Does Hatch-Waxman Need Modification? Regulatory And Legislative Developments Involving FDA's Proposed Rule On Generic Drug Labeling

The 1984 Hatch-Waxman Amendments to the Federal Food, Drug & Cosmetic Act, which facilitated the modern generic drug industry, is reported to be responsible for an estimated $1.2 trillion in reduced pharmaceutical spending in the last decade alone. Generic drugs now comprise approximately 85% of prescriptions dispensed in the United States, yet they account for less than 30% of the total prescription drug spending – a savings of more than $4 billion each week.

Despite these significant reductions in pharmaceutical spending from an economic standpoint, the absence of some regulatory guidance in Hatch-Waxman has led to significant controversy from a litigation standpoint. Two United States Supreme Court decisions, *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567 (2011), and *Mutual Pharmaceutical Co. v. Bartlett*, 133 S. Ct. 2466 (2013), have generated considerable debate because these decisions rely on the regulatory structure created by Hatch-Waxman to virtually eliminate a generic drug manufacturer's tort liability for failure to warn claims.

Responding to *Mensing* and *Bartlett*, on November 13, 2013, FDA issued a proposed regulatory rule that many argue will fundamentally alter the generic drug industry. The proposed rule would allow, for the first time, generic manufacturers to unilaterally update their labeling and then distribute the revised labeling before FDA reviews and/or approves the modification.[1] It is universally accepted that the proposed rule, if finalized in its current form, will effectively overrule *Mensing* and *Bartlett* and resurrect state failure to warn tort liability for generic drug manufacturers.

[1] FDA, Proposed Rule, *Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products*, 78 Fed. Reg. 67,985, 67,989, 67,995 (Nov. 13, 2013) (hereinafter "proposed rule").

While FDA's proposal has generated vigorous debate across a broad range of interested stakeholders, several recent developments – including agency delays, threatened legal challenges, and growing political opposition – have caused many to question whether the proposed rule will ever be finalized. But before discussing these recent developments and the political and legal hurdles still facing the proposed rule, it is important to understand the historical requirements for generic drug labeling, the rationale behind *Mensing* and *Bartlett*, and the arguments supporting and opposing FDA's proposed rule.

Historical Labeling Requirements for Generic Drug Manufacturers

Many argue that the success of the generic drug industry is rooted in the foundational requirement that a generic drug be the "same as" the brand-name product upon which it is based. Under the "sameness" requirement, a generic drug must be the brand-name's "pharmaceutical equivalent" (*i.e.*, the "same" active ingredient(s), route of administration, dosage form, and strength) and "bioequivalent" (*i.e.*, the equivalent rate and extent of absorption).[2] In addition, the statutory language of Hatch-Waxman expressly requires that the labeling for generic drugs must be "the same as the labeling approved for the [brand-name] drug."[3]

In the 30 years since the passage of Hatch-Waxman, only brand manufacturers have been allowed to add to or strengthen drug warnings without first obtaining FDA approval.[4] Because generic drugs have an ongoing federal statutory duty of "sameness," generic manufacturers are

[2] *See* 21 U.S.C. §§ 355(j)(2)(A)(ii)-(iv).

[3] *See* 21 U.S.C. § 355(j)(2)(A)(v).

[4] Brand manufacturers are permitted to make unilateral label changes in some circumstances under the changes being effected ("CBE") regulations. The CBE regulations permit brand manufacturers in appropriate circumstances to "add or strengthen a contraindication, warning, [or] precaution," or to "add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product." 21 CFR §§ 314.70(c)(6)(iii)(A); 314.70(c)(6)(iii)(C). When implementing labeling changes through the CBE process, brand drug manufacturers are not required to wait for pre-approval by FDA, which ordinarily is necessary to change a prescription drug label. Rather, the brand manufacturer can distribute the modified labeling to physicians and simultaneously file a supplemental application which is considered and evaluated by FDA. Importantly, however, a change effected under the "CBE" standard must still ultimately be approved by the FDA.

required to reproduce the labels of the branded counterpart. The United States Supreme Court described the different labeling duties of brand manufacturers and generic manufacturers by saying: "[a] brand-name manufacturer . . . is responsible for the accuracy and adequacy of its label . . . [and a generic manufacturer] is responsible for ensuring that its warning label is the same as the brand name's."[5] Thus, unilateral labeling changes by generic drug manufacturers have long been held to violate Hatch-Waxman's requirement that a generic drug's label be the "same as" its brand-name counterpart.

