BIOTECHNOLOGY INDUSTRY ORGANIZATION

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

Re: Docket No. FDA-2008-N-0038

Dear Sir/Madam:

The Biotechnology Industry Organization (BIO) thanks the Food and Drug Administration (FDA) for the opportunity to submit comments on the FDA's Consumer Medication Information (CMI) Initiative. BIO believes that patients and healthcare professionals should have access to up-to-date, relevant, and accurate product information available in an easily accessible form in order to inform individual medical decisions and ensure the safe utilization of medications. Under current practice, patients may receive several different types of patient-oriented written communication at the time of dispensing – such as Consumer Medication Information (CMI), Medication Guides (MedGuide), and Patient Package Inserts (PPI) – that may be non-standardized and duplicative. BIO encourages FDA to collaborate with stakeholders to develop a single patient-oriented medication document with standardized format and content informed by social science and behavioral research to be used to communicate product information to patients.

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.

BIO's healthcare members understand the need for patients and physicians to have up-to-date, relevant, and accurate information about the benefits and risks of a drug or biologic so they can

make well-informed choices about therapy. The professional physician label is the cornerstone of every prescribing decision and includes important benefit/risk information to guide medical decision-making. However, the professional label is written in a manner intended for physicians and other medical professionals. Additional consumer-friendly written materials can be useful to help patients understand the benefits and risks of a product, to increase patient compliance, and to help inform patients when a follow-up with their physician may be warranted.

Under current practice, a patient being dispensed a medication at a pharmacy or other healthcare setting may receive a combination of several separate documents including a CMI prepared by a third-party vendor, and/or a FDA-approved MedGuide, or a PPI. Patients may also receive product information from the brief summary section of direct-to-consumer advertising. These different types of written patient-oriented communications are the result of a series of laws, regulations, and guidance documents spanning several decades. The most notable of these is a 1996 law (P.L. 104-180) which established a voluntary private-sector initiative to provide useful written information for patients of new prescriptions 95% of the time by 2006. As demonstrated by a 2008 evaluation of CMI, the initiative has struggled to meet that goal.[1] The evaluation found that the quality and comprehensibility of CMIs can be variable; the format and content can be difficult for patients to read; and the information provided may be duplicative of other formats. This can contribute to suboptimal comprehension of important prescribing information. BIO is encouraged by FDA's ongoing evaluation of new initiatives to provide patients with the tools they need to understand and manage their medications to achieve optimal compliance and health outcomes.

I. A SINGLE PATIENT-ORIENTED WRITTEN COMMUNICATION:

BIO supports efforts to streamline this process to ensure that patients receive high quality and easily understandable medication information, and is pleased to offer the following recommendations.

- *A Single Document Solution*: BIO supports the development of a single patient-oriented medication document for drugs and biologics to be provided at the time of dispensing. A single document solution based on a uniform template would promote consistent information and formatting of patient information. Such consistency should 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. A single written communication may also serve to stimulate patients' communication with their health care provider about their medication regimen. BIO does not advocate the creation of yet another duplicative document for dispensers to distribute to patients, but envisions that this document would replace the current complement of patient documents, except in cases where MedGuides are required, as discussed below. For the purposes of these comments, we will refer to

[1] Kimberlin & Winterstein *Expert and Consumer Evaluation of Consumer Medication Information - 2008" Final Report to the U.S. Department of Health and Human Services and the Food and Drug Administration, November 4, 2008,* http://www.fda.gov/cder/news/CMI/final_report.pdf

this proposed, standardized single document as the "Patient-oriented Medication Document" or PMD.

- *Written by the Sponsor*: BIO believes that the PMD should be initially drafted by the drug 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 profile, they are in the best position to develop and routinely update the content of the PMD. Much like the current process for developing professional and patient labeling, the sponsor should initially draft the PMD, followed by FDA review, including written comments from FDA to the manufacturer regarding any Agency proposed changes to the labeling language. Sponsors may wish to contract with a third party to assist in drafting and/or distributing the PMD, but ultimate decisions regarding content should rest with the sponsor and FDA.

- *Based on a Pre-determined Template Specifying Content and Format*: BIO believes that FDA should establish a uniform template through regulation and guidance that specifies the content and format of the PMD. 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 supported 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.

