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February 28, 2012

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

Re: Docket No. FDA-2009-N-0247, Food and Drug Administration Report on Good Guidance Practices: Improving Efficiency and Transparency

Dear Sir/Madam:

The Biotechnology Industry Organization (BIO) thanks the Food and Drug Administration (FDA) for the opportunity to comment on the FDA *Report on Good Guidance Practices: Improving Efficiency and Transparency.*

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.

Regulatory transparency and clear articulation of FDA's policies and expectations through development and timely publication of guidance documents can help to foster innovation. BIO is pleased that the Agency has undertaken a review of the guidance development process and has developed reasonable recommendations to streamline the full life-cycle of guidance - from initiation to development to publication – so that guidance can be informed by the best available science and finalized in a timely manner.

BIO believes that a sound guidance development process should be driven by several key guiding principles:

- **Based on Sound, Modern Science**: Guidance development should promote scientific dialogue and exchange and reflect advancements in modern science. Good Guidance Practices should encourage exchange with external scientific and technical experts, such as through public workshops, throughout the lifecycle of guidance development.

- **Focused on Public Health Priorities**: To advance public health and drive innovation, FDA should target high-priority disease areas and that may be lagging in medical product development and commit to production of guidances.

- **Promoting Transparency and Accountability**: The guidance development process should promote transparency and accountability both internally and with the general public, for example through the publication of the prioritization, development timeline, and status of new guidances.

- **Providing Timely Advice**: Guidance documents should be developed and finalized within an established, available timeframe to ensure that the document reflects updated scientific methods and approaches. Older draft and final guidances should be periodically revisited.

- **Consistency in Application of FDA Guidance**: Staff training and public education on new guidances are important strategies to ensure consistent application of guidance documents and help stakeholders better understand the agency's expectations.

BIO is pleased to provide the following specific comments on FDA's recommendations for improving the guidance development process.

A. Initiating Guidances

1. Stakeholders are Encouraged to Submit Guidances and Topics to FDA

BIO appreciates FDA's openness to receiving guidance topics and complete guidances for consideration. It is also important to ensure there is adequate process around this proposal to ensure that FDA can respond to and track guidances submitted by the public. For example, we suggest that FDA publish whether it has accepted the guidance or topic and has initiated the guidance development.

As discussed in recommendation #A.5., workshops and scientific dialogue early in the guidance development process would help to inform the basis of a new guidance and identify topics. Further, we encourage FDA to establish a public vetting and prioritization process for identifying and prioritizing new guidance topics to ensure effective allocation of both FDA and stakeholder resources in new guidances.

2. The Guidance Agenda Should Be Posted on the Internet Only

BIO believes that posting the guidance agenda on the FDA website in addition to annual publication in the Federal Register would help to ensure that the agenda is updated in a timely manner. However, this recommendation should only be implemented if FDA can commit to periodically updating the web-based guidance agenda on a regular basis, such as every other month. Additional comments on the format of a web-based guidance Agenda are included in recommendation #A.5.

3. Each Center/Office Should Develop Written Guidance Initiation Process

It is appropriate for Centers and Offices to have consistent practices for eliciting or suggesting guidance concepts, including FDA's rationale for new guidance, revisions to existing guidance, and the development of guidance. Given limited FDA resources for guidance and policy development, it is important to prioritize those guidelines that will have the greatest public health impact, address emerging technologies and methodologies, and help to facilitate the development of new therapies to address unmet medical needs.

4. Uniform Listing Standard for the Annual Guidance Agenda

To enhance the guidance development process, we agree that FDA should more consistently utilize the Guidance Agenda. The Guidance Agenda issued annually is a very useful tool when employed strategically by the Agency. Unfortunately, it appears that many guidance documents do not develop beyond the agenda listing. FDA's recommendation to identify those guidances that will be issued within the year is a reasonable first step.

