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

March 8, 2011

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

Re: Docket No. FDA-2009-N-0247-0260: FDA Transparency Initiative: Improving Transparency to Regulated Industry

Dear Sir/Madam:

The Biotechnology Industry Organization (BIO) thanks the Food and Drug Administration (FDA) for the opportunity to provide recommendations on how the Agency can be more transparent towards regulated Industry. We support the goals of this initiative and we are pleased to see the Agency's commitment to advancing the principles of transparency, consistency, and accountability by leveraging modern communication tools and re-evaluating Agency processes. Clear, consistent and open communication with the public and regulated Industry, conducted in a manner that balances the importance of protecting competitive commercial information, is a critical FDA function and essential for protecting and promoting the public health.

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.

Overall, BIO applauds FDA's commitment to improving transparency to manufacturers, and believes that the report *Improving Transparency to Regulated Industry* includes many common sense approaches for enhancing FDA transparency and represents a good

starting point on which to base future enhancements. BIO thanks the FDA for considering our previous comments and recommendations on how to improve FDA transparency towards regulated Industry.[1] Creating transparency between the Sponsor and FDA will lead to better understanding on our part of why the Agency is taking certain actions, and allow Sponsors to provide a more informed and meaningful scientific response to FDA's thinking. In the end, this will enable a more efficient review, and the interests of the public are better served by a more open, scientific dialogue during the review process.

We are pleased to offer the following comments in support of many of the draft proposals, yet we also request that the Agency re-consider its position on several significant matters that represent missed opportunities. Below, we provide specific comments on the five draft proposals and nineteen action items.

I. MISSED OPPORTUNITIES:

While we are encouraged by the progress of the FDA's Transparency Initiatives, there are important areas that FDA's report is notably lacking. In particular, transparency as it relates to communications with Sponsors during drug development, scientific positions established during the review cycle, and transparency regarding additional analyses undertaken by FDA are not adequately addressed within the Phase III report.

i. *Earlier and More Frequent Communication with First-time Filers*

In the course of drug development, Sponsors sometimes have simple or clarifying questions which are not extensive enough to warrant formal meetings with FDA, but where the responses could have a significant impact on the development program. To obtain timely responses to such questions, Sponsors often have to engage in a lengthy exchanges of multiple formal letters with FDA, which is an inefficient use of both FDA's and the Sponsor's time. More timely and efficient scientific dialogue between FDA and the Sponsor during drug development could lead to early resolution of critical issues, alleviate burden on reviewers' time caused by multiple, unnecessary letters and meetings, and decrease research and development costs. For a small biotechnology company reliant on investment capital, this unnecessary delay can undermine the fiscal viability of the company and cost millions of dollars that would otherwise go into further research and development. Ultimately, this can be detrimental to the public health and the ability of the biotechnology Industry to drive economic development and generate new jobs.

Indeed, the report states that "The Task Force agrees that meetings and informal communications between Sponsors and FDA can provide useful information and greater predictability to Sponsors and can help avoid unexpected or late-emerging problems in the review of an application. The cost of drug development may increase when timely answers to Industry questions are not provided. FDA should provide as much information to Sponsors as possible." (p.26) However, the Task Force reaches the unfortunate

[1] Biotechnology Industry Organization, *FDA Transparency Towards Regulated Industry,* April 12, 2010, http://bio.org/letters/20100412b.pdf

conclusion that given current resources, it is not feasible to significantly increase the number of meetings and informal communications with FDA staff without decreasing review efficiency.

BIO urges FDA to reconsider its position and take active steps to facilitate additional scientific dialogue between FDA and the Sponsor during drug development beyond formal, written exchanges of letters. In the spirit of collaboration and cooperation, such exchanges would be resource-saving by improving the quality of information submitted to FDA and by preventing unnecessary meetings and exchanges of written correspondence. We suggest that FDA establish a process for providing responses to simple, clarifying scientific matters that wouldn't necessitate a formal meeting with FDA. This could be achieved by scheduling a teleconference with the appropriate review staff under pre-determined timeframes followed by documentation of the exchange, for example via email. This would be complementary to the process proposed under Action Item #4 for providing responses to procedural questions within 5 days.

ii. Ongoing Implementation of the GRMPs:

The report also does not go far enough to encourage consistency, predictability, and transparency in FDA's review practices and facilitate scientific dialogue and exchange between FDA and the Sponsor during the review process. BIO encourages FDA to continue to embrace and expand upon the principles of the Good Review Management Practices (GRMPs), which are designed to improve the efficiency, clarity, and transparency of the review. For example, many review divisions appear to have differing informal criteria for meeting with Sponsors, requesting clinical data, and interacting with Sponsors during the review process. This can lead to difficulty anticipating FDA regulatory expectations and uncertainty for Sponsors. FDA must have well documented training to ensure implementation consistently across review divisions. GRMPs increase predictability and improve transparency in the review process.