- *Reviewed and Approved by FDA*: As with all labeling, the PMD must be reviewed and approved by the FDA. Recent history has suggested that private sector initiatives to streamline and standardize CMI have not met their goals, and that FDA should take a greater role ensuring the future quality and consistency of the proposed PMD. FDA should approve the document as part of the pre-market approval process and a process should be established for approval of revisions to the document as necessary, e.g. when new benefit/risk information emerges. BIO believes the review process and timeframes should be the same as other changes to the labeling and should be integrated into the Good Review Management Principles and Practices.

- *Communicated within the Full Context of Benefits and Risks*: All drugs and biologics carry both benefits and risks that must be carefully weighed by patients and their doctors. The balance between the benefits of treatment and the risks of potential side effects will differ based on many factors, including the nature of the treatment and the condition, and each patient's unique medical profile. 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 the single PMD should provide patients with both risk and benefit information, because only then can patients make appropriately informed choices about a product's use. FDA and stakeholders should also explore formatting options to make new benefit and safety information more prominent so that it is brought to a patient's attention.

- *Clearly State Role and Limitations of Patient Information*: As beneficial as written information targeting patients can be, it is also important that patients understand that it does not replace advice from their physician. Accordingly, FDA should require that the PMD state that it is an-FDA approved summary of the full FDA-approved labeling; that it may not be comprehensive in addressing all patient needs and situations; and that discussions with their personal physician regarding their medication remain important. Consistent with the requirements for a MedGuide (21 CFR, part 208.20), the PMD should also include a statement similar to "Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide" followed by a statement that patients should ask health professionals about any concerns, and a reference to the availability of professional labeling.

- *MedGuides Should Serve as the Single Document for Drugs Subject to REMS*: BIO recognizes that MedGuides are a statutory concept codified under the FDA Amendments Act of 2007 (P.L. 110-085) for certain products subject to a Risk Evaluation and Mitigation Strategy (REMS). BIO believes that the MedGuide document should serve as the single patient document for products subject to REMS, in place of the proposed PMD. MedGuides generally focus on a particular adverse event(s) of concern, and can facilitate more thorough communication of the unique risks and mitigation considerations of the REMS products to inform and prevent serious side effects or to promote adherence to directions for use. However, in reference to the point above, we note that the MedGuide regulations (21 CFR, part 208) may need to be amended to allow for more comprehensive product information to be communicated in the complete context of its benefits and risks, and, depending upon the results of social science research, to facilitate patient understanding of the information in a format patients recognize. We also note that regulations mandating PPIs for certain drugs, such as oral contraceptives and estrogen products, may need to be considered to accommodate a single document solution.

- *Implementation Schedule:* If supported by the outcome of social science and behavioral research, the implementation of a single, FDA-approved PMD 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 believes that it is important that there be an appropriate, phased implementation schedule for applicable products. This schedule could be similar to the staggered timeframe approach used to implement the 2006 Physician Labeling Rule.

II. SOCIAL SCIENCE & BEHAVIORAL RESEARCH:

BIO believes that there is a need for additional social science and behavioral research around patient comprehension of written patient medication information. Such research should inform future efforts to streamline the format and content of the PMD template.

BIO encourages FDA and other stakeholders to collaboratively sponsor research to advance the field of how to best present risk and benefit information to patients, including optimal format, content, verbiage, length, and patient comprehension expectations that can be applied across all drugs. For example, BIO would support the development of a consortium to finance, prioritize,

and commission this research. Such a consortium or private-public partnership should include drug and biologics manufacturers, physician groups, pharmacy associations, patient organizations, and academic researchers, and could be coordinated through National Council on Patient Information and Education (NCPIE), the Centers for Education & Research on Therapeutics (CERTs), or the Reagan- Udall Foundation for the FDA. This research should:

- Focus on patient comprehension of various formats (tabular, Q&A, visual graphics, etc), content, verbiage, length, and delivery of written patient communication.
- To the extent practicable, be generalizable across a wide range of product classes.
- Focus on performance-based testing of patient comprehension, rather than basic content based-testing.
- Evaluate effectiveness of patient information systems in place in other countries.
- Involve a broad demographic of the U.S. population in a variety of settings.
- Future research could evaluate alternative means of communication for patient sub-populations such as the blind or illiterate who may not be able to utilize written documents.

