
Docket No. FDA-2013-N-0500

COMMENTS

of

THE WASHINGTON LEGAL FOUNDATION

to the

**FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH & HUMAN SERVICES**

Concerning

**SUPPLEMENTAL APPLICATIONS
PROPOSING LABELING CHANGES
FOR APPROVED DRUGS
AND BIOLOGICAL PRODUCTS**

IN RESPONSE TO THE PUBLIC NOTICE PUBLISHED
AT 78 *FED. REG.* 67985 (NOVEMBER 13, 2013)

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March 13, 2014

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Via Email

Division of Dockets Management (HFA-305)
Food and Drug Administration
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**Re: Supplemental Applications Proposing Labeling Changes for
Approved Drugs and Biological Products – Proposed Rule
78 Fed. Reg. 67985 (November 13, 2013)
Docket No. FDA-2013-N-0500; RIN 0910-AG94**

Dear Sir/Madam:

The Washington Legal Foundation (WLF) appreciates this opportunity to submit written comments in response to the Food and Drug Administration's (FDA) proposal to amend its regulations governing procedures for application holders of an approved drug or biological product to make unilateral changes in the product labeling.

The proposal would, among other things, permit holders of Abbreviated New Drug Applications (ANDAs) "to distribute revised product labeling that differs in certain respects, on a temporary basis, from the labeling of its reference listed drug (RLD) upon submission to FDA of a 'changes being effected' (CBE-0) supplement." 78 Fed. Reg. at 67985. WLF respectfully submits that this proposal is both ill-advised and in violation of FDA's statutory mandate, and urges FDA to withdraw the proposal.

The Hatch-Waxman Act, adopted by Congress in 1984 for the purpose of streamlining approval of generic drugs, requires that labeling for a generic drug must be "the same as the labeling approved for" the underlying brand-name drug. 21 U.S.C. § 355(j)(2)(A)(v). Self-

evidently, the labeling for a generic drug will not be “the same” as the labeling for the underlying brand-name drug if its manufacturer is authorized to distribute revised product labeling “that differs in certain respects” from the labeling of the underlying brand-name drug or RLD, even if only on a “temporary basis.” Accordingly, the FDA proposal would authorize conduct that Congress explicitly prohibited.

The proposal is also ill-advised. It would lead to patients and physicians being presented with multiple and potentially conflicting sets of health warnings for a single drug. Rather than promoting safety, it would lead to unnecessary confusion and uncertainty for the doctors who must decide whether the drug in question is appropriate for their patients. It would also significantly increase the exposure to product liability faced by generic manufacturers; the added expense would lead to increased prices (and potential shortages) for generic drugs, precisely the opposite of what Congress intended when it adopted the Hatch-Waxman Act.

The proposal states that FDA seeks to “create parity among application holders with respect to such labeling changes.” *Id.* WLF respectfully suggests that the best way to achieve “parity” would be to eliminate the ostensible authority of brand-name drug companies to make unilateral changes in their labeling. FDA has provided no evidence to suggest that the current authority of brand-name companies to make temporary labeling changes upon submission of a CBE-0 supplement has led to improved safety for patients.

I. *Interests of WLF*

The Washington Legal Foundation is a public interest law firm and policy center with supporters in all 50 States. WLF regularly appears before federal and state courts and administrative agencies to promote economic liberty, free enterprise, a limited and accountable government, and the rule of law. It devotes a substantial portion of its resources to defending the rights of individuals and businesses to go about their affairs without undue interference from government regulators. Among WLF's supporters are doctors and patients who desire to advance health care by ensuring that innovative and safe medical products reach the market without undue delay. WLF regularly litigates in support of patients who seek expedited access to life-saving medical products. *See, e.g., Abigail Alliance for Better Access to Investigational Drugs v. von Eschenbach*, 495 F.3d 695 (D.C. Cir. 2007), *cert. denied*, 552 U.S. 1159 (2008). WLF has opposed efforts to expand tort liability for manufacturers of drugs and biological products based on its conclusions that such efforts do little, if anything, to improve product safety and tend to restrict patient access to life-saving products by unnecessarily raising prices. *See, e.g., Mutual Pharmaceutical Co. v. Bartlett*, 133 S. Ct. 2466 (2013).

II. *FDA's Statutory Authority*

Congress adopted the Federal Food, Drug, and Cosmetic Act (the "FDCA"), 21 U.S.C. §§ 301 *et seq.*, to regulate the sale and distribution of drugs and medical devices to the public. Section 352(f) requires that all approved drugs bear "adequate directions for use." FDA does not approve the marketing of a new drug until after it has satisfied itself, among other things, that the drug is safe, effective, and adequately labeled for its intended use. 21 U.S.C. § 355(d).

