levine* may have limited the reach of pre-emption, there is still hope. Pre-emption still remains a potential defence under limited factual circumstances. Precisely what may fall under the exception articulated in *Levine* remains to be seen. Counsel on both sides are looking to test the boundaries of the Supreme Court's opinion. Absent Congressional intervention, the scope of *Levine* will be determined by courts across the country in the days ahead.