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May 31, 2012

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

Re: Docket No. FDA–2012–N–0170: Modernizing the Regulation of Clinical Trials and Approaches to Good Clinical Practice; Public Hearing; Request for Comments

Dear Sir/Madam:

BIO thanks the FDA for the opportunity to provide comments on Modernizing the Regulation of Clinical Trials and Approaches to Good Clinical Practice. BIO strongly supports efforts by FDA, industry, academia, and patient groups to modernize and streamline clinical trial infrastructure and methodologies to help expedite the development of innovative new therapies.

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.

Global Harmonization of Clinical Trials Oversight

BIO member companies conduct business in the global marketplace, and, wherever possible and appropriate, encourage the international harmonization of regulatory requirements. Global harmonization of clinical study requirements should be a goal so that, overall, FDA and industry resources expended on safety can be efficiently utilized.

Multi-site studies have become increasingly common in research, and this is particularly true for clinical trials of biopharmaceuticals. Unfortunately for multi-site studies, current rules and practice entail getting approval from multiple independent review boards (IRBs), which is inefficient and burdensome to clinical trial sponsors. Obtaining approval from multiple IRBs can delay research that otherwise could make new treatments available to patients more quickly. While in certain situations there may be a role for local IRBs, BIO strongly supports the concept of single IRB approval for a multi-site study. Use of a single IRB for a study would represent a significant advance in public health and research, and enhance a sponsor's ability to conduct such studies. It would maintain important oversight and protections for research subjects, but be less burdensome, more efficient, and minimize delays and inconsistencies in conducting research.

It should also be underscored that, no matter what country hosts clinical research, data collection, or analysis, that companies conduct testing in an ethical manner and provide comprehensive protection for all research participants. Participants throughout the world – including in developing countries – deserve protection based on the same fundamental ethical principles. BIO member companies conduct clinical trials in compliance with Good Clinical Practices (GCP), including those standards developed by the International Conference on Harmonisation (ICH-GCP), and in accordance with applicable local laws and regulations.

Pharmacovigilance and benefit/risk management are also global undertakings, and, as such, should be addressed from both a domestic and international perspective. Despite the global nature of modern drug development, presently a different dossier is prepared for each health authority for marketing approval (for example, NDA to FDA; MAA to EMA). BIO commends FDA for its efforts to develop and implement the electronic Common Technical Document (eCTD) to promote harmonized structure of regulatory submissions. While progress has been made, we recommend that FDA continue to collaborate with other regulatory agencies, so that there is one submission dossier with an agreed content and structure that allows submission of the same dossier to multiple agencies for marketing approval.

We also urge greater harmonization for the registration of clinical trials and the reporting of the results. There are enormous duplicative efforts involved with compliance with the 2007 FDA Amendments Act Title VIII versus EudraCT.

Creation of FDA "Experimental Space" and Chief Innovation Officer

While FDA has requested information on modernizing the regulation of clinical trials and approaches to good clinical practice, we also believe that there needs to be adequate infrastructure in place to include regulatory science and new scientific tools into the clinical trials enterprise. Advancements in molecular biology, genomics, and informatics have led to the development of novel 21st century drug development tools, but it is important that there be a clear process for translating and integrating these new methodologies from academia and public-private partnerships into FDA regulatory decisions at the reviewer level. BIO believes that an FDA "Experimental Space," led by a new Chief Innovation Officer, should be established with the responsibility and authority to ensure that promising new approaches are integrated into

Agency operations at all levels. The Chief Innovation Officer should be authorized to identify promising new scientific and regulatory approaches, with input from stakeholders inside and outside the Agency, and ensure that these approaches are integrated into Agency operations and harmonized with the approaches of other mature regulatory agencies. Examples of such approaches might include the qualification of a particular biomarker, the acceptance of novel clinical trial design methodologies, incorporation of electronic health record (EHR) technologies, alignment and rationalization of regulatory pathways for the approval of drugs/biologics and companion diagnostics, or adoption of novel methods in predictive toxicology.

Among the Chief Innovation Officer's duties should be the systematic analysis of the recommendations of all internal and external entities involved in advancing regulatory science, such as the FDA Science and Innovation Strategic Advisory Council, the FDA Science Board, the National Center for Toxicology Research, the FDA/NIH Joint Leadership Council, the Reagan-Udall Foundation, and key public-private partnerships such as the academic Centers of Excellence in Regulatory Science, the Biomarkers Consortium, the Patient Reported Outcomes Consortium (PROC) and the Predictive Safety Testing Consortium (PSTC).