In 1984, Congress amended the FDCA by adopting the Hatch-Waxman Act, Pub. L. No. 98-417, 98 Stat. 1585, which, among other things, was intended to streamline the approval of generic versions of previously-approved brand-name drugs whose patent protection has expired. Hatch-Waxman created the ANDA process; under that process, companies seeking to market a generic version of a previously-approved drug may rely on the safety and effectiveness data in the original NDA filing, 21 U.S.C. § 355(j), thereby facilitating quicker market entry by lower-cost drugs following expiration of the original applicant's exclusive marketing period. The only significant scientific information that must be included in an ANDA is evidence that the applicant's drug is "bioequivalent" to the original drug. 21 U.S.C. § 355(j)(2)(A)(4). If bioequivalence is demonstrated, Congress assumed that the generic drug shares the brand-name drug's safety and effectiveness.

That assumption significantly reduces the cost of developing and manufacturing generic drugs. As the Supreme Court has recognized, "[i]t is the special, and different, regulation of generic drugs that allowed the generic drug market to expand, bringing more drugs more quickly and cheaply to the public." *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2582 (2011). *See also, Bartlett*, 133 S. Ct. at 2480 (stating that it was "Congress' decision to regulate the manufacture and sale of generic drugs in a way that reduces their cost to patients"); 130 Congr. Rec. H8706 (Aug. 8, 1984) (statement of Rep. Waxman) (the previous lack of procedures for allowing generic manufacturers to piggy-back on the safety and effectiveness data in the original NDA filing "is an effective bar to generic competition because the generic companies cannot afford the millions of dollars to duplicate the test results already in the FDA's files.").

As amended by Hatch-Waxman, the FDCA provides that an ANDA submitted by a generic company must “show that the labeling proposed for the new drug is the same as the labeling approved for” the RLD. 21 U.S.C. § 355(j)(2)(A)(v). It further provides that FDA may not approve the ANDA unless the application demonstrates that the labeling “is the same.” 21 U.S.C. § 355(j)(4)(G).

III. FDA Regulatory History

Soon after the Hatch-Waxman Act amended the FDCA to include those statutory provisions, FDA adopted regulations confirming both that a generic manufacturer must ensure at all times that its product’s labeling is identical to its brand-name counterpart and that the “sameness” requirement prohibits generics from making unilateral labeling changes. As FDA explained in its Federal Register notice announcing its proposed rule change, it has maintained that position for the past three decades:

FDA has generally taken the position that a generic drug must maintain the same labeling as the RLD throughout the lifecycle of the generic drug product (see 21 C.F.R. § 314.150(b)(10)). Thus if an ANDA holder believes that newly acquired safety information should be added to its product labeling, it should provide adequate supporting information to FDA, and FDA will determine whether the labeling for the generic drug(s) and the RLD should be revised (see 57 FR 17950 at 17961; April 28, 1992).

78 Fed. Reg. at 67988. In particular, FDA has advised ANDA holders that they may not use the CBE-0 supplement process to “unilaterally change ANDA labeling in a manner that differs from the RLD.” *Id.*

FDA now proposes to change that three-decades-old policy in order for the first time to permit ANDA to use the CBE-0 supplement process to make unilateral changes to their product

labeling on a temporary basis, while they await word from FDA on whether it approves the labeling change on a permanent basis. FDA justifies the proposal as being based on “the need for an ANDA holder to be able to independently update its labeling as part of its independent responsibility to ensure that the labeling is accurate and up-to-date.”

IV. The Proposal Violates FDA’s Statutory Mandate

The FDCA could not be clearer that the ANDA holder has no authority to draft or revise the content of its product labeling. Rather, as noted above, its labeling must be “the same as the labeling approved for” the RLD. 21 U.S.C. § 355(j)(2)(A)(v). That rule is consistent with Congress’s determination that generic drugs could be marketed without additional safety and effectiveness testing precisely because they are bioequivalent to, and bear labeling identical to, the RLD. FDA’s contrary interpretation of its statutory mandate—whereby FDA claims authority to permit generic drug manufacturers to make temporary, unilateral labeling changes after submitting a CBE-0 supplement—is not plausible.

In support of its interpretation, FDA notes that it has a long history of interpreting its FDCA mandate as authorizing it to permit brand-name manufacturers to make temporary, unilateral labeling changes for the purpose of alerting physicians to “important, newly acquired safety information.” 78 Fed. Reg. at 67995. But that argument cuts against FDA’s position. Because FDA has a long history of interpreting its FDCA mandate as *not* authorizing it to permit generic manufacturers to make such labeling changes, the equivalent inference is that the FDCA does not grant such authority.

As the agency authorized to enforce the FDCA, FDA is entitled to interpret ambiguous

portions of the statute. Nonetheless, the Supreme Court has stated emphatically that courts will not defer to such interpretations when, as here, they are directly contrary to longstanding agency interpretations, particularly when the previous position has been enshrined in a formal regulation. *See, e.g., Wyeth v. Levine*, 555 U.S. 555 (2009).

