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January 11, 2011

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

Re: Docket No. FDA-2010-D-0319 Draft Guidance for Industry and Food and Drug Administration Staff on Dear Health Care Provider Letters: Improving Communication of Important Safety Information; Availability

Dear Sir/Madam:

The Biotechnology Industry Organization (BIO) thanks the Food and Drug Administration (FDA) for the opportunity to submit comments on the "Draft Guidance for Industry and Food and Drug Administration Staff on Dear Health Care Provider Letters: Improving Communication of Important Safety Information." (the Draft Guidance).

BIO represents more than 1,100 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:

Generally, this guidance document outlines the content and format requirements for a Dear Health Care Provider Letter (DHCP) letter, which BIO believes is very helpful to the Sponsor in writing the letter. We would like to suggest several recommendations for consideration in the Final Guidance:

I. DHCP Letters should be Aligned with REMS Programs

BIO suggests that there be consistent content and format recommendations for the three types of DHCP letters and letters sent as part of a Risk Evaluation and Mitigation Strategy (REMS). We note that the footnote to the Draft Guidance states that "Although not specifically intended for this purpose, the guidance may be used, in appropriate circumstances, to help develop correspondence to meet certain of the communication plan requirements for Risk Evaluation and Mitigation Strategies (REMS) under section 501-1(a)(3) of the Federal Food, Drug, and Cosmetic Act." (p.1) Since DHCP letters are significant components of a Communication Plan element of a REMS, we ask that FDA further clarify that the format and content recommendations in this guidance also apply to letters sent subject to a REMS program.

If there are additional, unique considerations that are relevant to letters sent under REMS, we request that FDA please elaborate upon those distinctions. For example, BIO asks FDA for clarification concerning letter heading of the DHCP letter when it is required as part of a REMS Communication Plan. The choice of using one of the three headings; "IMPORTANT DRUG WARNING", "IMPORTANT PRESCRIBING INFORMATION", or "IMPORTANT CORRECTION OF DRUG INFORMATION" may not convey the appropriate safety risk message when a DHCP letter is part of a REMS. We ask FDA to consider the use of other letter headings such as "IMPORTANT DRUG SAFETY INFORMATION", for a DHCP letter in a REMS Communication Plan as this more aptly communicates the letter's intent. The use of this header will also better define other communication materials that may be included within the REMS, such as healthcare provider safety guidelines or educational safety brochures thus providing greater clarity about the purpose of the communication.

Additionally, the Draft Guidance states "Similarly, a DHCP letter that announces the introduction of a new Medication Guide should be directed to pharmacists who would be required to distribute the Medication Guide to patients." (lines 207-209) Since nearly all REMS programs include a Medication Guide as an element, please clarify if the Draft Guidance indirectly ties these letters to REMS programs. Finally, please clarify that in certain circumstances not all pharmacists would need to receive a DHCP letter announcing a new Medication Guide, but rather just an appropriate subset of pharmacists.

II. Target Audiences Beyond Physicians Should be Further Clarified

We ask FDA to clarify the Agency's expectations that the target audience be broadened to a distribution list beyond prescribers. For example, the Draft Guidance states that:

> *"A DHCP letter should be directed to all health care providers who are likely to prescribe, dispense, or administer the drug and others who would have a need to know the information being disseminated. Ordinarily, potential prescribers — the gatekeepers to access to the drug — would be the most important audience for a DHCP letter. Therefore, a manufacturer should make certain to direct the letter to the full range of health care providers who would have occasion to prescribe the drug, including nurse practitioners and physician assistants who have*

> *prescribing authority. A DHCP letter should also be directed to other health care providers who may not have occasion to prescribe the drug, but for whom it would otherwise be important to know the information in the letter.* (Lines 196-204)

We request that FDA provide guidance on how the Sponsor would obtain such broad lists of non-prescribers, such as pharmacists, nurse practitioners, and nurses. In the past, FDA has typically requested manufacturers to distribute DHCP letters, depending on the information, to physicians that prescribe a drug. Companies have worked with medical organizations such as the American Medical Association, to purchase distribution lists to send the DHCP letters. While we understand FDA's intent to inform broader groups of healthcare providers (HCP) about the DHCP letter information, we are concerned about our ability to reach the target audiences that FDA suggests and the cost of mailing DHCP letters to additional HCP groups, such as non-prescribers. Given the increasing use of the internet and disseminating information electronically, we suggest that companies work with FDA to discuss methods of distributing DHCP letters to broader groups of HCPs other than direct mail.