BIO recognizes that a handful of drug sponsors with MedGuides subject to REMS are required to conduct evaluations of the effectiveness of the MedGuides within 18 months of approval. These smaller, individual, and varying evaluations may be useful to inform the labeling for those specific REMS products, but may not be appropriate for answering the broader social science research questions that are needed to realize the goals of the CMI Initiative. The 18 month MedGuide evaluations are intended to address the risk management strategies related to a single product, which usually has unique characteristics, risks, and patient populations. As a result, the outcomes of these evaluations may not be generalizable to other classes of products and the broader healthcare delivery system. Additionally, the REMS evaluations would not include the input of key stakeholders including pharmacists, patient advocates, and other manufacturers not subject to REMS. For these reasons, the 18 month evaluation of REMS MedGuides evaluations should not replace research needed to determine the format and content of a universal patient-oriented medication document. As noted above, a broad, consortium-driven social science review of patient-oriented documents and patient comprehension should be considered. Individual MedGuide evaluations should be limited in scope and conducted in a manner that is least burdensome for patients and pharmacists.

An additional concept that warrants further social science research is the "Drug Facts Box" format. Some stakeholders have suggested that a Drug Facts Box may enhance patient comprehension and make safety and efficacy information more patient friendly. BIO believes that the concept may hold promise and that the format should be further explored. However, the Drug Facts Box or a similar summary should only be included as an element of the single PMD if justified by the results of robust patient comprehension research. We are concerned that the Drug Facts Box approach could make it extremely difficult to provide meaningful information in such a small space. Current PPIs already contain information that is distilled down from the physician labeling and to reduce that further may dilute important product information to the extent that it is of little use. Research needs to be conducted to determine the type of qualitative or quantitative safety and efficacy information that can be presented in the Drug Facts Box. For example, presentation of clinical trial results in the drug facts box and comparison across products may lead patients to draw inappropriate conclusion of the data.

Furthermore, the risk of a patient reading only the Drug Facts Box and not reading any additional, more detailed and thorough information could result in patients making uninformed decisions about medicines. For that reason, BIO believes that a "Drug Facts Box" cannot and should not include all patient-oriented information relevant to proper administration of a medicine. If research were to support the use of a Drug Facts Box, we would suggest that FDA consider a tiered approach where a "Drug Facts Box" or a similar summary appears at the beginning of the PMD and is followed by more extensive information for patients that wish to access more detailed information. FDA should also explore the potential for the Drug Facts Box or PMD to replace the brief summary required for direct-to-consumer print advertising.

III. DISSEMINATION OF THE PATIENT MEDICATION DOCUMENT:

In addition to streamlining the content and format of the PMD, greater efforts should be taken to ensure that the document is distributed to patients efficiently and effectively. BIO recommends that if a patient is supposed to receive the PMD with their prescription, then it should be provided with each prescription that is dispensed. This will help educate patients on emerging information regarding the benefits and risks of the product, and how to manage the medication on an ongoing basis.

In light of recent advances in information technology, BIO believes that manufacturers and pharmacists should leverage electronic systems to enhance the dissemination and accessibility of patient communications. BIO believes that the proposed FDA-approved PMD should be electronically accessible on a public website, such as the manufacturer's product site, the FDA web page, and/or a National Library of Medicine database. In order to disseminate the most up-to-date information, pharmacists should be able to electronically access, distribute, and print the PMD from a consolidated database. To the extent practicable, existing pharmacy information technology and distribution systems should be utilized.

IV. THE ROLE OF WRITTEN PATIENT COMMUNICATIONS IN AN INPATIENT SETTING:

BIO also recognizes that the role and dynamic of written patient communications 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 benefits and risks 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 written patient communications.

BIO recommends that manufacturers be permitted to develop and distribute a PMD for a drug or biologic regardless of where it is 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 utilizing the document with each patient, subject to the provider's professional judgment and practice of medicine. Healthcare providers may find that these documents can serve as valuable educational

tools or visual instructions to complement spoken directions to patients. However, we also recognize that written communications can have inherent limitations in an inpatient setting, such as in an emergency situation when a patient is unresponsive. We do note, however, that certain products subject to REMS are required to have the MedGuide distributed to the patient prior to each administration of the medication, and those products should continue to comply with all required elements of the REMS.

CONCLUSION:

BIO appreciates this opportunity to comment on FDA's Consumer Medication Information Initiative. We encourage FDA to consider a single document solution for written patient-oriented medication information with a template informed and justified by relevant social science research in order to further enhance patient comprehension of a drug or biologic's benefits and risks. We would be pleased to provide further input or clarification of our comments, as needed.

Sincerely,

/S/

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