BIOTECHNOLOGY INDUSTRY ORGANIZATION

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

October 29, 2010

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

Re: Docket No. FDA–2010–N–0437, Development and Distribution of Patient Medication Information for Prescription Drugs

Dear Sir/Madam:

The Biotechnology Industry Organization (BIO) thanks the Food and Drug Administration (FDA) for the opportunity to submit comments on the Development and Distribution of Patient Medication Information (PMI). BIO supports the development of effective PMI that reinforces communication between the patient and healthcare professionals, enables understanding of benefits and risks of a product, and promotes safe and effective use of medication. In previous comments to FDA, BIO endorsed the development of a single patient-oriented document written by the Sponsor, reviewed and approved by FDA, and based on a template that has been validated through social-science research of patient comprehension. BIO also believes that technology should be leveraged to enhance dissemination and distribution of PMI. We are pleased to elaborate upon our previous comments and to further address the questions raised in the Federal Register (FR) notice and at the September 27-28th public hearing.

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.

I. How can we best ensure PMI quality and compliance with content and format criteria?

A. PMI Should Be Drafted by the Manufacturer:

In order to ensure appropriate quality and compliance with format and content criteria for PMI, BIO believes that both the manufacturer and the FDA must take a more active role in PMI development. BIO believes that the PMI should be written by the Sponsor. Drug and biologics manufacturers, along with FDA, have the most detailed knowledge of the benefits, risks, and unique scientific characteristics of a given product. Because drug and biologics manufacturers are responsible for the surveillance and continuous review of marketed products' benefit-risk profiles, they are in the best position to develop and routinely update PMI.

B. Based Upon an FDA-Standardized Template:

We suggest that FDA establish a uniform template through regulation and guidance that specifies the content and format of the PMI. The template should be determined after consulting with relevant stakeholders; should be based on the results of social science and behavioral research on patient comprehension of medication information; and should be implemented only if validated by such research. The template should be drafted in a manner that promotes standardization while also retaining a level of flexibility so that new approaches can be adopted as research and technology advance. A consistent template would seek to increase patient comprehension by creating a common format with which patients could become familiar over time, so they could recognize where to find relevant information in the document regardless of the product or class.

BIO welcomes an ongoing dialogue with the Agency and other stakeholders on how to develop clear standards and processes for PMI development and we would like to work with FDA to determine if it is possible to standardize the language used in PMI. This could be achieved through an FDA-approved list of language to be used in PMI that is mapped to concepts that appear in the US Prescribing Information (USPI), and would include lay-friendly, standardized descriptions of benefit and risk information, potential adverse reaction symptoms, and appropriate patient actions. Initially this list could include terms utilized for the most frequently used products and would grow over time. The language would be created by an independent coalition to include FDA representatives, medical experts, patient education and communication experts, and pharmaceutical manufacturers. The language would be tested by patients prior to use. Additionally, we would welcome guidance on how the Patient Counseling Section within the USPI should be aligned with the PMI so that this section could be more useful to physicians and patients.

As a benefit from this approach, patients would see the same terms used from product-to-product, benefiting from increased standardization that has become the norm with food and over-the-counter (OTC) product labeling today. FDA would streamline review due to use of already approved language and manufacturers would streamline development of PMI content due to use of standardize language associated with concepts found in the USPI.

Additionally, to achieve a true one document solution in which PMI replaces Consumer Medication Information (CMI), Patient Package Inserts (PPI), and Medication Guides (MedGuides), we support FDA's stated intention to remove MedGuides from the framework for Risk Evaluation and Mitigation Strategies (REMS). The requirement that MedGuides be part of REMS has placed significant workload demands on FDA and industry without clear added value. This change would have the dual benefit of enhancing benefit/risk communication towards patients while reserving full-scale REMS implementation for Elements to Assure Safe Use (ETASU), so that all stakeholders in the healthcare delivery system can focus resources on the most critical risk minimization activities.