Moreover, in two recent decisions, the U.S. Supreme Court has interpreted the FDCA to prohibit generic drug manufacturers from making unilateral labeling changes. *PLIVA*, 131 S. Ct. at 2582; *Bartlett*, 133 S. Ct. at 2470. FDA notes that *PLIVA* stated that FDA could change its CBE-0 regulations if it wished to do so. *PLIVA*, 131 S. Ct. at 2582. FDA undoubtedly has authority to amend its own regulations, but that is not the issue. The issue is whether *Congress*, in enacting the FDCA, permitted ANDA holders to make unilateral labeling changes, or permitted FDA to give ANDA holders such authority. The Supreme Court has answered that question “no”: “federal *law* prohibits generic drug manufacturers from independently changing their drugs’ labels.” *Bartlett*, 133 S. Ct. at 2470 (emphasis added). FDA is not permitted to second-guess that statutory interpretation; if it seeks the authority to authorize unilateral labeling changes, FDA should ask Congress to grant it.

In support of its position, FDA also cites the FDCA’s misbranding provision, 21 U.S.C. § 352, and its authority under 21 U.S.C. § 271(a) to issue regulations for the “efficient enforcement” of the FDCA. 78 Fed. Reg. at 67995. Those provisions add nothing to FDA’s argument. That FDA has authority to prevent distribution of a drug as “misbranded” because it does not bear adequate safety warnings does not imply authority to grant the drug’s manufacturer authority to make unilateral labeling changes in order to prevent the drug from being potentially

“misbranded.” Nor does the authority to issue regulations for the “efficient enforcement” of the FDCA imply an authority to issue regulations that countermand an explicit provision of the FDCA.

V. The Proposal Is Ill-Advised

The proposed regulation is not only unauthorized by Congress; it is also ill-advised. WLF does not claim significant medical expertise and thus does not fully comprehend the safety ramifications of FDA’s proposal. It nonetheless respects the conclusions of numerous health officials who are not beholden to the plaintiffs’ bar that the proposal will do nothing to advance patient safety and, to the contrary, is likely to lead to unnecessary confusion and uncertainty for the doctors who must decide whether the drug in question is appropriate for their patients. *See, e.g.,* March 6, 2014 letter to FDA from the Academy of Managed Care Pharmacy and 20 other groups (“[T]he proposed rule creates the regulatory framework whereby multiple different warnings can simultaneously exist in the marketplace for multiple generic versions of a drug. This would be inconsistent with FDA’s longstanding, unwavering emphasis on consistency in drug labeling and potentially confusing for health care professionals.”).

FDA’s proposal admits the possibility of confusion but proposes to deal with that confusion by creating a website on which it will post temporary label changes initiated by NDA and ANDA holders. 78 Fed. Reg. at 67989. WLF fails to understand how such a website would solve the confusion issue. All it would accomplish would be to highlight the existence of the confusion. That confusion will remain until FDA provides an answer as to which version of the product labeling is accurate.

The proposal would also significantly increase the exposure to product liability faced by generic manufacturers; the added expense would lead to increased prices (and potential shortages) for generic drugs, precisely the opposite of what Congress intended when it adopted the Hatch-Waxman Act. FDA admits that a significant motivating factor in its proposal is a desire to reverse the Supreme Court's decisions in *PLIVA* and *Mensing* and to permit those who allege they have been injured by a generic drug to file a failure-to-warn tort claim against the manufacturer. *Id.* at 67988-89. But any regulatory change that increases tort suits against generic manufacturers will cause generic drugs to become less affordable to needy patients. WLF respectfully suggests that the billions of dollars that would be diverted by the proposal to the legal system could be better devoted to direct improvements in healthcare.

Moreover, it is not at all clear, after the dust is settled and thousands of lawsuits have been adjudicated, that FDA will have accomplished its litigation-promoting purpose. The Supreme Court has already determined (in *PLIVA* and *Bartlett*) that Congress intended to preempt failure-to-warn tort suits against generic manufacturers. It is doubtful that the Court will reverse its statutory interpretation simply because FDA chooses to amend a regulation to permit ANDA holders to make unilateral, temporary labeling changes.

Finally, WLF notes that FDA has had many years of experience with a system that permits generic manufacturers to make unilateral labeling changes. Yet FDA has never come forward with any studies demonstrating that its system has led to improved healthcare results. In the absence of such evidence, there can be little justification for expanding that system to generic manufacturers, an expansion that is highly likely to lead to considerable confusion among

doctors and may well lead to decreased health care quality.

The proposal states that FDA seeks to “create parity among application holders with respect to such labeling changes.” *Id.* at 67985. WLF respectfully suggests that the best way to achieve “parity” would be to eliminate the ostensible authority of brand-name drug companies to make unilateral changes in their labeling. In the absence of evidence from FDA suggesting that the current authority of brand-name companies to make temporary labeling changes upon submission of a CBE-0 supplement has led to improved safety for patients, it is time to re-think the current policy.

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CONCLUSION

The Washington Legal Foundation respectfully requests that FDA withdraw its proposal to amend its regulations governing procedures for application holders of an approved drug or biological product to make unilateral changes in the product labeling.

Sincerely,

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