



1201 Maryland Avenue SW, Suite 900, Washington, DC 20024
202-962-9200, www.bio.org

August 25, 2009

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

Re: Docket No. FDA- 2008-D-0253. Presenting Risk Information in Prescription Drug and Medical Device Promotion

Dear Sir/Madam:

The Biotechnology Industry Organization (BIO) is pleased to submit these comments in response to the Food and Drug Administration's (FDA's) draft guidance *Presenting Risk Information in Prescription Drug and Medical Device Promotion*.

BIO represents more than 1,200 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. BIO members are involved in the research and development of innovative healthcare, agricultural, industrial and environmental biotechnology products, thereby expanding the boundaries of science to benefit humanity by providing better healthcare, enhanced agriculture, and a cleaner and safer environment.

General Comments

BIO welcomes FDA's efforts through the Division of Drug Marketing, Advertising, and Communications to provide formal advice regarding the presentation of risk information in promotional materials. Our members develop and market innovative products that treat a range of human illnesses, thus addressing important medical needs of patients and society that might otherwise be unmet. BIO member companies are deeply concerned with the effective and safe use of the products its members provide for patients. BIO recognizes that drugs (including therapeutic biologics) and medical devices are associated with both benefits and risks. The benefits and risks together must be understood and carefully considered by patients and physicians as they make initial therapeutic decisions

and throughout therapy. To support sound therapeutic decisions, we believe that patients and physicians need timely, accurate, and relevant information about the benefits and risks of a drug or device. BIO believes that balanced promotional labeling and advertising provide valuable information about the benefits and risks of therapy.

BIO agrees with FDA's premise that benefits and risks of therapy must be considered in balance. BIO urges FDA to consider the balance of benefit and risk not only within individual promotional pieces but also within other types of information pieces that are available to patients and physicians. We believe that it is critically important that all regulated sources of information provide a balanced view of the benefits and risks of therapy. Neither the medication guide nor the highlights section of the full prescribing information provides meaningful contextual information regarding the important benefits of therapy or the risks of disease. Risk evaluation, management, and mitigation plans appropriately focus on risk of therapy; however, the products marketed under these programs may have clear benefits that create an important context for therapeutic decisions which are often inadequately communicated in the program support materials. As the Agency considers the important topic of risk information in prescription drug and device promotion, BIO urges FDA to consider the importance of balanced benefit and risk information in other communications within its influence, including patient directed labeling, highlights, and other documents that are made available to patients and physicians in association with risk mitigation and management programs.

BIO agrees with FDA that it is critically important to disclose risk information appropriately and effectively in prescription drug and medical device promotion. BIO shares FDA's concerns about over-warning regarding risks, particularly those that are not included in the product labeling. Over-warning about risks is a significant consideration because it may result in actions that have unintended consequences for patients. Indeed, even appropriate risk communications can cause unintended consequences for patients, physicians, and public health. For example, flight from therapy with poor health outcomes has been observed after the announcement of new risk information both in the context of labeling updates and in association with new signal communications. Such occurrences underscore the importance of appropriate contextual information for risk assessment and therapeutic decision making. Materials that provide information about risks of therapy, and also the benefits of treatment and risks of untreated serious illnesses could be powerful tools in limiting the adverse potential of over-warning. Information related to the effect of discontinuing therapy is likewise potentially valuable to patients as they consider with their physicians the benefits and risks of treatment. BIO supports FDA's continued efforts to assure that risk information is transparent and appropriately presented and fully balanced so that patients and their healthcare team can make the informed decisions for continued health.

BIO champions the sponsors' critical role in updating labeling as new and important safety information emerges and by extension their pivotal role in developing, creating, and disseminating appropriate benefit and risk communications through all labeling, promotional, and other communication endeavors. BIO is vitally interested in assuring that information about our products supports and aids patients and physicians in making informed individual therapeutic decisions. We seek to assure that information about the benefits and risks of our products is cohesive, understandable, and appropriate in the

broader context of under-treated or untreated serious disease. BIO supports FDA's continued efforts to assure that product information is accurate, truthful, and relevant.

BIO respectfully offers the following comments about the draft guidance.

1. Policy Overview – Net Impression and Reasonable Consumer Standard

The draft guidance discusses the concept of the *net impression* (line 112) of a promotional piece and emphasizes the importance of evaluating the message communicated by “all elements” of the piece as a whole. BIO endorses FDA's view that the totality of the message is important to assess in promotional labeling and advertising. To this end, we believe that it is important to consider all elements - benefits, risks, and effect of underlying disease - of the messaging about a product. BIO believes that 21 CFR §202 provides a strong framework to assure that promotions are accurate, truthful, not misleading, and to provide balance across the key elements of product communication. Additionally, in order to further clarify net impression, we ask that the Agency explain how it decided which factors listed in the guidance contribute to the net impression of a piece. Our interpretation of the guidance is that factors such as consistent use of language, use of signals, and framing of risk information contribute to the net impression of a piece. It would be helpful, however, if FDA fully explained the rationale used in determining the factors.

BIO supports FDA's conclusion that under the *reasonable consumer standard* (line 154), the Agency will consider the “reasonable consumer” to be a reasonable member of the targeted audience. However, BIO is concerned that draft guidance includes insufficient methodology to define what a reasonable consumer would think and what would be the net impression drawn by a reasonable consumer. Experience with readability testing of European patient information leaflets indicates that such a standard is very high and not entirely predictable. It may be difficult for the Agency or sponsor to accurately predict the assessment of a reasonable consumer in all cases. BIO encourages the Agency to affirmatively endorse that, when available, quantitative or qualitative market research developed by sponsors may be used to define a reasonable consumer view of promotion. BIO likewise encourages the Agency to clearly define the critical elements of such research that would be deemed to provide evidence of a reasonable consumer's view.

