Biotechnology Industry Organization

January 22, 2013

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

Re: Docket No. FDA–2012–D–0847: Draft Guidance for IRBs, Clinical Investigators, and Sponsors: IRB Responsibilities for Reviewing the Qualifications of Investigators, Adequacy of Research Sites, and the Determination of Whether an IND/IDE Is Needed

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Organization (BIO) thanks the Food and Drug Administration (FDA) for the opportunity to submit comments on the "Draft Guidance for IRBs, Clinical Investigators, and Sponsors: IRB Responsibilities for Reviewing the Qualifications of Investigators, Adequacy of Research Sites, and the Determination of Whether an IND/IDE Is Needed." BIO commends FDA on releasing this Draft Guidance, which will continue to strengthen human subject protection during clinical research, while optimizing the efficiency with which the Institutional Review Board (IRB) review process can be performed.

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:

BIO shares the Agency's strong commitment to protecting the rights and welfare of human subjects involved in biomedical research and recognizes the critical role of IRBs in this function. [1,2,3] To advance this commitment, BIO enthusiastically supports efforts

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[1] FDA Guidance, *Using a Centralized IRB Review Process in Multicenter Clinical Trials*, http://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm127013.pdf

[2] *ICH E6 Good Clinical Practice: Consolidated Guidance*, Section 3, http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073122.pdf

[3] *Federal Register*, Vol. 76, p. 44512-44531, July 26, 2011

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by FDA to continue to provide guidance for meeting the requirements of 21 CFR Part 56 while using a central IRB review for multi-site studies.[4,5] In this new Draft Guidance, the connection with the recommendations from the FDA Guidance on *Using a Centralized IRB Review Process in Multicenter Clinical Trials* may be lost. BIO's position is that use of a single, central IRB for a clinical study represents a significant advance in public health and research and also enhances a Sponsor's ability to more efficiently conduct such studies. A centralized IRB process maintains important ethical oversight and protections for human research subjects, while being less burdensome and more efficient, with fewer delays, duplications of effort, and inconsistencies in initiating and conducting clinical research. Maintaining connectivity to this important topic and previous guidance is critical when discussing new guidance on IRBs.

This is evidenced by a recently published study showing that major impediments to the broad adoption of central IRBs have included perceived concerns about a lack of specific knowledge regarding local research sites, principal investigators (PIs), local patient populations, and community values.[6] Furthermore, in its Advanced Notice of Public Rule Making (ANPRM) on the Common Rule, the Department of Health and Human Services (HHS) Office for Human Research Protection (OHRP) and FDA acknowledge these concerns by stating, "For research where local perspectives might be distinctly important (*e.g.*, in relation to certain kinds of vulnerable populations targeted for recruitment) local IRB review could be limited to such consideration(s), but again, IRB review is not the only mechanism for addressing such issues."[7]

FDA has been careful in its guidance to allow central IRBs flexibility in developing their own agreements with local IRBs, stating only, "For sites at institutions that have an IRB that would ordinarily review research conducted at the site, the central IRB should reach agreement with the individual institutions participating in centralized review and those institutions' IRBs about how to apportion the review responsibilities between local IRBs and the central IRB (21 CFR 56. 114)."[8]

BIO recommends that the Agency maintain continuity between previous guidance on the use of centralized IRBs by adding IRB and/or centralized IRB language to this Draft

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[4] BIO Comments on ANPRM on Human Subjects Research Protections, http://www.bio.org/sites/default/files/BIO%20Common%20Rule%20ANPRM%20comments%20FINAL-10%2026%202011_0.pdf

[5] BIO Comments on FDA Draft Guidance on Using a Centralized IRB Process, http://www.bio.org/advocacy/letters/comments-fda-draft-guidance-using-centralized-irb-process

[6] Klitzman R (2011) How local IRBs view central IRBs in the US *BMC Medical Ethics* 12:13 http://www.biomedcentral.com/1472-6939/12/13

[7] *Federal Register*, Vol. 76, p. 44512-44531 (quotation from p. 44522), July 26, 2011

[8] FDA Guidance, *Using a Centralized IRB Review Process in Multicenter Clinical Trials*, http://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm127013.pdf

Guidance. In addition, for clarity and to address the aforementioned concerns that show there are major impediments to the broad adoption of central IRBs, BIO recommends that FDA offer further specificity on the potential division of responsibilities between local and central IRBs during centralized ethical review for multi-site trials. BIO proposes that Section 3 (*Must an IRB review the adequacy of the research site?*) of this Draft Guidance is a rational location to provide greater certainty and linkage between this guidance and past guidance to the relationship between local and central IRBs. Additionally, further elaboration on the statement, "IRB review is not the only mechanism for addressing such issues"[9] within the context of Section 3 of this Draft Guidance would empower central IRBs to address local concerns with greater flexibility and certainty.

CONCLUSION:

BIO appreciates this opportunity to comment on the "Draft Guidance for IRBs, Clinical Investigators, and Sponsors: IRB Responsibilities for Reviewing the Qualifications of Investigators, Adequacy of Research Sites, and the Determination of Whether an IND/IDE Is Needed." We would be pleased to provide further input or clarification of our comments, as needed.

Sincerely,

/S/

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[9] *Federal Register*, Vol. 76, p. 44512-44531 (quotation from p. 44522), July 26, 2011