



founded 1881

March 11, 2014

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Docket No. FDA-2013-N-0500
Supplemental Applications Proposing Labeling Changes for Approved Drugs
And Biological Products, 78 Fed. Reg. 67985 (November 13, 2013)

Dear Sir or Madam:

In the November 13, 2013, *Federal Register*, the Food and Drug Administration invited comments on the above-referenced proposed rule, which would amend regulations covering changes to product labeling for drugs under abbreviated new drug applications in advance of FDA's review of such changes.

The Consumer Healthcare Products Association (CHPA), founded in 1881, is the national trade association representing manufacturers and distributors of over-the-counter (OTC) or nonprescription medicines and dietary supplements in the United States. Our members make OTC drugs covered by both abbreviated new drug applications and new drug applications (including reference listed drugs on which ANDAs are based). As such, we have an interest in the subject matter of the proposed rule.

While we recognize FDA's effort to address the disparity among application holders is an important objective, the proposed rule raises significant concerns. If adopted as proposed, the proposed rule would create uncertainty and the potential for consumer confusion, particularly for OTC drugs. We ask that FDA consider the uniqueness and differences between how prescription and OTC drugs are labeled in resolving questions raised by the proposed rule.

1. Allowing temporary differences in safety-related labeling risks consumer confusion – a risk FDA has acknowledged as a concern. In the proposed rule itself, FDA acknowledges concerns about temporary differences in safety-related labeling for therapeutically equivalent drugs, especially if multiple ANDA holders submit CBE-0

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supplements that differ from each other and from the RLD. 78 Fed. Reg. 67985, 67989 (November 13, 2013). FDA also acknowledges interpretation of postmarketing safety data is complex, requiring judgment-based decisions about which reasonable persons with relevant expertise may disagree. 78 Fed. Reg. 67985, 67991 (November 13, 2013).

While specific across a class of products rather than a single NDA with multiple ANDAs, the analogous case of OTC medicines containing non-steroidal anti-inflammatory drugs (NSAIDs) provides a useful illustration of FDA's interest in label consistency. In this particular instance, a key FDA concern was *not* allowing label differences among products in the class. For this reason, FDA assured the agency's interpretation of postmarketing safety data, not different manufacturers', drove a class approach to labeling through rulemaking. In this instance, FDA provided 150 days rather than the usual 90 for comments, stating "because of the complexity of the proposed rule, FDA is providing an additional 60 days (beyond the normal comment period) for comments" 71 Fed. Reg. 77314 (December 26, 2006).

FDA had earlier requested that NDA holders of OTC NSAIDs follow very specific templates to assure consistency. See letter from Charles Ganley, Director, Office of Nonprescription Products, FDA, to NDA holders of OTC NSAIDs, July 15, 2005, requesting label changes via Changes Being Effected Supplements with firms requested to submit prior approval supplements for any deviation from the templates. While we acknowledge data-driven differences among ingredients in a class can lead to different labels, this case illustrates the importance of avoiding consumer confusion.

Finally, allowing consumers to locate safety information and allow effective comparisons between similar products, thereby helping consumers select the most appropriate product, has long been an FDA goal in OTC drug labels. See OTC labeling requirements final rule, 51 Fed. Reg. 13254 (March 17, 1999). This proposed rule runs counter to that policy.

2. The potential for confusion is heightened in the OTC category. FDA seeks to at least partially address the confusion potential of temporary differences in safety-related labeling for therapeutically equivalent drugs through a proposal for a dedicated Web page where FDA would promptly post CBE-0 labeling changes while FDA reviewed the supplement. 78 Fed. Reg. 67985, 67989 (November 13, 2013). The usefulness of this approach in general is questionable at best, and runs counter to the very nature of OTC drug labels. Consumers of OTC drugs rely almost entirely on the product label for relevant information about the product, given OTC medicines are purchased directly by the consumer through self-selection without the intervention of a physician or pharmacist. It is not practical to expect consumers to refer to a website to seek out or evaluate differences among product labels. The physical package label the consumer sees at shelf when choosing a product, and that same package label they take home and have available to them when using an OTC drug, is at the core of OTC drug availability. It is for this reason many OTC NDA holders, and almost all sponsors of prescription-to-nonprescription switch NDAs, conduct label comprehension studies to test how well consumers comprehend the information on the outside of the drug package, on the inner container,

and, if applicable, any insert or other informational material. See “Guidance for Industry: Label comprehension studies for nonprescription drug products,” FDA, August 2010; and FDA briefing document for Nonprescription Drugs Advisory Committee, November 9, 2012.

