THE COMMITTEE ON ENERGY AND COMMERCE

MEMORANDUM

March 31, 2014

To: Members, Subcommittee on Health

From: Majority Committee Staff

Re: Hearing on "Examining Concerns Regarding FDA's Proposed Changes to Generic Drug Labeling"

On Tuesday, April 1, 2014, the Subcommittee on Health will hold a hearing entitled "Examining Concerns Regarding FDA's Proposed Changes to Generic Drug Labeling." The Subcommittee will convene at 3:00 p.m. in 2123 Rayburn House Office Building. The hearing will focus on a proposed rule issued by the Food and Drug Administration (FDA) on November 13, 2013, which, if finalized, fundamentally would alter longstanding policy regarding generic drug labeling changes under the 1984 Hatch-Waxman amendments to the Food, Drug, and Cosmetic Act (FDCA).

I. Witnesses

Panel One

Janet Woodcock, M.D., Director, Center for Drug Evaluation and Research, U.S. Food and Drug Administration.

Panel Two

Michael D. Shumsky, Partner, Kirkland & Ellis LLP;

Ralph G. Neas, President and CEO, Generic Pharmaceutical Association;

Allison M. Zieve, General Counsel, Public Citizen.

II. Background

Congress enacted the Hatch-Waxman Act in 1984, amending the FDCA to provide an abbreviated approval pathway for generic drug products and jumpstarting the modern generic drug industry. Under section 505(j) of the FDCA, an abbreviated new drug application (ANDA) will be approved if it shows that the generic product has the same active ingredient(s) as the brand-name product (otherwise known as the reference listed drug (RLD)); the same route of administration, dosage form, and strength as the RLD; and is bioequivalent to the RLD.[1] In

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

addition, the generic applicant must "show that the labeling proposed for the [generic] drug is the same as the labeling approved for the [RLD]. . . ."[2]

For over two decades, FDA has held that these "sameness" requirements apply to the generic product as long as it remains on the market—not only at the point of approval. With respect to labeling, FDA repeatedly has stated that a generic manufacturer would be in violation of the statute if it deviated from the FDA-approved labeling for the branded product.[3]

Further, the agency always has placed "a very high priority [on] assuring consistency in labeling" in order to "minimize any cause for confusion among health care professionals and consumers as well as to preclude a basis for lack of confidence in the equivalency of generic versus brand name products."[4] In fact, in 2008, FDA testified to Congress that the agency:

> carefully controls the content and labeling of medical products, because such labeling is FDA's principle tool for educating health care professionals and consumers about the risks and benefits of the approved products to help ensure safe and effective use. . . . FDA continually evaluates the latest available scientific information to monitor the safety of products and to incorporate new information into product labeling when appropriate. FDA takes care that labeling neither underwarns nor overwarns.[5]

Currently, as has been the case since enactment of the Hatch-Waxman Act, if a generic manufacturer believes that newly acquired safety information should be added to its product labeling, FDA has required that the company provide adequate supporting information to the agency. FDA then will determine, based on its broader knowledgebase and scientific expertise, whether the labeling for the brand-name drug—and all therapeutically equivalent generic products on the market—should be revised.[6] On the other hand, a brand-name drug manufacturer can submit a "changes being effected" (CBE-0) supplement and, prior to obtaining FDA approval, change the drug's labeling to reflect newly acquired safety information and immediately distribute the revised labeling. FDA will review the proposed change and approve it as proposed or request modifications. If and when the revised labeling is ultimately approved,

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[2] *Id.* at § 355(j)(2)(A)(v). According to FDA, the primary purpose of labeling (commonly referred to as the "package insert" or "prescribing information") for prescription drugs is to provide health care practitioners with the essential scientific information needed to facilitate prescribing decisions, thereby enhancing the safe and effective use of prescription drug products and reducing the likelihood of medication errors. Prescription drug labeling is directed to health care practitioners, but may include FDA-approved patient labeling. The statute does permit minor labeling differences to account for the fact that the drugs are produced or distributed by different manufacturers.