Further, we recommend that the website also include guidance development timeframes and key milestones, project status, and completion dates. This will promote transparency with the public and support accountability. As discussed above, the website should be updated on a regular basis, such as at least every other month.

Prioritization of guidances listed in the guidance agenda will also improve transparency. This may contribute to early opportunities to provide feedback on identified topics while in the concept phase via a public docket or stakeholder meetings.

5. Improved Dialogue with Stakeholders regarding the Guidance Agenda and Topics

Early consultations with industry and other stakeholders are critical to developing successful Guidance. We suggest that FDA open dialogues with industry before beginning to draft new policy to understand the underlying science and technology and practical impacts of potential Agency actions. We support the Agency's practice of holding public workshops to discuss and/or present a draft of a guidance document to an Advisory Committee when highly controversial or unusually complex new scientific

issues exist. We strongly suggest that FDA continue this practice and build upon this type of public dialogue. As a complementary or stand-alone approach, FDA could adopt the "concept paper" approach utilized by the European Union. This approach provides additional input prior to guidance development.

It also bears mentioning that in some instances, FDA's established Good Guidance Practices have been interpreted as impeding Agency engagement with the scientific community on a topic that is subject to ongoing guidance development. BIO believes that FDA's Good Guidance Practices should encourage scientific dialogue and exchange with stakeholders throughout the guidance development lifecycle to ensure that the draft and final guidances are informed by the most current science and technological approaches.

B. Prioritizing, Work Planning, and Tracking Guidances

1. Systematic Prioritization Process for each Center/Office

BIO supports FDA's efforts to prioritize guidances so that resources can be directed in the most efficient and effective manner. As previously discussed, we also suggest FDA include a process to solicit public input on guidance topics and prioritization criteria before the criteria are finalized. Such a process would ensure input from technical experts and interested stakeholders. Prioritization of guidance documents should also be published with the guidance agenda.

2. Work Planning and Tracking Strategies to Raise Awareness of Time-Frames

BIO agrees that the guidance development process should include clear timelines and accountabilities. These timelines should both inform internal work planning and also be publically communicated via the guidance agenda web site so that stakeholders can be able to determine the status of a guidance under development.

C. Developing Guidances

1. **Develop Best Practices for Working Groups**
2. **Implement Strategies to Expedite the Guidance Drafting Process**

BIO supports FDA's initiatives to best leverage its own internal capabilities and organizational resources to develop guidances in the most effective and efficient manner.

D. Reviewing and Clearing Guidances

1. **Identify Cross-Cutting Issues Early**
2. **Resolve Policy Issues before the Review/Clearance Phase**
3. **Streamline the Review/Clearance Process**

BIO supports an empowered and well-coordinated medical policy development function at FDA and believes these are reasonable approaches for achieving internal alignment on policy and minimizing the burden of clearance processes.

4. Inter-Center/Office Agreements that Establish Goals for Review/Clearance Time-Frames

BIO welcomes this proposal and agrees that the guidance development process should include clear timelines. As discussed previously, these timelines should be accessible on the FDA web-based guidance agenda so that the public can determine the status of a guidance under development. Having a timeline for guidance development drives greater accountability and predictability within the Agency

5. Encourage Compliance with Review/Clearance Timeframes
6. Enhance Processes to Expedite and Facilitate the Review/Clearance Process
7. Establish Clear Expectations with Regard to Limited Review Cycles

BIO supports these recommendations to promote expeditious review and clearance of guidance documents.

E. Issuing Guidance and Outreach

1. Establish Milestones for Reviewing Comments, Revising the Guidances, and Issuing Final Guidance

One of the strengths of the Good Guidance Practices and the Administrative Procedure Act is the ability to solicit and incorporate public feedback on the draft guidance through the notice-and-commenting process. This encourages public involvement in the process and ensures that FDA's recommendations are informed by the best available external scientific and technical experts.