Many OTC NDAs also include self-selection studies to determine if a consumer can, after reading a product label, make a correct decision about whether or not the product is appropriate for her to use based on the indications and warnings. Self-selection studies might be combined with a label comprehension study, or with an actual use study to provide data to help predict if a drug will be used properly, safely, and effectively in an OTC setting. *Id.*

The larger point is that NDA holders work with FDA in the review of these studies to reduce the potential for confusion, ultimately providing consumers with labeling for selection at the store shelf and safe, effective use at home. It is not at all clear how this thorough process of developing an OTC drug label would translate to posting on a website aimed at healthcare professionals. It is even less clear how a consumer would utilize OTC labeling posted on a website to make a self-selection decision at point of sale. While websites can certainly advance safe and effective use, they cannot substitute for the package label, where today consumers see the same label for therapeutically equivalent products. If consumers were to see different or, even worse, conflicting labels, which should they believe? What label should guide their decisions on safe use of the medicine?

One additional factor related to potential for confusion which is unique to the OTC category is the presence of store brands. Major retailers regularly carry brands that are therapeutically equivalent to RLD brands under their own brand name (ie, “Store X brand NSAID”). These retailers contract with ANDA holders to provide them with these products – in other words, the manufacturer and the distributor are different entities. In the interest of enhancing competition, the same retailer may frequently contract with *more than one* ANDA holder for their own, retailer-branded *same* therapeutically equivalent product, creating the possibility of not just two brands of differently labeled, therapeutically equivalent products, but the *same* “Store X brand NSAID” product with two different labels manufactured by two different ANDA holders. The proposed rule would put the responsibility on the consumer to compare and evaluate products with potentially different labels, while FDA may also be evaluating the merit of the labeling changes under the agency’s own timeframe.

3. The potential for confusion is further heightened for OTC drugs given label changes involve multiple steps in the design, label printing, and manufacturing process. Even if, as the agency proposes, labeling differences among therapeutically equivalent products were resolved promptly, the reality of the OTC label process would lead to long lags in what consumers would see at shelf, potentially exposing consumers to differing labels between RLD brands and store brands. To change an OTC label, NDA or ANDA holders must go through a complex series of steps in package engineering, label design and layout, packaging components, label printing, validation and approval in the manufacturing

process, and ultimately applying labels in the manufacturing process itself. These steps have to occur in sequence, not concurrently. Apart from the special circumstances of a recall not at issue here, by the time an OTC drug label reaches a store shelf, months have been involved. FDA routinely acknowledges this reality by providing compliance dates of 6 months to a year beyond effective dates of rules related to OTC drug labels. In the case of NDA OTC NSAIDs, this acknowledgement was inherent when the agency requested label changes through a template with six months for implementation after submission of a CBE supplement. See letter from Charles Ganley, Director, Office of Nonprescription Products, FDA, to NDA holders of OTC NSAIDs, July 15, 2005.

If a firm filed a CBE-0 with an already prepared OTC label, and FDA subsequently approved that label change, other ANDA or NDA holders of therapeutically equivalent products would not be able to ship products with the new label for some months after firm filing the CBE-0. In that interim time period, consumers would continue to see different labels on the otherwise same product, again increasing the potential for confusion.

The proposed rule represents a significant change in what entity initiates label changes. The proposed rule fails to account for differences between how prescription and OTC drugs are labeled. We ask that FDA consider the uniqueness and differences between how prescription and OTC drugs are labeled in resolving questions raised by the proposed rule.

Thank you for the opportunity to comment on this important proposed rule and for considering these views.

Sincerely,



David C. Spangler
Senior Vice President, Policy,
and General Counsel & Secretary