In its current version the GRMPs are woefully outdated and do not incorporate important aspects of the review, such as early consultation with the Office of Surveillance and Epidemiology (OSE) and review of Risk Evaluation and Mitigation Strategies (REMS). We encourage FDA to update the GRMP guidance and staff operating procedures. We also ask FDA to continue to fully implement and adhere to the *21st Century Review Program*, which will encourage greater consistency and predictability in the review process as part of a clear and transparent regulatory decision making process.

iii. Transparency in Advisory Committee Meeting Processes:

BIO supports enhanced transparency throughout the drug review process by standardizing best practices of communication across review divisions. For example, leading up to an Advisory Committee, there are widely varying communications practices across divisions, including exchange of draft briefing documents, slides, and questions. BIO supports an ongoing, open dialogue with the review division to ensure that important review issues are addressed, while avoiding duplication between the Sponsor and FDA.

This is of particular importance in a public setting, such as Advisory Committees, and it is our view that greater transparency leads to more informed discussions by the advisory committee members.

We suggest that FDA communicate to the Sponsor well in advance the issues, concerns, and positions it will raise with the Committee, so the Sponsor can be prepared to address those issues and the Committee Members can provide well-informed advice. We ask that the questions to be asked of the Committee be formulated and presented to the Sponsor, with the briefing materials, at least 20 days in advance of the Advisory Committee meeting. Also, we suggest a policy that FDA review division management and review staff meet with the Sponsor before any Advisory Committee meeting to iron out differences regarding data and methodology, so the Committee can focus where their advice is most needed instead of on trying to figure out which analyses are reliable. In addition, we ask FDA to share its presentation and questions in advance with the Sponsor. Access to these materials fosters the opportunity for meaningful company analysis and preparation, without which a well-organized, thoughtful, and targeted presentation becomes difficult at best. By allowing for informed presentations, access to these materials maximizes the benefits of the Advisory Committee process.

iv. Agency Interactions with Manufacturer Regarding Public Communication about Emerging Safety Issues with a Manufacturer's Product

FDA should be more open with the Sponsor regarding its determination when a new safety issue may exist, including sharing data and analyses used as the basis for such a determination. Adequate communication among FDA, regulated Industry, and the public is a critical component of an FDA public health intervention. In the event of a safety issue or enforcement action, we recommend that FDA notify the company involved well in advance of any external FDA communication so that the company and other affected companies may develop complementary communications to the public and healthcare providers, or work collaboratively with FDA to establish a joint communication plan. We suggest, where feasible, that FDA engage with Sponsors at least 48-72 hours in advance of communicating emerging safety information or results of manufacturing site inspections (Form 483) to the public. Companies need to prepare to respond to inquiries from media, international health authorities, advocacy groups, and consumers that will be triggered by FDA public announcements.

We respectfully request that FDA reconsider the current process of communicating with manufacturers about emerging safety issues specific to a manufacturer's product. FDA's rationale in this section is only in the context of the manufacturer of a specific product. There is often spillover to other manufacturers with the same active ingredient, in the same therapeutic class or in the same therapeutic category. This spillover occurs around the world. Sufficient notification of other manufacturers who may be impacted by an announcement of an emerging safety issue is critical to ensure appropriate communication to the public.

v. Advisory Opinion Process

FDA's Transparency initiative, in section V.A., responds to a request from a group representing several manufacturers that the Agency establish an advisory opinion process to provide binding advice in response to specific requests on proposed promotional and scientific exchange activities. The Task Force did not endorse this request, responding that FDA already provides feedback on specific promotional pieces, and that binding advisory opinions could "place inappropriate restrictions on FDA's ability to respond to emerging issues . . ."(p. 44) We respectfully request that FDA reconsider this proposal for several reasons:

1. FDA's current practice of providing feedback on specific promotional pieces does not address the need for clarification regarding a proposed activity, as distinguished from a specific prepared promotional piece;
2. A binding opinion mechanism could still enable FDA to maintain flexibility, as needed; and
3. Other Agencies have successfully implemented similar Advisory Opinion processes.

First, the current process to request FDA's advisory review on specific promotional materials, while very useful for particular prepared advertising or promotion, does not satisfy the need for clarity with regard to whether a proposed activity would be considered by the Agency to be scientific or promotional. In contrast, an advisory opinion would allow interested parties to ask FDA's opinion about a proposed activity or practice in advance of conducting the activity, *i.e.*, by presenting a case study or theoretical fact situation to the Agency. We understand that review of a proposed piece may not be sufficient without describing to FDA the context and fact situation surrounding the distribution. For example, particular information may itself be considered scientific, but there may be a lack of regulatory clarity as to whether the means of dissemination may render the activity promotional.

Second, the concerns articulated by the Task Force regarding the binding nature of advisory opinions can easily be addressed. The report expresses reservation that a binding process could limit FDA's ability to respond if there are changed circumstances. FDA could design a process that would allow it to change its opinion based on a demonstrated public health need. For example, the HHS Office of the Inspector General (OIG) can reconsider an advisory opinion where the public interest requires following notice to the requestor and an opportunity to respond.[2] The report also expresses reservation that requestors "may fail to provide, or subsequently change" information material to FDA's consideration of the request. To the extent that later activities do not reflect what was proposed, however, FDA's opinion would not be binding. In addition, OIG has addressed this issue by requiring that requesters certify to the accuracy and completeness of the information upon which the opinion is based. Incomplete and/or changed information may render the opinion void.

