November 14, 2014

Margaret Hamburg, MD
Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Dr. Hamburg:

Patient safety and safety-related labeling is of the utmost concern for both innovator and generic pharmaceutical companies. As we have discussed with you and your staff, both GPhA and PhRMA member companies believe that any regulation on patient labeling should maximize patient safety and minimize the chance for any confusion about safety warnings – especially for medicines that are marketed simultaneously as innovator and/or one or more generic versions ("multisource drugs"). Assuming that FDA is moving ahead with its proposed rule on safety labeling (***Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products [Docket No. FDA-2013-N-0500];*** hereinafter "the Proposed Rule"), GPhA and PhRMA believe that there are sensible revisions that can be made that will help eliminate the chance for confusion over safety warnings in a multisource environment.

While GPhA and PhRMA have expressed concerns about the Proposed Rule as written (see attached GPhA and PhRMA Comments posted to the Docket on March 13, 2014), we do support the basic goals set forth in the FDA proposal: (1) assuring that all application holders meet their responsibility of reporting safety related information; and (2) making newly evaluated safety information available to practitioners and the public as soon as possible.

GPhA and PhRMA have come to an agreement to support an alternative solution to the proposed rule on safety labeling that will meet all of our shared public health goals regarding multisource drugs – the Expedited Agency Review (EAR). The EAR proposal is consistent with comments that GPhA and PhRMA have submitted to FDA in the docket. Therefore, we would like to request a listening meeting with you and your key Leadership Team members so we can present, in detail, our proposal, and better explain how the Agency and key industry stakeholders can work together to effectively modernize the labeling change notification and review process when new safety information becomes available. These procedures will help ensure that patients and healthcare professionals receive accurate and timely label change notification.

We hope that the GPhA and PhRMA representatives can meet with you at the earliest opportunity.

Sincerely,

Ralph G. Neas
President and CEO
GPhA

John J. Castellani
President and CEO
PhRMA

Attachments

Alternative to the Proposed Rule on Labeling

Expedited Agency Review ("EAR") Post the First Generic Entrant

A. Summary

An "Expedited Agency Review" ("EAR") would establish defined time parameters for FDA to take action on a label change made: 1) following FDA's receipt and review of "*new safety information*"[1] from an NDA/ANDA holder; or 2) following review of data received through the Sentinel System and/or other databases including global sources that are suggestive of a need for a label change. The EAR process would replace the changes being effected process for safety-related labeling changes now permitted under 21 CFR §314.70(c)(6)(iii). The EAR would require FDA to provide NDA and ANDA holders with prompt notice of approval of a required label change, and it would specify the timeframes for NDA and ANDA holders to make a corresponding labeling change.

NDA and ANDA holders presently are active participants in the surveillance, receipt, and submission to FDA of pharmacovigilance data. They submit adverse event data to FDA in 15-day, quarterly, and annual reports. At the same time, NDA and ANDA holders are poorly situated to determine whether the information they possess truly is "*new*", because no individual applicant holder has access to all the available data – the proprietary data from clinical studies conducted by NDA holders, and/or the data held and/or provided by each individual applicant holder. Coincident with implementation of the EAR process, FDA would issue a guidance document on the identification and submission of "*new safety information*" to define NDA and ANDA holders' responsibilities in the process.

Unlike individual applicant holders, FDA possesses all the significant clinical trial data on a pharmaceutical product and all the adverse event and periodic reports from all manufacturers. In addition, FDA has enhanced its position as the primary repository of safety information for pharmaceutical products through creation of the Sentinel System. The Sentinel System is FDA's national electronic system that is utilized to track the safety of marketed drugs, biologics, and medical devices – see attached Appendix.

That approach has been limited by both a lack of data precision and an inability to perform signal identification. Active surveillance by the Sentinel System will allow FDA to identify an increased risk of common events that healthcare providers may not suspect are related to medical products. Therefore, public health can be protected more effectively by using the Sentinel System and relying far less on the historical passive reporting processes.

[1] "New safety information" has the definition provided in the Guidance for Industry: Safety Labeling Changes – Implementation of Section 505(o)(4) of the FD&C Act, dated July 2013.

The need for an EAR can derive from two sources: 1) NDA and ANDA holders who submit expedited and periodic reports and who believe data they are submitting to FDA might constitute "*new safety information*" can request an EAR; or 2) FDA can determine that it is in possession of "*new safety information*" from all the resources available to it and begin an EAR on its own initiative. Once an NDA or ANDA holder requests an EAR or FDA determines on its own initiative that an EAR should be undertaken, FDA must make a decision on the appropriateness of a label change within XX days (or sooner if FDA determines the circumstances warrant more expedited action). During that XX-day period, FDA engages the NDA and ANDA holders in discussions regarding the potential for a label change. Once FDA determines whether a label change is required, FDA immediately notifies the NDA and all ANDA holders of the decision. If the decision is to implement new labeling, NDA and ANDA holders implement the change within 30 days (or sooner if FDA determines the circumstances warrant more expedited action).

The goals of prompt dissemination of new labeling and assurance that different labels will not exist in the marketplace at the same time can be facilitated through e-labeling. The public health benefit of e-labeling is clear as it will speed up the availability of accurate, real-time, and consistent labeling of marketed products for pharmacists, physicians, and patients – see attached Appendix.

In an e-labeling environment product users will have immediate access to the latest information to reduce prescribing errors and adverse drug events as well as improve patient care. That is precisely the type of information that FDA states that it hopes to make available with its proposed labeling rule.

B. Process.

Step 1. NDA or ANDA holder requests EAR or FDA initiates EAR on its own.

Step 2. FDA begins review of all available safety data and engages NDA and ANDA holders in discussion of potential label change.

Step 3. If FDA determines through a review of all available safety data that a labeling change is required, FDA informs the NDA and ANDA holders of the content of the final labeling language immediately (within 15 days) and instructs the NDA and ANDA holders to update their labeling within 30 days via e-labeling.

Step 4. All application holders update labeling via e-labeling within 30 days.