



July 11, 2007

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

Re: Docket No. 2007N-0121: Use of Medication Guides to Distribute Drug Risk Information to Patients

Dear Sir or Madam:

The Biotechnology Industry Organization (BIO) appreciates the opportunity to provide the following comments regarding questions posted in advance of the Food and Drug Administration's (FDA) open public meeting on June 12-13, 2007 on Medication Guides. 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 healthcare, agricultural, industrial and environmental biotechnology products.

General Comment: FDA Should Amend 21 CFR Part 208 to Allow Medication Guides to Contain Drug Benefit Information as well as Drug Risk Information

Currently, Medication Guides communicate to patients the risks of certain drugs and biologics. The purpose of Medication Guides is to inform and prevent serious side effects or to promote adherence to directions for use. Thus, the information provided to patients in the Medication Guide, unlike the information provided in professional labeling such as package inserts, is almost exclusively focused on the risks of a therapy and contains virtually no information about its benefits. This can have important implications in terms of how patients make choices about a therapy.

Both FDA and industry have embraced the concept that drug safety is not absolute, but rather a matter of balancing predicted benefits against known risks. According to the *FDA Guidance for Industry: Development and Use of Risk Minimization Action Plans*, "FDA's determination that a product is safe, however, does not suggest an absence of

risk. Rather, a product is considered to be safe if the clinical significance and probability of its beneficial effects outweigh the likelihood and medical importance of its harmful or undesirable effects. In other words, a product is considered safe if it has an appropriate benefit-risk balance for the intended population and use.”ⁱ Physicians are expected to make therapeutic decisions based on knowledge of both the risks and benefits of a product, as described in the package insert. Patients should have a similar right to make therapeutic choices based on complete information. Accordingly, Medication Guides should evolve to include both benefit and risk information based on the Package Insert. Therefore, BIO believes that the Medication Guide should provide patients with both risk *and* benefit information, because only then can patients make fully informed choices about a product’s use.

The FDA’s efforts to improve risk communication have resulted in an increase in the number of Medication Guides to approximately 240 products. Although there are rules regarding the requirement for a Medication Guide (21 CFR Part 208), it appears that these rules have been inconsistently applied across departments within the Agency. For example, certain therapies or product classes have Medication Guides, while other therapies with major adverse effects do not. Thus, BIO recommends that FDA examine how Medication Guide rules have been applied to various products and attempt to create more consistency in the application of these rules.

The following is BIO’s response to the questions raised in FDA’s April 9, 2007 Federal Register notice, as set forth in questions to manufacturers.

Responses to Manufacturers’ Questions:

1. *What steps do you take to ensure compliance with the Medication Guide requirements? What challenges do you encounter in complying with the requirements to distribute Medication Guides with the product to pharmacies and others? How do you ensure that pharmacies are receiving a sufficient supply of Medication Guides?*

The regulations require that manufacturers ensure that Medication Guides are available for distribution to patients by either providing them in sufficient numbers to distributors, packers, or dispensers, or that the manufacturer provide the means to distributors, packers or authorized dispensers the means to make sufficient copies of the Medication Guide available.” For self-administered products, to comply with the requirements, a Medication Guide is provided in the box along with the finished drug product. As such, there are no challenges for ensuring compliance. A patient receives a Medication Guide every time the prescription is refilled.

For products that are not self-administered, there can be challenges in ensuring that patients receive a medication guide prior to every use. For example, IV therapies are not delivered directly to the patient but through an intermediary. Product is first shipped to pharmacies where the pharmacist prepares the solution

for the infusion and then sends the solution to the infusion center. Ideally, the infusion sites have a sufficient supply of Medication Guides, and healthcare professionals at the site provide patients with a Medication Guide prior to the infusion as part of the pre-infusion process. However, this process may not happen consistently. BIO would be pleased to work with FDA and other stakeholders to explore ways of improving this process.

2. *Have means other than paper, such as electronic files, been used to supply Medication Guides to pharmacies or third-party vendors? If so, please describe your experience. If not, please explain why not.*

Currently, BIO has not received any feedback from member companies who have explored the use of electronic Medication Guides.

3. *How do you instruct pharmacies that Medication Guides must be dispensed with certain prescription drugs per Section 208.24(d)?*

In general, the outer box labeling alerts the pharmacist that a Medication Guide must be dispensed with the product. This has been found to be sufficient instruction.

4. *Should standardized language and/or a uniform symbol on the container label be used for the required instruction to dispensers? If so, please propose standardized language and suggest a uniform symbol that might be appropriate.*

It is the position of BIO that a uniform symbol on the container label of the product should be required and BIO recommends the symbol **MG** be placed in the lower left corner of the label. Pharmacists would become accustomed to looking for the symbol if it is placed in a consistent location. The symbol would alert pharmacists to the need to provide a Medication Guide for every prescription filled.

5. *What can be done by means of packaging, such as "unit-of-use," to ensure that a Medication Guide is shipped with the drug product so that it is distributed with each prescription? What are the advantages and disadvantages of using unit-of-use packaging for any product that requires a Medication Guide?*

The Medication Guide can be added to the package insert as a separate perforated section for inclusion with the finished drug product during the packaging operation. The advantages are as follows:

- Pharmaceutical packaging lines routinely include the package insert as a labeling component with the finished product
- Package inserts are included in the finished good bill of materials
- Each finished product will contain a Medication Guide

However, it is important to note that there are several disadvantages to this approach:

- Limited space in the package to include extra documentation
- Added complexity on the packaging line; changing parts for automated equipment
- Increased printing and folding complexity due to additional text

6. *What are the advantages and disadvantages of developing Medication Guides to cover a class of drugs rather than having a separate Medication Guide for each product in a class?*

BIO believes that each product should be evaluated based on its own risk-benefit profile and that a product's risks and benefits should be individually communicated to patients rather than through class labeling. It is well-known that even within a class of drugs there may be major differences in both risks and benefits, whether due to molecular differences, or differences in dosing, indication, pattern of use within an indication, formulation, or route of administration. In addition, many new drugs act on several targets, so the idea of a "class" becomes an oversimplification. Just as we inform prescribers of the specific risks and benefits of a drug through the package insert, so too we should inform patients of the specific risks and benefits of a drug through the Medication Guide. A significant role of the patient information is to help prevent medication errors and to improve compliance. Individual product information in the Medication Guide would be preferable to adequately address dosing, overdose, administration techniques, and proper storage.

BIO appreciates this opportunity to comment on the *Use of Medication Guides to Distribute Drug Risk Information to Patients*. We would be pleased to provide further input or clarification of our comments, as needed.

Sincerely,

/s/

Sara Radcliffe
Vice President, Science and Regulatory Affairs

ⁱ FDA, Guidance to Industry: Development and Use of Risk Minimization Action Plans (4 March 2005)