However, the procedures for issuance of formal regulations differ from those for issuance of guidance in that FDA is not required to detail what comments the Agency received, how the comments were evaluated and weighed, and which were accepted and rejected. BIO does not believe that it would be a wise investment of limited FDA resources for the Agency to issue a lengthy statement of comments received and evaluated on draft guidances, as is typically done when FDA issues a new regulation, which could further delay the issuance of final guidance. However, we do recommend that FDA implement an efficient and concise mechanism for acknowledgement of the key themes raised in public comments and identify significant changes made in the final guidance. This could be achieved through a short one-page cover memo accompanying the final guidance.

Additionally, BIO suggests that FDA consider adopting the practice of other Federal agencies, such as the Centers for Medicare and Medicaid Services (CMS), which release

a red-line version to accompany certain final guidances to help the public better understand the changes made since publication of the draft guidance.

We also believe that final guidances would benefit from an executive summary section at the start of the guidance that recaps the recommendations made within the guidance, for example through several concise bullets.

Finally, FDA should also communicate to industry the effective date that the Guidance will apply to products already under development but not yet submitted to FDA for review.

2. Use Innovative Forms of Guidance that Comply with GGP Requirements, Such as Issuing Notice to Industry Letters as Level I Guidance "for Immediate Implementation"

BIO supports efforts to issue guidance and advice to industry as expeditiously as possible. However, as previously noted, it is important to provide adequate opportunities for public comment, consistent with the Administrative Procedure Act, to ensure that FDA guidance and new FDA policy are informed by sound science and public input. While we understand this practice is more prevalent in medical device regulation, we believe that the utilization of Notice to Industry Letters as Level I guidances "for immediate implementation" should be limited, and generally reserved for addressing key public health emergencies or emerging threats.

3. Periodically Evaluate Draft Guidance to Determine if any Draft Guidance that has been in Draft Form for More than Three Years should be Withdrawn, Finalized, or Issued as Revised Draft

We appreciate FDA's proposal to revisit guidances that have been in draft form for longer than three years. Sponsors often find it difficult to ascertain whether FDA staff enforces draft guidances, even those pending after several years.

We also request that FDA communicate clear rules for their staff and Industry explaining how draft guidance documents are to be applied during the development and review process.

Additionally, guidances that have been in draft form for a significant period of time may no longer reflect the current state of science. Such guidances should be reviewed and either re-opened for comment and finalized or withdrawn. Scientific workshops may help provide input should the guidance need to be revised as a new draft.

In other instances, the guidance may not have been finalized due to legitimate considerations that arose during the public comment period, but not communicated back to regulated industry and FDA staff. This may contribute to confusion and inconsistency in interpreting FDA's expectations.

4. Establish Expectations that Issues Raised by Comments be Resolved within a Certain Timeframe after the Comment Period Closes

Please see our comments in recommendation #E.1.

5. Establish Goals to Finalize Draft Guidance that Receives no Comments Expeditiously

BIO believes this is a reasonable recommendation. In many cases, but not all, a lack of comments can signify tacit comfort with the guidance as written.

6. Use Social Media Tools to Increase Outreach for Recently Issued Significant Guidance

BIO believes that training and education should be part of the guidance implementation process. Training on new guidelines should include both industry, and regulators. Regulator training is essential to ensure consistency in application of guidance documents across review divisions. It is also important that there be an opportunity for industry to ask questions regarding new guidelines or expected regulatory practices. Responses to industry questions should be addressed through an appropriate forum that engages all relevant stakeholders and provides a consolidated, universal response within an acceptable time frame.

In addition, outreach via social media and archived webcasts could better facilitate educating regulated industry on how to better understand the new guidelines.

7. Provide a Centralized Databases with Links to New, Revised and Withdrawn Guidance Documents

BIO supports this practice and also agrees with the proposal to establish an archive section for old or withdrawn guidances.

CONCLUSION:

BIO appreciates this opportunity to comment to the Transparency Task Force on Good Guidance Practices. 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)