Further, we seek clarification regarding the applicability of the reasonable consumer standard to both healthcare professional and consumer audiences. The guidance states that FDA will consider the different “knowledge and experience” (line 176) of healthcare professionals and consumers when evaluating pieces intended for each audience. However, as healthcare professionals will in many cases have higher levels of education, training, and experience than consumers, we see potential difficulties in adapting the reasonable consumer standard for use with pieces intended for each audience. If applied too broadly, employing the reasonable consumer standard for both audiences may have the unintended effect of causing promotional pieces to be generally targeted toward audiences with less understanding of drugs and disease states, which could result in healthcare professionals being less engaged by the

pieces. It would be helpful if the Agency could further describe the rationale used for applying the same standard to both consumers and healthcare professionals and discuss any alternative approaches considered.

2. Factors Considered in the Review of Risk Communication – Use of Language

BIO generally endorses the underlying concepts for the considerations regarding the use of language and signals, and how information is framed and ordered.

BIO notes that the draft guidance does not provide a standard approach to define language appropriate to target audiences. This suggests that different terms could be selected for the same events by sponsors or the Agency, thus creating perceived and artificial advantages or disadvantages for a product. Industry associations and other regulatory Agencies in English speaking regions have developed standards assuring consistent conversion of medical terminology into language accessible to consumers. In Europe, there has been consistent support for translation across geographies and languages in the context of patient directed communications. A glossary for conversion of medical terms could be developed for general use in the United States. In the interest of clarity and consumer education, and anticipating that specific quantitative data supporting a presentation of information may not be available, BIO encourages the Agency to use and make transparent a standard approach to making medical terms accessible to consumers. For example, this standardized approach could be comparable to the Medical Dictionary for Regulatory Activities (MedDRA) or similar systems used to support pharmacovigilance efforts, and could be informed by social science research regarding consumer comprehension of medical terminology.

3. Considerations of Content – Quantity and Location

BIO notes that the draft guidance suggests the quantity of risk information should increase with the quantity of benefit information. It is important to note that the overall benefit risk profile of each drug is different. The risk information to balance a particular benefit presentation may not be measured in the quantity of information, but rather the quality of both the benefit and risk information presented and considered within context of other communications about a product. BIO urges FDA to acknowledge that the benefit risk profile of products is, in general, specific to each product. BIO encourages FDA to acknowledge that there is not necessarily a quantitative relationship between benefit and risk that defines balanced messaging, and to refine the draft guidance accordingly.

In addition, BIO notes that the guidance includes specific direction regarding print advertisements (lines 545-625) that may be confusing in the context of the provisions of 21 CFR §202.1 (e)(7) (vii), (ix), and (xi), (xii) which provide specifically for risk information to be included in a separate part of an advertisement and require that direction be provided as to the location of the risk information in a separate part of an advertisement. BIO requests that FDA affirmatively state that advertisements

developed consistent with the provisions of 21 CFR §202.1 (e)(7) will be considered compliant.

4. Presentation of Risk Information in Consumer Materials

The draft guidance states that consideration of the target audience is critical in determining which risk information is material and that promotional materials should convey benefits and risks in language understandable to consumers. The draft guidance also cites the requirement in 21 CFR §202.1(e)(3)(iii) that the brief summary must disclose each specific side effect and contraindication. Side effects and contraindications are stated to include side effects, warnings, precautions, and contraindications and include any such information under such headings as cautions, special considerations, important notes, etc., contained in the labeling for the advertised product. BIO requests that FDA provide guidance on how patient-directed promotional pieces can comply with the brief summary requirement while still providing risk information in consumer-friendly language.

5. Examples

BIO notes the Agency's effort to enhance the guidance through examples. However, we are concerned that the examples appear in some cases to be contradictory, suggesting that they reflect concerns that the Agency may have had regarding company presentation of specific risk information. To illustrate, Example 11 suggests that some information may not be material for some audiences, whereas Example 9 suggests that very similar information must be included without consideration to the audience. There is no indication in the guidance which of the examples would be considered the highest priority to the Agency and under what circumstances. These observations suggest that the examples may not be informative when applied to other situations. BIO requests that the Agency revise the guidance to address concepts that are important to achieve balance and provide specific citations to the provisions of the Act or the CFR to support these concepts.

6. Online Promotion

One important issue that industry faces is the application of the guidance to the internet. As more and more Americans turn to the web for information about their health, we believe it is important that FDA allow industry to use the internet to present balanced product information in a clear and transparent manner.

We understand that FDA will apply the general, high-level principles of the guidance to enforce and regulate internet promotion. However, we believe that the draft guidance, which does not distinguish between online advertisements versus traditional promotional methods, does not address the unique and distinctive issues raised by internet promotion. As such, the guidance does not provide sufficient assistance for sponsors to prepare online advertisements. For example, the guidance

does not address whether companies can use hyperlinks to appropriately communicate important risk information, especially if the hyperlink is clearly displayed (e.g., a link that states: [IMPORTANT RISK INFORMATION](#)).

We suggest that FDA discuss the unique issues inherent to online advertising in a separate subsection in the draft guidance.

Conclusion

Thank you for this opportunity to comment on the draft guidance *Presenting Risk Information in Prescription Drug and Medical Device Promotion*. We look forward to continued dialogue on this important topic and suggest that the Agency consider additional venues for interested parties to share concerns and comments regarding communications about the benefits and risks of drugs and devices.

Sincerely,

/s/

Andrew J. Emmett
Director for Science and Regulatory Affairs
Biotechnology Industry Organization (BIO)