March 11, 2014

Margaret A. Hamburg, M.D. Commissioner
Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Dear Commissioner Hamburg:

Re: FDA Docket No. FDA-2013-N-0500 and RIN 0910-AG94: Comments on Labeling Changes for Approved Drugs and Biological Products

The undersigned organizations applaud the Food and Drug Administration (FDA) for their proposed rule regarding "Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products"[1] and hereby submit the following comments in support of the proposed rule. The proposed rule properly addresses significant regulatory gaps in the FDA's current generic drug labeling regulations, which allow a generic drug manufacturer to maintain a label even if it knows that label to be inaccurate and out-of-date. In addition to raising serious safety concerns, the current regulations have had severe legal consequences for patients harmed as a result of unsafe generic drug labels. See, *PLIVA v Mensing*, 131 S. Ct. 2567 (2011).

Without question, this proposed rule is first and foremost a safety rule change. Under the proposed rule, whenever new information becomes available to a generic manufacturer that makes their product's current label inaccurate, a generic company "must take steps to change the content of its labeling." This obligation will arise not only under their current requirements, i.e., reporting post marketing adverse drug experiences to the FDA and requesting a label change, but also requires immediate labeling changes, commonly referred to as "changes being effected supplement." Because of the public health issues at stake, the agency would make this new information publicly available on a web page where the FDA will promptly post information regarding the labeling changes.

The new rule would reasonably and fairly expect generic companies, just like brand name drug companies, "to update labeling promptly to include a warning about a clinically significant hazard as soon as there is reasonable evidence of a causal association with a drug." In short, the proposed rule would "create parity" between brand name and generic drug companies to independently ensure safe product labels. American patients and prescribing physicians deserve no less.

The need for this rule change grew significantly more urgent when in 2011, in *PLIVA, Inc. v. Mensing*, 564 U.S. ___, 131 S.Ct. 2567, the U.S. Supreme Court immunized the generic drug industry for marketing drugs with labels they know to be inaccurate and out-of-date because current regulations prevent generic companies from independently changing drug labels. In its

[1] Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, *Pages 67985 – 67999* [FR DOC # 2013-26799] https://www.federalregister.gov/articles/2013/11/13/2013-26799/supplemental-applications-proposing-labeling-changes-for-approved-drugs-and-biological-products

proposed rule, the FDA stresses 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." Justice Sotomayor's dissent spelled out the safety implications of this decision:

> Today's decision eliminates the traditional state-law incentives for generic manufacturers to monitor and disclose safety risks. When a generic drug has a brand-name equivalent on the market, the brand-name manufacturer will remain incentivized to uncover safety risks. But brand-name manufacturers often leave the market once generic versions are available, meaning that there will be no manufacturer subject to failure-to-warn liability. As to those generic drugs, there will be no "additional… layer of consumer protection."[2]

Justice Sotomayor was referring to a case decided just two years before *Mensing*, *Wyeth v Levine*,[3] where the Court recognized the important role that lawsuits play keeping unsafe drugs off the market. The Court said, "[S]tate law offers an additional, and important, layer of consumer protection that complements FDA regulation." The Court noted, "FDA has limited resources to monitor the 11,000 drugs on the market and manufacturers have superior access to information about their drugs, especially in the postmarketing phase as new risks emerge."

Mensing did more than increase drug safety risks, however. It also eliminated important rights for the consumers of unsafe generic drugs. For example in 2009, patients who had experienced seizures and other serious adverse effects from Budeprion XL,[4] which was supposed to match the more well-known brand name, Wellbutrin XL, started bringing lawsuits against Teva Pharmaceuticals and Impax Laboratories, the distributor and manufacturer of Budeprion XL.[5] The patients argued that even though the companies knew there were problems, "they failed to disclose this information or warn patients and doctors about the differences between the medications." Between the start of the case and the settlement, the Supreme Court decided *Mensing*."[6] The companies then asked that the case be dismissed based on *Mensing*. However, they agreed to a mediation session with the patients and eventually settled. But the court pointed out that the patients were "leaving this litigation with much less than they sought when these cases were originally filed" acknowledging that *Mensing* made establishing liability much more difficult and emphasized the number of similar cases thrown out by "numerous courts" since the *Mensing* decision.[7]

The generic drug industry is opposing this rule change for two main policy reasons: increased costs and confusion. The cost argument is specious. First, a generic company's obligation to conduct post-market surveillance and provide the FDA with newly acquired safety information is