Failure To Warn Tort Liability For Generic Manufacturers In Light Of *Mensing* And *Bartlett*

Because generic drug manufacturers are prohibited from modifying their labeling unless FDA first approves a change to the branded drug label, two United States Supreme Court decisions have held that injured consumers of generic drugs have no right to recover for injuries allegedly caused by inadequate warnings in generic drug labeling.

In *Mensing* (2011), the plaintiffs claimed that the generic drug manufacturer could be liable under state tort law for failing to issue stronger warnings about its product – either through the CBE process or "Dear Doctor" letters – before the brand manufacturer issued such warnings. In rejecting this argument, the Court held that federal law precluded generic manufacturers from unilaterally changing their labels through any of the means suggested. The Court specifically stated that it is "impossible for the [generic] [m]anufacturers to comply with both their state-law duty to change the label and their federal law duty to keep the label the same [as the brand-name label]."[6] Therefore, the Court held that the plaintiffs' claims were preempted under federal law.

[5] *Mensing*, 131 S. Ct. at 2574.

[6] *Id.* at 2578.

Two years later, in *Bartlett* (2013), the Supreme Court rejected an argument that generic manufacturers could comply with both state and federal labeling duties by voluntarily removing the product from the market. The Court held that these state-law design defect claims, which effectively hinged on the adequacy of a generic drug's warnings, were also preempted under the same rational as *Mensing*. The Supreme Court once again based its decision in large part on the fact that generic manufacturers are "prohibited from making any unilateral changes to a drug's label" under federal law.[7]

The outcomes of *Mensing* and *Bartlett* are in stark contrast to another Supreme Court decision in *Wyeth v. Levine*, 129 S. Ct. 1187 (2009). In *Wyeth*, the Court held that state-law failure to warn claims involving brand manufacturers are not preempted as a matter of law because brand manufacturers, unlike generic manufacturers, are able to utilize the CBE process to make unilateral label changes. Thus, *Wyeth* reached a different result than *Mensing* and *Bartlett* because the Court held that the CBE process enables brand manufacturers to comply with both state law duties to warn and federal labeling obligations.

Recognizing that federal preemption for generic manufacturers can lead to a harsh result that makes "little sense" to injured consumers, the *Mensing* decision concluded by noting that "it is not this Court's task to decide whether the statutory scheme established by Congress is unusual or even bizarre."[8] Instead, the Supreme Court noted that the "regulations that apply to brand-name drug manufacturers are meaningfully different than those that apply to generic drug

[7] *Bartlett*, 133 S. Ct. at 2471.

[8] *Mensing*, 131 S. Ct. at 2582.

manufacturers."[9] The Court also acknowledged that "Congress and the FDA retain the authority to change the law and regulations if they so desire."[10]

Attempts To Nullify *Mensing*

Soon after *Mensing*, a consumer advocacy group filed a citizen petition with FDA requesting that the agency permit generic drug manufacturers to revise product labeling through the same CBE rules available to brand manufacturers.[11] Certain Congressional lawmakers also voiced serious concerns over the *Mensing* decision and implored FDA to take action to devise a system that allows consumers injured by generic drugs to seek a remedy in court.[12]

In April 2012, democrats in the Senate and House of Representatives introduced bills that would permit generic drug manufacturers to update warning information unilaterally. These bills never emerged from committee. Nevertheless, they generated support from Attorney Generals in 41 states and territories who endorsed a letter stating:

> This preemption holding produces arbitrary and unfair results, as both the majority and dissenting opinions [in *Mensing*] recognized. Consumers whose prescriptions happen to be filled with the brand-name version of a drug are protected by state law from inadequate warnings, but consumers whose pharmacists fill their prescriptions with the generic version are now denied this protection . . . . Fortunately, as the Supreme Court made clear . . . Congress can readily cure this problem by amending federal law. Congress should do so . . . .[13]

In the aftermath of *Bartlett* in 2013, those expressing concerns about the lack of fairness of generic drug preemption grew louder – encouraged in part by FDA's announcement in its

[9] *Id.*

[10] *Id.*

[11] Citizen Petition *available at* http://www.citizen.org/fda-petition-generic-drug-labeling-2013 (Attachment A).