The Chief Innovation Officer's responsibilities should include the development of implementation plans for pilot programs to incorporate recommendations from governmental, private organizations and academic regulatory science initiatives into Agency regulatory decision making. Implementation plans should be published for public comment for at least 60 days prior to initiation of any pilot program. Most importantly, the Chief Innovation Officer should have the authority to establish and oversee the implementation of pilot programs within the Centers, and ensure participation by cross-disciplinary pilot teams.

Health IT in Clinical Trials

Using health information technology (IT) such as electronic health records (EHRs) in clinical research will improve and speed up the drug development process, decrease costs, reduce medical errors, and improve health care quality. However, there are significant barriers preventing wide-spread use of health IT in clinical research, including slow adoption by providers and a lack of standards development. FDA, using a collaborative, consensus-based approach with all external stakeholders, could facilitate elimination of these barriers. We recommend that FDA develop its vision for utilizing health IT and EHRs, including straw proposals for external stakeholder discussion and comment, so that milestones for achieving that vision can be developed. This will ensure that the vision has the broad consensus needed to move a plan forward that is both in the public interest and feasible for implementation.
The widespread adoption of interoperable EHRs can facilitate the secure exchange of electronic health information, which can be used to speed the drug development process by improving the efficiency of clinical research.

Specifically, EHRs can help companies more effectively identify, recruit, and enroll patients for clinical trials. Companies often face challenges recruiting subjects to participate in clinical trials studying drugs for a rare disease or for trials that require a large number of patients. Difficulty recruiting eligible subjects increases the time (and cost) to develop a drug, but electronic health

records can be used to notify a physician if a patient is eligible for a clinical trial. This functionality will allow clinical trial investigators to more efficiently identify potential study participants eligible to participate in a trial.

Sponsors can also use health IT to better inform clinical study design. Data from EHRs can allow companies to simulate different clinical research models to determine the most efficient study design to assess the safety and effectiveness of a drug. Using health IT, sponsors can better understand the physiology of the target disease, the pharmacology of the drug compound to be tested, and the statistical methods that will be used to analyze the clinical trial results. This information can be used in designing the trial, which may improve the chance of clinical trial success.

Further, health IT can be used to more efficiently collect study data. Sponsors can eliminate redundant and time-consuming manual data entry by using EHRs to automatically populate case report forms.

Health IT can also allow investigators to protect subjects enrolled in a clinical trial by more effectively monitoring for adverse events. Sponsors can enroll patients in an electronic registry that allows the sponsor to track the patient's experience with the drug in real-time, relying on information contained in the patient's EHR. As a result, safety signals may be detected and addressed more rapidly, helping to ensure patient safety.

Despite the vast potential for improving clinical research through the use of health IT, significant barriers remain. Adoption of EHRs in clinical practice remains relatively low; interoperable standards and the secure exchange of data need to be ensured; and validation methods are needed.

Despite the promise of health IT, companies are less likely to use different approaches to clinical trial research, even if those methods lead to more efficiency and better protections for clinical subjects, if FDA is limited by inadequate IT infrastructure, expertise, and/or authority to apply data generated in clinical research using health IT in the Agency's regulatory decision making. As such, FDA must address its needs that would allow the Agency to develop and issue standards to guide companies in their use of health IT and EHRs.

BIO members welcome technological advances that will assist them in conducting clinical investigations in a more efficient manner. In fact, smaller, emerging companies not burdened by legacy systems and practices may have greater flexibility and willingness to adopt new EHR systems.

Building Quality into Clinical Trials

BIO supports the goals of enhancing human subject protection and the quality of clinical trial data, and applauds the Agency's efforts in issuing the August 2011 draft guidance, "Oversight of Clinical Investigations – A Risk-Based Approach to Monitoring." We look forward to the release of the final guidance and effective implementation of the risk-based approach in sponsor

companies and investigational sites. Biotechnology companies welcome proposed strategies for monitoring activities that will assist them in conducting clinical investigations in a more modern, risk-based manner. Adoption of modern, risk-based approaches should be directed toward enhancing the efficiency and effectiveness of clinical trial monitoring, with an emphasis towards achieving consistent implementation of monitoring requirements. BIO would welcome opportunities to further discuss specific approaches and lessons learned that would help shift toward modern, risk-based approaches for clinical trials that would potentially have global applicability. Please see BIO's comments the draft guidance, posted on our website, for more recommendations.

Approaches such as centralized clinical trial monitoring and a focus on the most critical data elements can help Sponsors and FDA deploy resources to the areas that will best promote the integrity and quality of clinical trial data.

Conclusion

BIO appreciates this opportunity to comment on Modernizing the Regulation of Clinical Trials and Approaches to Good Clinical Practice. We would be pleased to provide further input or clarification of our comments, as needed.

Sincerely,

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Kelly Lai
Director, Science & Regulatory Affairs
Biotechnology Industry Organization (BIO)