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[2] *PLIVA v Mensing*, 131 S. Ct. 2567 (2011) (Sotomayor, dissenting).
[3] *Wyeth v Levine*, 555 U.S. 555 (2009).
[4] http://www.propublica.org/article/no-substitute-when-a-generic-drug-isnt-what-it-seems
[5] In Re: Budeprion XL Marketing & Sales Litigation http://www.gpo.gov/fdsys/pkg/USCOURTS-paed-2_09-md-02107/pdf/USCOURTS-paed-2_09-md-02107-2.pdf
[6] *Id*., (citing PLIVA)
[7] *Ibid*.

unchanged by this rule, as are the costs involved. As to liability costs, this $43 billion industry[8] has had legal immunity only since 2011. State tort lawsuits coexisted with FDA generic drug regulation for decades before that.[9] All during that time period, the prices of generic drugs have remained low while the industry's market share has grown to extraordinary levels.[10] Further, this rule creates no new obligation for a generic manufacturer to conduct clinical trials or anything similar.

As to concerns expressed by some generic drug manufacturers that confusion might result from different generic drugs temporarily having different generic drug labels, the FDA has already taken important steps to address this issue. In fact, that is why the rule provides that updated safety information will be immediately posted on a dedicated FDA-controlled web site. According to the rule, the "FDA would promptly post information regarding the labeling changes proposed" and "the public may subscribe to FDA's free email subscription service to receive an email message each time there is an update to this proposed FDA Web page." This ensures that the most important safety information regarding a label change is readily and publicly available to patients and prescribing physicians, addressing any confusion resulting from a label change.

Moreover, the FDA properly acknowledged that strict adherence to the 1992 regulatory scheme, which requires generic labels to be identical to the brand, cannot continue in the current marketplace without grave risks to public safety. The 1992 policy simply did not contemplate the realities of the current marketplace. Nearly 80 percent of prescriptions are filled with the generic version of the drug, and many brand name drug manufacturers will remove their brand-named drug from the market after generic drug entry. This has resulted in a substantial amount of labels that may have inaccurate safety information due to a brand drug that no longer exists. As the agency notes, "concerns related to temporary differences in labeling between generic drugs and their [brand name counterparts] *are outweighed by the benefit to the public health* that would result from all [drug companies] having the ability to independently update drug product labeling to reflect newly acquired information regarding important drug safety issues." [emphasis added]

We believe the new rule actually presents less chance for labeling confusion than existing regulations. Under current regulations, a brand name drug can already initiate an immediate labeling safety change pending FDA review. As a result there already are instances where the brand and the generic have different labels for varying lengths of time. There is currently no requirement for labels to be updated within a certain timeframe. The proposed rule improves upon that by requiring that all labels be updated within 30 days. Overall, this will improve the safety of generic drug labels.

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[8] Generic drugs are a $43.1 billion industry. Steven E. Kuehn, "Generics Industry: Under Pressure," *PharmaManufacturing.com*, June 4, 2013, http://www.pharmamanufacturing.com/articles/2013/1306-generics-industry/

[9] The current generic drug regulatory scheme was first established by the 1984 Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act. 21 U.S.C. Food and Drugs, Chapter 9 § 301 et seq. Even before that, "[T]he legislative history of the [1938] FDCA suggests that Congress chose not to create a federal cause of action for damages precisely because it believed that state tort law would allow injured consumers to obtain compensation." *Mutual Pharmaceutical v Bartlett*, 133 S. Ct. 2466, ---- (2013) (Sotomayor, dissenting);

[10] As the agency notes, generic drugs account for over 80 percent of drugs prescribed today and "[a]mong drugs for which a generic version is available, approximately 94 percent are dispensed as a generic."

In sum, there's no question that consumers benefit from cheaper generic versions of drugs. There are good reasons why 80 percent of all drug prescriptions are filled by generic drugs today. However, no consumer saves money if a generic drug label is unsafe and she is medically harmed as a result - and then has no recourse in the courts. And as the law now stands, whether or not an injured patient has such legal recourse depends entirely on whether they have been prescribed a brand-name or generic drug, a situation which even the Supreme Court suggested was "bizarre."[11]

The Court said that "Congress and the FDA retain the authority to change the law and regulations if they so desire." Following this directive from the Court, the FDA has done precisely that with this proposed rule. This is an urgent safety rule change and we fully support its implementation.

Very sincerely,

Alliance for Justice
Brain Injury Association of America
Center for Justice & Democracy
Connecticut Center for Patient Safety
Mothers Against Medical Error
New Yorkers for Patient & Family Empowerment
Public Justice
Texas Watch

[11] "We acknowledge the unfortunate hand that federal drug regulation has dealt Mensing, Demahy, and others similarly situated. But "'it is not this Court's task to decide whether the statutory scheme established by Congress is unusual or even bizarre.'" *PLIVA, Inc. v. Mensing*, 131 S. Ct. ___ (2011).