BIOTECHNOLOGY INDUSTRY ORGANIZATION
1201 Maryland Avenue SW, Suite 900, Washington, DC 20024
202-962-9200, www.bio.org

January 24, 2011

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

Re: Docket No. FDA–2010–D–0529 Draft Guidance for Industry on Qualification Process for Drug Development Tools; Availability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Organization (BIO) thanks the Food and Drug Administration (FDA) for the opportunity to submit comments on the "Draft Guidance for Industry on Qualification Process for Drug Development Tools (DDT)."

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:

We would like to suggest several recommendations for consideration under the Final Guidance:

I. Consortium versus Proprietary DDT Qualification Processes

Although the guidance defines "Sponsor" as a company or a consortium, based on the explained procedure in the Draft Guidance it seems that the primary audience is a consortium. The Draft Guidance describes a procedure that points at collaborative group

effort that together can share the burden of the development of the drug development tools and submission of the data to the FDA. We suggest if the Draft Guidance is specifically written for and is intended for consortia, to avoid confusion it should clearly state so, and a separate qualification process should be put in place for situations where a single Sponsor develops a DDT for its own proprietary use.

The Draft Guidance, or a separately developed single Sponsor procedure, should address the following two situations.

a. In the case of complex or controversial DDT development programs for which the Center for Drug Evaluation and Research (CDER) holds a public discussion, how will proprietary data be handled and protected? Will the public discussion be in the form of an advisory committee process? If so, what will be the level of participation expected of the Sponsor in these instances?

b. One purpose of qualifying a DDT is to ensure that it can be used reliably in multiple drug development programs, rather than in just one drug-specific program. Further, a qualified DDT will be publicly disclosed. These two facts may sometimes lessen the proprietary value of a DDT to the DDT developer. It is therefore critical that FDA procedures for qualification recognize the importance of maintaining incentives for private sector investment in DDT development.

II. Qualification Process for Biomarkers Referenced in Prescribing Information

As stated in Section I. "Introduction," the Draft Guidance describes the qualification process for DDTs, including biomarkers, for use in drug development programs. We realize that the guidance is not intended to discuss the review of DDTs submitted as part of regulatory applications, such as biomarkers referenced in prescribing information. However, we request that the Agency clarify that biomarkers described in the pharmacodynamics (PD) sections of the prescribing information for future products do not need to be qualified using the DDT qualification process.

Further, BIO recommends that the guidance clarify that the DDT qualification process is restricted to biomarkers used for regulatory and clinical practice decision making on safety, efficacy, and dose/regimen/route of administration. The DDT qualification process is overly comprehensive and rigorous for exploratory biomarkers applied to describe the mode of action. There are no specific criteria for acceptance of biomarkers based upon their ultimate intended use. We are concerned that this apparent lack of clarity and the implication that all DDT activities, regardless of intended use, are held to the same level of evidence may lead to a decreased exploration of biomarkers by Sponsors.

III. Inclusion of Meeting Timelines and Process

BIO recommends that the Draft Guidance be revised to include information about the timelines (even if only estimates) that apply to the various steps in the DDT qualification

process (*e.g.*, response to the Letter of Intent (LOI), scheduling of requested meetings, communication of final decision). We request that the guidance also provide specifics with regard to the detailed requirements of the briefing package.

IV. Process for Qualification of a Proprietary Drug Development Tool

We request that the guidance address how FDA will respond in the event it receives an LOI for a biomarker that is being developed in a proprietary manner by another party (who might hold a patent on the biomarker). Specifically, we request information about how proprietary information will be protected. Please note that while we realize that this guidance is not intended to discuss the review of DDTs submitted as part of regulatory applications, it is also critical for FDA to protect proprietary information regarding DDTs submitted as part of regulatory applications.

V. Publicizing DDTs in Development

BIO acknowledges that, as described in Section VI, the Agency plans to make information about qualified DDTs available to the public. To avoid a scenario during the timeframe prior to qualification in which separate groups are unknowingly developing the same DDT in parallel, we encourage the Agency to publicize DDTs being developed by these groups before DDTs reach the qualification stage. Any such publication of information must be consistent with the Agency's obligation to protect proprietary information. We also encourage the Agency to facilitate collaborative development of DDTs.

VI. Evidentiary Requirements

For each DDT to be qualified there needs to be a reasonable level of evidence regarding its utility in the drug development process. "Reasonable level of evidence" should be defined based on the purpose and the context of the DDT's use, as well as consideration of the tools' risks and benefits. We recognize that the evidentiary standards for qualification would be different for each tool and that detailed guidance for each tool is outside of the scope of this general guidance. However, this guidance can describe the general principles which would be applicable to any qualification process.

Various groups (within FDA, National Institutes of Health (NIH) and Institute of Medicine (IOM)) have been engaged in similar thought processes and have established scientific frameworks for qualifying a biomarker in the context of its use. We recommend that the Agency draw from the information that is already available in the public domain to establish its own evidentiary standards[1].

[1] Examples include an Institute of Medicine Report (IOM) *Evaluation of Biomarkers and Surrogate Endpoints in Chronic Disease* and *A Prototypical Process for Creating Evidentiary Standards for Biomarkers and Diagnostics*: Clinical Pharmacology & Therapeutics. 2008 Feb;83(2):368-71.)

VII. Reconciliation with Previous Patient Reported Outcomes (PRO) Precedent and PRO-Specific Comments

Finally, the qualification process described in this guidance is inconsistent with the process negotiated between the PRO Consortium and FDA for subjective rating scales. We ask that the guidance be modified to reconcile these processes.

The guidance mentions that consortia, in which several developers are working together to develop a DDT, are a way to increase efficiency and lessen the resource burden. BIO members' experience with PRO related consortia suggest that reaching agreement among members of a consortium is time consuming and resource intensive. To facilitate individual companies' investment and participation in consortia, it would be helpful for the Agency to delineate clearly how qualifying a PRO as a DDT can improve the quality and speed of drug development.

FDA's final PRO guidance published in late 2009 outlined the review timelines and FDA requirements to support a PRO labeling claim. We recommend that the final DDT guidance clarify whether the PRO DDT requires the same level of evidence as the PRO guidance.

Because of the public nature of DDT developed via consortia, the process of qualifying a PRO as a DDT may be most suitable when the PRO instrument is already publicly available. We request that the guidance further elaborate on evidence requirements and process for a DDT qualification of existing PRO instruments versus new PRO instruments.

CONCLUSION:

BIO appreciates this opportunity to comment on the "Draft Guidance for Industry on Qualification Process for Drug Development Tools; Availability." 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)