Biotechnology Industry Organization

July 8th, 2013

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA–2013–D–0446: Draft Guidance for Industry on Expanded Access to Investigational Drugs for Treatment Use – Questions and Answers; Availability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Organization (BIO) thanks the Food and Drug Administration (FDA) for the opportunity to submit comments on the "Draft Guidance for Industry on Expanded Access to Investigational Drugs for Treatment Use – Questions and Answers."

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:

In general, the Draft Guidance is well written and provides very useful clarification of the implementation of FDA's regulations on expanded access to investigational drugs for treatment use under an investigational new drug application (IND). However, we note that the guidance document does not offer adequate information on the appropriate design of an expanded access protocol. In fact, there are two statements in the guidance document (Line 56 and Lines 66-68) that present seemingly contradictory views about the collection of safety and effectiveness information under expanded access uses. Therefore, it would be very helpful to Sponsors for FDA to provide the basic design parameters for an acceptable expanded access use protocol that enables the appropriate collection of data, yet still qualifies as an expanded access protocol rather than a standard protocol. This is especially important as expanded access use of an investigational drug is sometimes the first time the drug is being used in a high-risk population, and data collection can yield new and vital information.

In addition to design parameters, BIO requests guidance on the execution of the expanded access IND or protocol, including responsibilities regarding safety reporting of serious adverse events and adverse events (for both Sponsors and Sponsor-

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Investigators) and requirements for submission of the patient outcome (Individual Patient IND or protocol) or the final clinical study report (Intermediate-size or access IND or protocol).

It is also unclear whether data generated from an expanded access IND should be included in a package insert, and if so, what information would need to be included.

CONCLUSION:

BIO appreciates this opportunity to comment on the "Draft Guidance for Industry on Expanded Access to Investigational Drugs for Treatment Use – Questions and Answers." 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 W. Womack, Ph.D.
Director, Science and Regulatory Affairs
Biotechnology Industry Organization (BIO)

SPECIFIC COMMENTS

SECTION	ISSUE	PROPOSED CHANGE
II. BACKGROUND		
Line 49:	BIO believes that further clarity is needed on the number of subjects in "intermediate-size" populations.	BIO requests that FDA provide approximate numbers of subjects in "intermediate-size" populations.
III. QUESTIONS AND ANSWERS		
Q2: What types of regulatory submissions can be used to obtain expanded access to a drug under the three expanded access categories?		
Lines 78-85:	The guidance document refers to both *access* protocols and *access* INDs, whereas the regulations refer to these as *treatment* protocols or *treatment* INDs (21 CFR 312.320). Consistent terminology throughout the document that aligns with existing regulations would be helpful for purposes of clarity and for enabling discussions with the Agency.	BIO recommends that FDA revise to read: "…to an existing IND (i.e., an ~~*access*~~ *treatment protocol*), or; (2) a new IND submission… (i.e., an ~~*access*~~ *treatment IND*)." Also, BIO recommends that reference to the physician's Individual Patient IND submission should be included here, for clarity, as part of the option for submitting a new IND, as stated later in Line 104.
Q4: When should an access IND submission be used?		
Lines 98-104:	If there is no investigational new drug application (IND) currently in effect for an investigational agent, what information is required in an access IND to assess the acceptability of exposing patients to an investigational agent? Are the same procedures and processes followed for	BIO requests that FDA explain the specific information required in an access IND to assess the acceptability of exposing patients to an investigational agent if there is no IND currently in effect for that investigational agent. BIO also requests that FDA confirm whether the same procedures and processes will be followed for evaluation of the information in an access IND as with a standard IND.

SECTION	ISSUE	PROPOSED CHANGE
	evaluation of the information in an access IND as with a standard IND?	
Q6: How does FDA categorize and sub-categorize access submissions for administrative purposes?		
Lines 136-153:	BIO believes that the differences in the various types of expanded access submissions outlined in Question 6 are not clearly explained, resulting in the following questions: • If an individual patient IND is also an emergency IND, which sub-category label is preferred? • If a protocol is submitted as an intermediate size protocol, and patient enrollment expands beyond that originally planned, is a protocol amendment needed to enroll additional patients and does the protocol change categories to become a treatment protocol?	BIO requests that FDA provide further clarity and/or definitions, which separate and delineate the 8 sub-categories outlined in question 6, so that the Sponsor may more easily identify which sub-category applies to the expanded access submission.
Q9: Under 21 CFR 312.310(c)(1), individual patient access is generally limited to a single course of therapy for a specified duration, unless FDA expressly authorizes multiple courses or chronic therapy. What does this mean for the treatment of a chronic condition?		
Lines 247-269:	Because individual patients being treated under expanded access are often high risk and may suffer from complications and co-morbidities typically not seen in the Phase 3 population, dosing duration and monitoring procedures may change	BIO recommends that FDA include guidance on treatment changes that may occur after protocol initiation and how protocol amendments should then be handled by both Sponsors and Sponsor-Investigators.

SECTION	ISSUE	PROPOSED CHANGE
	throughout the course of treatment. Answer 9 does not offer guidance with regard to the steps the Sponsor or Sponsor-Investigator should take if the best course of action is to extend the duration of dosing past that originally determined, due to the individual patient's prognosis.	
Q10: Is Institutional Review Board (IRB) review and approval required for individual patient access uses?		
Lines 288-290:	Answer 10 concludes with the statement, "… FDA is currently considering whether other options might better facilitate individual patient expanded access while providing appropriate ethical oversight." BIO believes that Expedited IRB Review for some cases, particularly for extended use access for subjects previously enrolled in completed clinical studies after open label extensions (OLEs), will ensure continuous uninterrupted access to study drug.	BIO recommends that FDA consider appropriate cases for Expedited IRB Review, particularly for extended use access for subjects previously enrolled in completed clinical studies after open label extensions (OLEs), to ensure continuous uninterrupted access to study drug.
Q17: When can emergency use access begin?		
Lines 362-369:	In the case of an Emergency IND filed by a Sponsor-Investigator, Answer 17 indicates that the Sponsor-Investigator (Physician) will receive notification of approval via a telephone call, but the Sponsor will receive	BIO recommends that FDA modify Answer 17 to include notification to the drug supplier (Sponsor) of approval for emergency Sponsor-Investigator INDs and protocols, so that drug may be shipped to the physician requesting access.

SECTION	ISSUE	PROPOSED CHANGE
	neither FDA approval nor IRB approval indicating that dosing the patient may proceed and yet will need to ship drug on the Sponsor-Investigator's statement that approval has been received.	