[12] *See* April 11, 2012 letter from Rep. Henry A. Waxman to Hon. Margaret Hamburg (Attachment B); May 9, 2012 letter from Sen. Tom Harkin, Sen. Patrick Leahy, and Sen. Al Franken to Hon. Margaret Hamburg (Attachment C).

[13] May 11, 2012 letter to Sen. Patrick J. Leahy and Sen. Al Franken (Attachment D).

amicus curiae brief in *Bartlett* that it was "considering a regulatory change that would allow generic manufacturers . . . to change their labels in appropriate circumstances."[14]

Then, on November 13, 2013, FDA released its proposed rule which, as discussed above, would enable generic drug manufacturers to update their labeling through the CBE process. In the preamble to the proposed rule, FDA voiced concerns that *Mensing* "alters the incentives for generic drug manufacturers to comply with current requirements to conduct robust postmarketing surveillance, evaluation, and reporting, and to ensure that the labeling for their drugs is accurate and up-to-date."[15] FDA also claimed that the proposed changes are necessary to reflect growth of generic drug use and "create parity between [brand and generic manufacturers] with respect to submission of [CBE] supplements for safety-related labeling changes based on newly acquired information."[16]

Debating the Legality of the Proposed Rule

FDA's publication of the proposed rule ignited a heated debate over whether the proposed rule, if finalized, would be lawful. Critics note that FDA does not have the authority to overrule Congress or enact regulations which conflict with the plain text of a federal statute. They argue that FDA's proposed rule would unlawfully violate the statutory "sameness" requirement of Hatch-Waxman because it would necessarily result in generic drug labels that would differ from their branded counterparts. This argument appears to find support in *Bartlett*, where the Supreme Court noted that Congress explicitly enacted a regulatory structure that "leaves generic drug manufactures incapable of modifying either the drug's composition or their

[14] June 24, 2013 letter from various Senators and Representatives to Hon. Margaret Hamburg (Attachment E).

[15] *See* Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, 78 Fed. Reg. 67,985-02, 67,988-89 (November 13, 2013).

[16] *See* 78 Fed. Reg. 67,989.

warnings."[17] In fact, FDA itself – in regulations, industry guidance, and litigation briefing – has consistently interpreted Hatch-Waxman as precluding generic manufacturers from making labeling changes to deviate from the brand-name labeling.[18]

These legal concerns have also been raised by various Congressional lawmakers. In a sharply worded letter dated January 22, 2014, Republican members of the House Energy and Commerce Committee and the Senate Health, Education, Labor, and Pensions Committee expressed "grave concerns" that the proposed rule "would conflict directly with the statute, thwart the law's purposes and objectives, and impose significant costs on the drug industry and healthcare consumers."[19]

Responding to these claims, FDA contends it has ample authority to extend CBE rules to generic drugs under the same "authority over labeling for drugs" which permitted FDA to issue CBE rules for brand-name drugs. FDA also argues that the proposed rule promotes, not undermines, the "sameness" principles of Hatch-Waxman because the proposed rule would require all generic manufacturers to implement safety-related changes to drug labeling within 30 days after the change is approved by FDA. FDA argues that this requirement will reduce the differences in the labeling of brand and generic drugs because the current regulations do not impose a specific time requirement for generic manufacturers to implement FDA-approved label

[17] *Bartlett*, 133 S. Ct. at 2480.

[18] *See, e.g.*, 57 Fed. Reg. 17,961 (1992) (in promulgating its final rule implementing labeling requirements for generic manufacturers, FDA rejected the suggestion that the regulations should permit generic manufacturers to deviate from the brand-name labeling "to add contraindications, warnings, precautions, adverse reactions, and other safety-related information."); Center for Drug Evaluation & Research, Guidance for Industry: Changes to an Approved NDA or ANDA 24 (Nov. 1999) (FDA's guidance on labeling changes reiterates that generic manufacturers may not modify labeling to deviate from the brand-name labeling); *Mensing*, 2009 U.S. Briefs 993, 16-17 (Mar. 2, 2011) (FDA's amicus brief in *Mensing* acknowledges that FDA "has consistently taken the position that a [generic manufacturer] may not unilaterally change its approved labeling.").

