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November 20, 2006

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

Re: Docket No. 2006D-0303, Draft Guidance for Industry on Public Availability of Labeling Changes in "Changes Being Effected" Supplements. [FR Doc. 06-07983] Vol. 71 (September 20, 2006) Pages 54999-55000.

Dear Sir or Madam:

The Biotechnology Industry Organization (BIO) provides the following comments. BIO represents more than 1,100 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and 31 other nations. BIO members are involved in the research and development of health-care, agricultural, industrial and environmental biotechnology products. BIO appreciates the opportunity to comment on the Food and Drug Administration's (FDA's) *Draft Guidance for Industry on Public Availability of Labeling Changes in "Changes Being Effected" (CBE) Supplements* (the draft guidance).

The central proposal in the draft guidance is that FDA will make revised labeling proposed in a CBE supplement publicly available on its website and through the DailyMed shortly after the supplement is received (and likely before FDA has reviewed or approved it). BIO recognizes that FDA is proposing this new approach with the goal of making the most current labeling widely available to healthcare practitioners and the public, and we support this goal. However, we believe that FDA's proposal will not achieve the intended goal, and will confuse rather than assist practitioners and the public, unless FDA addresses the issues we raise below. If these issues are not addressed, we believe FDA should not implement the draft guidance but should instead focus on improving processes for the prompt review and approval of CBE supplements and prompt posting of approved labelling.

We give specific comments on the proposal, and then we describe three related general concerns.

Specific Comments

Guidance Document, Section III "Discussion," p. 2: *"A sponsor should not submit a CBE supplement to FDA until the sponsor is ready to distribute the labeling that it proposes in that CBE supplement. FDA will consider the submission of a CBE supplement to be consent by the sponsor to post the proposed labeling on FDA's Web site and on the DailyMed. The Agency welcomes discussions with sponsors before they submit a CBE supplement."*

Comment: BIO is concerned that the recommendation to discuss CBE supplements with FDA prior to submitting them, to ensure that the proposed labeling from the supplement is ready to distribute, may delay the release of important CBE labeling safety information to the public. Discussing CBE supplements with FDA is not currently required in the regulations. The suggestion in the draft guidance that such a step is recommended could serve to delay communication of a supplement's safety information to the public. We request that this recommendation be removed.

In addition, we request clarification of the statement that a CBE supplement should not be distributed until a sponsor is "ready to distribute the labeling." First, "ready" is not clear in that some companies choose not to implement labeling changes at the time when, or shortly after, FDA receives the CBE supplement. The draft guidance should not preclude the possibility that a CBE supplement is submitted in advance of the time that a sponsor intends to distribute labeling. Second, it is not clear what the term "distribute" encompasses in this context. Labeling information may be disseminated to the public in a number of ways before trade product is distributed, e.g., along with samples, accompanying promotional materials, and on company websites. We request that (provided FDA addresses the other concerns we raise in our comments) FDA clarify that CBE supplements should be submitted at the time proposed labeling is "distributed" by any of these means.

Related General Concerns

BIO has three additional concerns related to this draft guidance that should be addressed within FDA, if the ultimate goal is for DailyMed to serve as the definitive and most up-to-date source of labeling content in the United States healthcare environment.

1. We have observed a trend toward FDA requesting minor revisions in the words, position, and construct of CBE labeling text, although these minor changes do not improve the safety message being conveyed through the labeling supplement. We recognize that FDA may have legitimate reasons to modify labeling proposed in a CBE supplement; indeed that is the reason why such supplements are submitted for review. However we note that the combination of this trend and the proposals in the draft guidance will frustrate rather than foster FDA's efforts to improve communication to healthcare practitioners and the public, because the result will be several variations of the labeling posted on DailyMed in a fairly short period of time. Furthermore this trend may

result in sponsors becoming reluctant to utilize the CBE provision at all, because they expect that FDA will require such minor modifications after CBE labeling has already been distributed. BIO requests that FDA refrain from modifying CBE labeling text as a rule, and that the text be modified only if there is substantive value to be gained.

2. We have noted inconsistencies in the interpretation of 21 CFR 314.70 within the review divisions with regard to what labeling supplements qualify as CBE versus Prior Approval (PA). Specifically, some divisions are insisting that supplements with safety wording be submitted as PA instead of CBE supplements. If this trend continues, the result will be that fewer updated labels will be posted promptly to DailyMed, and sponsors will become reluctant to propose CBE instead of PA supplements. BIO requests that CBE supplements be accepted as currently defined in CFR 314.70 and that PA supplements be reserved for situations when labeling discussions are necessary.

3. We note that currently not all labeling is posted to DailyMed in an expeditious manner, so that healthcare providers and the public cannot rely on DailyMed as the definitive and timely source of labeling content. We are concerned therefore about what may happen if FDA does require modifications based on its review of a CBE supplement. Specifically, we are concerned that the corrected label may not be posted and the uncorrected label may not be removed in a timely manner. This problem may be particularly acute when multiple CBE supplements are pending for the same product (this may happen, for example, where there are delays in review of labeling supplements); in such cases it will be particularly important that labels are posted and removed from the site in an orderly and expeditious fashion. We recognize that there have been incremental improvements in the timely posting of labeling on DailyMed, and we request that FDA ensure that all labeling is posted in a timely manner.

Conclusion

BIO appreciates this opportunity to comment on FDA's *Draft Guidance for Industry on Public Availability of Labeling Changes in "Changes Being Effected" (CBE) Supplements*. We look forward to seeing the final guidance, and would be pleased to work with FDA to provide further input or clarification of our comments, as needed.

Sincerely,

/s/

Sara Radcliffe
Managing Director
Science and Regulatory Affairs