C. Communicated in the Context of Both Benefits and Risks:

Both the Agency and industry recognize that drug safety is not absolute, but rather a matter of balancing benefits against risks. Likewise, patients should be able to make therapeutic choices based on complete information. Therefore, BIO recommends that the template for PMI should provide patients with both risk and benefit information, because only then can patients make appropriately informed choices about a product's use. We propose that FDA and stakeholders also explore formatting options to make new benefit and safety information more prominent so that it is brought to a patient's attention.

Some stakeholders have suggested that benefit information should be presented in a quantitative, numerical fashion to facilitate comparisons across products in a class. BIO cautions that this approach is problematic and could be misleading to patients as proposed. Clinical trial results for products in the same class are often based upon vastly different clinical protocols with unique factors and statistical limitation. Quantitative comparison across different trials may lead patients to draw inappropriate conclusion of the data, and additional research is required to determine how quantitative information may be presented without being misleading.

Rather, we suggest that safety, benefit, and administration information be provided in a qualitative, narrative manner using language that can be easily read and understood by a patient who has the disease for which the medication is being prescribed. This narrative benefit information provides useful context to the patient about what to expect from the therapeutic communicated in language that an average patient can fully understand. A similar approach is utilized in Vaccine Information Statements produced by the Centers for Disease Control and Prevention (CDC), which can serve as a useful model for the content of the FDA prototype. The use of "action-driven wording" also helps to provide direction and clear advice for patients and healthcare providers on how to manage a risk. BIO applauds FDA for using this type of narrative description of expected benefits and potential side effects in the PMI prototypes currently being evaluated.

D. Reviewed and Approved by FDA:

In order to ensure high quality and consistent PMI and address legal concerns, BIO suggests that the PMI should be reviewed and approved by the FDA. Much like the current process for developing professional and patient labeling, the Sponsor should initially draft the PMI, followed by FDA review, including written comments from FDA to the manufacturer regarding any

Agency proposed changes to the labeling language. FDA should approve the document prior to use and a process should be established for approval of revisions of PMI as necessary, e.g. when new benefit/risk information emerges. BIO believes the review process and timeframes should be the same as for other changes to the labeling and should be integrated into the Good Review Management Principles and Practices. We also propose that the PMI and Physician Labeling receive simultaneous review at the end of a review cycle to assure alignment and efficient use of FDA resources.

FDA has raised resource concerns regarding the Agency's ability to review and approve PMI documents and has suggested a "quality framework for developing, distributing, and amending the PMI." BIO would like to learn more about the FDA quality systems proposal. Additionally, FDA has also suggested that user fees may be necessary to help support the review and approval of PMI documents. However, BIO does not believe that additional industry user fees beyond what are currently paid through PDUFA are necessary since much of this type of review work is already taking place under current resource levels.

With respect to new drugs, under current practice FDA is already approving most new drugs with some type of patient labeling and this work is ongoing under current resources. For example, in 2009, FDA approved 97 NDAs/BLAs and approved 91 new or modified MedGuides.[1,2] Additionally, the single document solution is based upon the premise that this single document would be more concise and streamlined than that current patient documents and would lead to less redundancy with other types of FDA-approved patient labeling, such as MedGuides and PPI. Therefore, under a PMI approach FDA would be reviewing shorter documents and fewer redundant documents, which should reduce workload on the Agency. For example, MedGuides approved or modified in 2010 average nearly six pages, with the longest ranging from twelve to twenty-one pages. FDA's PMI prototypes currently being tested envision a document that is only one or two pages, which should be considerably easier for FDA to review and approve.[3]

The FR notice states that PMI would have to be developed for thousands of individual products which would place a considerable burden on the Agency. However, the majority of these products are generics that can rely on the innovator PMI without additional FDA review or approval. According to the Generic Pharmaceuticals Association, 10,072 of the 12,751 drugs listed in the FDA's Orange Book have generic counterparts.[4] Therefore, nearly 80% of currently marketed products would not require extensive FDA review and approval of the PMI.