[3] *See* FDA, *Abbreviated New Drug Application Regulations—Final Rule*, 57 Fed. Reg. 17950, 17961 (Apr. 28, 1992) (stating that FDA will revoke a prior approval if the ANDA's "labeling . . . is **no longer consistent** with that for the listed drug.") (emphasis added); FDA, *Guidance for Industry: Changes to an Approved NDA or ANDA*, at 24 (Apr. 2004). *See also* 21 C.F.R. § 314.150(b)(10) (stating that FDA approval of an ANDA will be withdrawn if the agency finds that "the labeling for the drug product that is the subject of the abbreviated new drug application is **no longer consistent** with that for the listed drug.") (emphasis added).

[4] FDA, Division of Generic Drugs, *Policy and Procedure Guide* 37 (1989).

[5] *The Safety of Medical Products Regulated by FDA: Hearing Before the House Comm. On Oversight & Gov't. Reform*, 110th Cong. (2008) (statement of Randall Lutter, Dep. Comm'r for Policy, U.S. Food & Drug Admin.). at 2.

[6] *See* 57 Fed. Reg. at 17961.

all generic products on the market are required to conform their labeling. The CBE-0 supplement process is currently only available to generic drug manufacturers for such conforming changes.

III. ***PLIVA, Inc. v. Mensing***

On June 23, 2011, the U.S. Supreme Court held in *PLIVA, Inc. v Mensing*[7] that a generic drug manufacturer could not be held liable in State court for failure to include adequate warnings in its product labeling since Federal law prevents them from independently changing their safety-related labeling to strengthen warnings.

In an *amicus curiae* brief filed with the Supreme Court, FDA highlights the fact that the agency has "consistently taken the position that an ANDA holder may not unilaterally change its approved labeling,"[8] but notes that generic drug manufacturers "should discharge their duty to provide adequate warnings" by promptly bringing new safety information to the agency's attention.[9] FDA then states:

> Situations where an ANDA holder alone has a basis to believe stronger warnings should be added to its drug's approved labeling have not been known to arise frequently. And when one does, there tend to be unique, fact-specific considerations; as the parties and several amici point out, the Hatch-Waxman Amendments have fostered a diverse marketplace for generic drugs. For that and other reasons, FDA has not promulgated a formal regulation for this process.[10]

IV. **FDA's Proposed Rule on Generic Labeling Changes**

On November 13, 2013, FDA issued a proposed regulation, which would permit generic drug manufacturers to use the CBE-0 supplement process to unilaterally change their safety-related product labeling. In justifying the proposal on legal grounds, the agency states that under section 505(j) of the FDCA a generic drug is only "required to have the same labeling as the RLD at the time of approval," while acknowledging that "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."[11] In justifying the proposal on policy grounds, the agency states that "as the generic drug industry has matured and captured an increasing share in the market . . . FDA believes it is time to provide ANDA holders with the means to update product labeling to reflect data obtained through postmarketing surveillance . . . ."[12] To address "concerns about temporary differences in safety-related labeling for drugs that FDA has determined to be therapeutically equivalent, especially if multiple ANDA holders submit CBE-0 supplements with labeling

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[7] 131 S. Ct. 2567 (2011).
[8] Brief of Amicus Curiae United States at 20, PLIVA, Inc. v. Mensing, 131 S. Ct. 2567 (2011) (Nos. 09-993, 09-1039 and 09-1501).
[9] *Id.*
[10] *Id.* at 20-21.
[11] FDA, Proposed Rule, *Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products*, 78 Fed. Reg. 67985, 67988 (Nov. 13, 2013) (to be codified at 21 C.F.R. pts. 314 & 601).
[12] *Id.*

changes that differ from each other and from the RLD," the agency is proposing to "establish a dedicated Web page . . . on which FDA would promptly post information regarding the labeling changes proposed . . . ."[13] In the proposed rule, FDA mentions that if this proposal were finalized, "it may eliminate the preemption of certain failure-to-warn claims with respect to generic drugs."[14]

V. Staff Contacts

Should you have any questions regarding the hearing, please contact Paul Edattel, Carly McWilliams, or John Stone at 202-225-2927.

[13] *Id*. at 67988-67989.
[14] *Id*. at 67989.