[19] *See* January 22, 2014 letter to FDA from Republican members of the House Energy and Commerce Committee and the Senate Health, Education, Labor, and Pensions Committee (Attachment F).

changes, and many generic manufacturers delay making such changes for several months or longer.

Debating the Public Health Benefits of the Proposed Rule

There is also significant debate regarding FDA's motivation for issuing the proposed rule and whether the proposed rule would create any legitimate public health benefits. From a policy perspective, critics view the proposed rule as being motivated by litigation interests rather than legitimate concerns for patient safety or public health. The preamble to the proposed rule makes clear that it is designed in large part to eliminate the preemptive shield for generic manufacturers that has been firmly established in the wake of *Mensing*. This intended consequence arguably runs counter to FDA's longstanding position that its regulations cannot be designed as a means of impacting civil tort liability.[20] Critics also note that while there was little or no involvement from relevant industry groups during the rule development process, FDA has acknowledged that it had meetings with members of the Plaintiffs' bar before the proposed rule was released.[21]

Putting aside FDA's motivations, there is significant disagreement over whether the proposed rule would provide any meaningful benefit to the public health system. FDA contends that the proposed rule will have important benefits to both physicians and consumers. FDA claims that the exponential growth and maturity of the generic drug industry supports taking steps to ensure that health care practitioners and the public have access to the most current drug

[20] *See, e.g.*, Requirement for Labeling Directed to the Patient, 42 Fed. Reg. 37,636, 37,637 (July 22, 1977) ("[W]hether particular labeling may alter a manufacturer's liability in a given instance cannot be considered as a dispositive factor by the Commissioner in reaching a decision . . . ."); Labeling and Prescription Drug Advertising; Content and Format for Labeling for Human Prescription Drugs, 44 Fed. Reg. 37,434, 37,437 (June 26, 1979) ("It is not the intent of FDA to influence the civil tort liability of the manufacturer or the physician."); Prescription Drug Product Labeling; Medication Guide Requirements, 63 Fed. Reg. 66,378–01, 66,383 (Dec. 1, 1998) ("Tort liability can not [sic] be a major consideration for FDA which must be guided by the basic principles and requirements of the act in its regulatory activities.").

[21] *See* April 1, 2014 hearing of the House Energy and Commerce Committee Subcommittee on Health, *Examining Concerns Regarding FDA's Proposed Changes to Generic Drug Labeling*, testimony of Dr. Janet Woodcock, transcript and video *available at* http://democrats.energycommerce.house.gov/index.php?q=hearing/hearing-on-examining-concerns-regarding-fda-s-proposed-changes-to-generic-drug-labeling-subc.

safety information, which can then be used to better inform potential treatment decisions. FDA argues that to place this burden solely on the brand manufacturer, which often exits the market when generic drugs become available, and/or FDA, which does not have the resources to vigorously monitor and analyze post-marketing safety data alone, threatens patient safety.

Opponents of the proposed rule disagree with FDA's analysis, highlighting the potential negative public health consequences if different labeling simultaneously exists in the marketplace for the "same" drug. Specifically, they argue that different warnings on generic drug labels could suggest diminished safety or effectiveness and, in some circumstances, may drive physicians and/or patients to select brand-name drugs rather than a generic version. This lack of uniformity, opponents argue, could lead to confusion among healthcare professionals and consumers and may ultimately undermine confidence in the entire generic industry.

Also, given that generic manufacturers often do not have access to the clinical and safety data held by the brand manufacturer, the proposed rule would require generic manufacturers to make unilateral labeling changes based primarily on post-marketing adverse event information. This could result in the addition of safety information to labeling when that information is not scientifically accurate and/or is driven by reducing potential litigation exposure. It is also uncertain whether generic manufacturers are equipped – especially without incurring significant additional costs – to make these labeling assessments.

