



April 24, 2006

Dockets Management Branch (HFA-305)
Food and Drug Administration
5600 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. 2005D-0011. Draft Guidance for Industry: Labeling for Human Prescription Drug and Biological Products – Implementing the New Content and Format Requirements

Dear Sir/Madam:

The following comments are provided by the Biotechnology Industry Organization (BIO). 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: Labeling for Human Prescription Drug and Biological Products – Implementing the New Content and Format Requirements*.

This draft guidance represents an important step in the right direction toward clearer, more easily understood product labeling. In our comments below we offer both general and section-specific recommendations for enhancing the usefulness of the draft guidance to BIO member companies.

GENERAL COMMENTS

It is important that the requirements and recommendations contained in the physician labeling rule (PLR) (21 CFR 201.56 and 201.57), the two final and two draft guidance documents released along with the PLR (listed in the Federal Register, Vol. 71, No. 15, January 24, 2006, pp. 3922-4000), and Structured Product Labeling (SPL) are consistent and work together to facilitate prescribers'

use of labeling. BIO is concerned about inconsistencies among these documents.

First, we request clarification of how the new content and format requirements in the PLR will be implemented in SPL (e.g. in style sheets, and tagging of sections in the full package insert in SPL for presentation in the *Highlights* section of the Prescription Drug Labeling (PDL)).

Second, Section V. A. 2 (Lines 578-581) of the draft guidance state that – consistent with the final rule (§§ 314.70(b) and (c) and 601.12(f)) – revision of the *Highlights* (other than minor exceptions) require a prior approval supplement (PAS). However per §314.70(c)(6)(iii), a changes-being-effected (CBE) supplement allows for a labeling change that (1) adds or strengthens a contraindication, warning, precaution, or adverse reaction, (2) add or strengthens a statement about drug abuse or dependence. We are concerned about inconsistencies and delays that may result from the lag time between the sponsor revising this type of information in the comprehensive prescribing information section via a CBE while simultaneously revising the *Highlights* section via a PAS. BIO asks for clarification of how potential inconsistencies and delays will be avoided by FDA, and recommends that the Agency treat *Highlights*-related PASs with a high priority to ensure the timely revision of the *Highlights*.

Third, BIO also notes that information in the *Highlights* section regarding warnings is repeated in the *Black Box* as well as the *Warnings* section of the label. The agency states in the “background” section of the draft guidance that the PLR is intended to make prescription drug labeling easier for healthcare practitioners to read and use. BIO is concerned that the new format may in fact cause confusion, in that it now requires prescribers to review information in the *Highlights*, *Black Box* and *Warnings* section of the label.

Section III. CONSIDERATIONS FOR REVISING LABELING

Line 120: For products that were approved many years ago but that are now the subject of an efficacy supplement that triggers revision of the label to fit the new format, BIO foresees difficulty in constructing some new sections of labeling, if those sections require data that were not part of the sponsor’s original application. It should be acceptable to display the information in the old format while adding new information complying with the PLR as additional postmarketing reports become available. Alternatively, FDA should permit companies to omit sections in the PDL if there is insufficient information for these sections.

Line 138-140: The submission of an efficacy supplement (e.g. for a new indication) triggers the requirement to revise the product’s labeling to

conform to the PLR. However, the review of the efficacy supplement and the revised labeling for other purposes are two separate issues and should not necessarily have to occur together. If the two activities have to occur together this may result in unnecessary delays in ensuring that the label is up-to-date and accurate. Therefore, we suggest that FDA should permit renewal and revision of labeling in the old format until an efficacy supplement is approved. At that time, the new indication and the other revisions can be put into the new format.

Section IV. HIGHLIGHTS

Line 310: BIO notes that the *Adverse Reactions* section is no longer included in *Highlights* under the heading of the *Recent Major Changes* section as it was in the proposed rule. We ask for clarification in the final guidance of whether this was an oversight, or whether the Agency assumes that important adverse reaction information would qualify for inclusion in the *Warnings and Precautions* section, thereby making inclusion of the *Adverse Reactions* section under this heading redundant.

Lines 364-371: Please clarify what should be listed in the *Recent Major Changes* heading. Does this pertain to any changes that were approved by FDA within one year of the date upon which the converted labeling is submitted to the Agency, or is it defined differently (e.g. changes that were incorporated into the labels printed in the prior year)?

Lines 422-425: BIO suggests that when no contraindicated situations have been identified, this section simply state, '*None.*'

Section V. PROCEDURAL INFORMATION

Line 563: It would be helpful for FDA to expand upon the last bullet of this list (or expand Footnote 9) by also listing the types of supplements that count as "a labeling supplement with clinical data" and that are not already included in the bullets above.

Lines 667-669: These lines state that "Applicants should propose content and location of class labeling statements in the new format in the draft labeling submitted with their applications or supplements." We request that FDA clarify that subsequent applications submitted by sponsors of drug that are other members of the class will not be required to use identical verbiage and placement.

Section VI. FORMATTING

Line 704: BIO recommends that when subsections are used, they be identified with another decimal point (e.g. 8.6 Renal Impairment, 8.6.1 Severe Renal Impairment, 8.6.2 Mild to Moderate Renal Impairment) to help with tagging for SPL2b.

In conclusion, BIO appreciates the opportunity to comment on this Draft Guidance. We look forward to additional opportunities to discuss the issues outlined above.

Sincerely,

/s/

Sara Radcliffe
Managing Director
Science and Regulatory Affairs