We recognize that there will be some legacy products that will require FDA approval of the PMI. However under current practice and resources, MedGuides are regularly required or modified for

[1] FDA, "Approved Risk Evaluation and Mitigation Strategies", accessed October 27, 2010, http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111350.htm
[2] FDA, "Drug and Biologics Approval Reports", accessed October 27, 2010, http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/default.htm
[3] FDA, "Medication Guides", accessed October 27, 2010, http://www.fda.gov/Drugs/DrugSafety/UCM085729
[4] Generic Pharmaceuticals Association, "Facts at a Glance", accessed October 27, 2010, http://www.gphaonline.org/about-gpha/about-generics/facts

currently marketed products. If available resources are not sufficient for this task, then we are committed to securing additional appropriated funding for the agency to review these documents.

II. What are the components of an effective framework for ensuring patient access to PMI?

In light of recent advances in information technology, FDA, manufacturers and pharmacists should leverage electronic systems to enhance the dissemination and accessibility of PMI. The FDA-approved PMI should be electronically accessible on a public website or database such as the National Library of Medicine's DailyMed website or a newly created website specifically for PMI. This website should provide prescribers, pharmacists, and patients with single point of access to PMI.

One of the strengths of a short, concise, standard letter-sized PMI is that it can be downloaded and printed in a variety of settings using off-the shelf printing technology. BIO believes that pharmacists should be able to electronically access and print the document from a consolidated database, thereby ensuring that the most up-to-date document is provided to the patient. To the extent practicable, existing pharmacy information technology and distribution systems should be utilized. We do recognize that this may involve some reengineering of existing pharmacy databases and workflow systems. However, these changes are technologically feasible and should be pursued by pharmacists and the FDA if it is in the best interest of the patient and can improve health outcomes.

Electronic distribution of the PMI can also allow patients to elect to receive the PMI through a variety of electronic media, such as via email or mobile device.

BIO also recognizes that access to PMI can change depending on the healthcare setting where the product is dispensed or administered. This is particularly true in hospitals, infusion centers, and cancer or dialysis clinics where the medication is generally administered directly by a healthcare provider who is physically present to educate a patient on the product's effects and answer questions. In fact, many biologic products are administered by healthcare professionals in such settings. This raises unique challenges and opportunities regarding benefit/risk communication and the distribution of PMI.

BIO recommends that PMI should be electronically accessable to patients regardless of where products are dispensed, so that it can be made available to the patient whether or not the product is intended to be administered directly by a healthcare professional. BIO believes that physicians and other healthcare providers should consider offering PMI with each patient, subject to the provider's professional judgment and practice of medicine. Healthcare providers may find that PMI serves as a valuable educational tool or visual instruction to complement spoken directions given to patients. However, we also recognize that PMI may have inherent limitations in an inpatient setting, such as in an emergency situation when a patient is unresponsive.

III. What approaches should be considered to ensure that FDA can rapidly move from the current system to a new PMI paradigm?

If supported by the outcome of social science and behavioral research, the implementation of a single, FDA-approved PMI for applicable products will require formidable effort from both FDA and industry. Given the considerable workload necessary for industry to develop these documents and for FDA to review them, BIO suggests there be a phased implementation schedule for submitting PMI to FDA and distribution. This schedule could be similar to the staggered timeframe approach used to implement the 2006 Physician Labeling Rule and could also include an appropriate piloting phase. After the pilot phase, FDA may wish to focus the initial deployment on the most commonly prescribed outpatient products and those with MedGuides in order to reach the most patients and have the greatest initial impact while other drug product PMI are being developed, approved, and distributed in subsequent phases. Additionally, given the high volume of generic products prescribed and the important benefit/risk considerations inherent with all pharmaceutical products, the product PMI should be written by the innovator company and distributed with both the original and generic versions.

IV. Conclusion:

BIO appreciates this opportunity to comment on the development and distribution of Patient Medication Information for Prescription Drugs. We would be pleased to provide further input or clarification of our comments, as needed.

Sincerely,

/S/

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

Previous BIO Comments on Patient Medication Information:

- BIO Comments on Providing Effective Information to Consumers about Prescription Drug Risks and Benefits, November 25, 2009, http://bio.org/reg/20091125.pdf
- BIO comments on Consumer Medication Information (CMI), April 29, 2009, http://bio.org/reg/20090429.pdf