Given the potential increased product liability exposure and regulatory compliance costs, the proposed rule will almost certainly lead to an overall increase in the cost of generic drugs. These increased costs will be borne by consumers, insurers, and government healthcare programs. Some argue that these increased costs and potential liabilities may also result in

certain generic manufacturers exiting the market, which could result in an increased risk of drug shortages and/or increased reliance on brand-name drugs.

Finally, given that the proposed rule would result in brand and generic labeling with dissimilar warnings, precautions, and other safety information, physicians and pharmacists could be subject to new tort liability because of the particular brand or generic drugs they prescribe or dispense. Having numerous different labels for therapeutically equivalent drugs could also deter physicians and pharmacists from reviewing all of the labels and/or could significantly increase their workloads. These concerns have been raised by certain pharmacy and physician groups which do not support the proposed rule and have requested that FDA "fully explore the potential unintended consequences."[22]

Debating the Costs of the Proposed Rule

Another aspect of the proposed rule that has generated substantial controversy is whether FDA's cost-benefit analysis considered all of the likely costs associated with implementation of the proposed rule. FDA's initial projections estimated that the annual net social cost of the proposed rule is between $4,237 and $25,852, with the present discounted value over a 20-year horizon of between $44,890 and $384,616.[23] These figures are based primarily on the costs of "submitting and reviewing" the paperwork associated with anticipated labeling changes.

However, the accuracy and completeness of FDA's estimates have been called into question by numerous lawmakers and industry groups. For example, two republican legislators wrote a letter to the Office of Information and Regulatory Affairs requesting White House

[22] *See* March 6, 2014 letter to Dr. Margaret A. Hamburg (Attachment G).

[23] FDA, Proposed Rule, *Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products*, 67,986.

scrutiny of FDA's cost-benefit analysis.[24] This letter criticizes FDA's failure to consider any litigation-associated costs "despite the fact that reinstating tort liability for generic manufacturers was a stated intent of the rule." The letter also references a February 2014 economic analysis performed by Matrix Global Advisors that estimated that the annual costs of the proposed rule would jump to $4 billion if additional costs were considered.[25] The letter further cites to a public interest comment submitted to FDA by the Mercatus Center, which contends that FDA failed to: (1) estimate any costs associated with increased monitoring or researching, developing, and drafting label changes; (2) quantify increased costs incurred if generic manufactures submit multiple proposed label changes for the same adverse event; and (3) quantify the costs to FDA of maintaining a proposed website where information about pending CBE label changes would be provided to the public.[26]

Similarly, on June 4, 2014, a report from a House of Representatives Committee on Appropriations concluded that the proposed rule "fails to provide a net health benefit to consumers and providers" and directed FDA to "complete a new economic analysis of the rule, paying particular attention to the cost of pharmaceutical products."[27] To date, FDA has not published any new or revised economic analysis of the likely impact of the proposed rule.

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[24] *See* June 25, 2014 letter from Rep. Bon Goodlatte and Sen. Lamar Alexander to Hon. Howard A. Shelanski Attachment H).

[25] Brill, Alex, *FDA's Proposed Generic Drug Labeling Rule: An Economic Assessment*, Matrix Global Advisors (Feb. 5, 2014) (Attachment I).

[26] Nesbit, Todd, *Public Interest Comment on Docket No. FDA-2013-N-0500*, Mercatus Center George Mason University (Mar. 4, 2014) (Attachment J).

[27] Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations Bill, 2015, *available at* https://www.congress.gov/congressional-report/113th-congress/house-report/468/1.

Recent Developments and Final Thoughts

Based at least in part on the large number of public comments received from various stakeholders, on November 18, 2014, FDA announced that it did not expect to finalize the proposed rule until September 2015, at the earliest. While an FDA spokesperson noted that agency officials "routinely adjust dates" for finalizing proposed rules, some believe this delay may have been influenced by the recent mid-term elections where republicans obtained a majority in both the House of Representatives and the Senate. This recent delay – combined with the strength of the opposition's arguments – cause many to speculate whether FDA will ultimately finalize and implement the proposed rule. If it does, it likely will only be the beginning of a lengthy and expensive legal challenge that may end up right back where this controversy began – in the Supreme Court.