III. Assessing the Effectiveness of DHCP Letter is not yet Appropriate

The Draft Guidance states that "To determine whether a DHCP letter has had the intended effect, we recommend that manufacturers conduct an evaluation of the extent to which the target audience received the DHCP letter and is aware of the information that was communicated in the letter. For letters that are intended to modify behavior in the target audience, ideally there would also be an evaluation of the extent to which DHCP letter changed behavior in the manner described in the letter." (lines 374-380)

FDA's request for manufacturers to assess the impact of DHCP letters seems to go beyond the scope of the current regulations or requirements for the dissemination of DHCP letters. Conducting evaluations of awareness of information or extent to which the letter changed behavior typically can be quite burdensome and time-consuming. Also, evaluation of changes in behavior would be difficult. We note that currently for REMS DHCP letters, the assessment (surveys of physician understanding of serious risks) of these letters is directly related to the REMS requirements and content of the letter (such as the risk of the product) and not behavior modification.

If FDA chooses to finalize such effectiveness evaluations, we suggest that FDA provide guidance as to the methods on how assessments or evaluations should be conducted, the specific objectives of such evaluation, and which division within FDA that companies would work with in conducting and analyzing the results of the assessment or evaluation information. Additionally, we request that FDA clarify what should be the basis of comparison to determine whether a DHCP letter is effective, particularly for those letters that are part of an initial FDA approval and where it is difficult to determine what impact the DHCP makes in the absence of prior safety data to show an effect of before and after the DHCP.

IV. Additional Area of Clarification

In the past FDA has requested that companies submit DHCP letters to FDA on Form FDA 2253 so that FDA has a copy of the DHCP letter to post on their website. Also, at times, FDA requests the product risk information, or "fair balance" be presented in DCHP letters. Recently, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has provided guidance to companies that fair balance, or important safety information, is not necessary to be included in DHCP letters. In lieu of incorporating fair balance or important safety information, DDMAC has given advisory comments to include a statement in the letter, as applicable, such as "these are not the only risks associated with the use of this product. Please see the enclosed full prescribing information for more information about these risks associated with the use of this product. The information is also available at www.product.com." Thus, we believe it would be helpful if FDA would also provide guidance regarding the inclusion of product risk information in the DHCP letters and if FDA will continue to request that companies submit DHCP letters on Form FDA 2253, since typically such letters would not be considered promotional.

CONCLUSION:

BIO appreciates this opportunity to comment on the "Draft Guidance for Industry and Food and Drug Administration Staff on Dear Health Care Provider Letters: Improving Communication of Important Safety Information." Specific, detailed comments are included in the following chart. 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)

SPECIFIC COMMENTS

SECTION	ISSUE	PROPOSED CHANGE
III. FDA CONSULTATION ON DEVELOPMENT OF HDCP LETTERS		
Line 66:	Spelling error- HDCP	Please correct spelling to "DHCP"
IV. WHEN TO USE A DHCP LETTER/WHICH TYPES OF DHCP LETTER TO USE		
Line 99:	The Draft Guidance specifies 21 CFR 200.5; however, line 207-209 describes use of a DHCP letter to announce a Medication Guide.	Please clarify if FDA intends to include/incorporate other types of letters, such as REMS or recall letters.
Line 187:	The Draft Guidance states "The letter heading should repeat whichever statement appears on the envelope in the same format (a smaller font may be used, as needed)."	Please clarify whether "same format" includes color. If so please reword to: "The letter heading should repeat whichever statement appears on the envelope in the same format, including color (a smaller font may be used, as needed)."
Lines 227:	Spelling error - Hepatoxicity	Please correct spelling to "Hepatotoxicity"
Line 338:	Reference should also be made to refer to product.com website, if applicable.	Please add: "Refer to product website, if applicable"
Line 374:	Spelling error - Assesssment	Please correct spelling to "assessment"
Line 341-352:	This provision elaborates on additional details that could obscure more important information should generally be omitted from a DHCP letter or placed in a location that would not cause it to divert attention from more important information.	Whilst we understand the FDA's concern of not wanting to divert attention of the content, some information such as the patient exposure as well as the company's proposed plans to further investigate the problem (*e.g.* using a registry, genotyping, data-mining, solicited proactive surveillance) might need to be included to provide appropriate context to the safety concern being addressed.