Third, a similar advisory opinion process is employed by other federal agencies, including the OIG. In the OIG context, the advisory opinion process has netted important

[2] 42 C.F.R.§1008.45

public health and compliance advances. For example, compliance mechanisms to secure out of pocket assistance to needy patients through third party foundations have been established through this process.[3] As a result, a public health need has been met and potentially costly mistakes have been avoided. In the FDA context, implementing such a process would net important public health gains because it would allow regulated entities to rely on FDA's unique public health expertise in considering proposed educational, scientific or other activities or information dissemination intended for health care professionals and would foster compliance with FDA requirements.

BIO believes FDA can and should establish a process to ensure that its unique public health expertise can be brought to bear in evaluating arrangements to make scientific information available to health care professionals in a manner that affords it the regulatory flexibility to respond to public health issues while fostering transparency and compliance for regulated entities. Companies want to comply with the law and an advisory opinion process would benefit all parties by providing clarity, certainty and enhanced compliance.

vi. Resolution of Scientific Disputes within FDA:

Finally, FDA needs a well-documented and timely process to manage scientific disputes within a review. Different interpretations of data are expected in science; however, timely decisions and a transparent process for FDA's management of these situations are absolutely essential.

II. COMMENTS ON DRAFT PROPOSALS:

DRAFT PROPOSAL 1: FDA should maintain on the FDA Web site a list of presentations given by FDA employees to external audiences.

BIO supports this proposal and the FDA Action to maintain a list of presentations given by FDA employees to external audiences and post slide presentations to external audiences Sponsored by or co-Sponsored by the Agency. However, BIO believes that FDA should use this opportunity to take this proposal a step further, and to provide links to the actual presentations, rather than just a list of the presentations. In order to ensure fair, open, and equitable access, FDA should make a concerted effort to post presentation slides or transcriptions of scientific policy presentations by FDA staff to outside groups. While the proposed list is a step in the right direction, it would still require a request to FDA for the presentation, minimizing the value of quick and efficient electronic access.

Alternatively, in instances when interested members of the public request a copy of presentations from the Agency, we recommend including a proposed general timeframe in which responses to such requests will be provided. We also ask the Agency to include links to presentations of key meetings (*e.g.*, the Drug Information Association (DIA) or

[3] OIG Advisory Opinion 10-12

the Food and Drug Law Institute (FDLI) and speeches by FDA senior management within 5 business days of the date of the presentation. Furthermore, we recommend that a reasonable timeframe for posting all other staff presentations be established (*e.g.*, within 90 days of the presentation).

Further, we recommend that the list should be searchable by topic and date of the presentation and updated on a regular basis.

We would also like to better understand the 508 compliance process and why this presents a barrier to posting presentations. It may be useful to evaluate the potential burden to the Agency of complying with section 508 accessibility standards with the burden of processing numerous requests for copies of presentations, as the work required by the Agency may be equal, or only negligibly different.

DRAFT PROPOSAL 2: When the Office of the Commissioner (OC) receives a request to reconsider a scientific decision of an FDA employee from an interested person outside the Agency pursuant to 21 C.F.R. § 10.75, OC should inform the submitter within three weeks whether OC will review the request, and should inform the submitter when a decision or an update on the status of the review may be expected.

BIO agrees with this draft proposal. However, FDA must establish mechanisms to prevent the misuse of this process, including accidental or intentional disclosure of confidential commercial information.

DRAFT PROPOSAL 3: FDA will inform Industry about the progress of certain high priority guidances in development by disclosing a timeline from the start of the Agency's work on a draft guidance to publication of the final guidance.

BIO welcomes this proposal and agrees that the guidance development process should include clear timelines 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

We encourage FDA to increase transparency beyond only high priority guidance documents and recommend that status and progress be provided for all planned guidances.

Prioritization of guidance in annual listings will also improve transparency. Early opportunity to provide feedback on identified topics while in the concept phase via a public docket or stakeholder meetings will provide greater transparency to the process.

Additionally, we ask the Agency to consider the following actions to make the progress on "high priority" guidances more useful.

- If the recommendation to expand timelines to all guidances is not adopted, expand the definition of "high priority" guidance to include clarifying Agency policy in therapeutic areas that significantly impact the development of products not yet under review by FDA.
- Include concepts and FDA's rationale for new guidance, revisions to existing guidance and the development stage of the guidance.
- Include the effective date that the Guidance will apply to products already under development but not yet submitted to FDA for review.
- Include a process on how public input can be provided to guidance in the development phase at FDA.
- Include a process to solicit public input on guidance prioritization criteria before finalization in order to enhance input from technical experts and interested stakeholders.
- Explain how changes or additions to guidance will be communicated.
- Provide emerging guidance and policy in a "Points to Consider" document.
- Establish an archive section for old guidances.
- Periodically review and update special controls guidance documents.
- Communicate clear rules for reviewers and Industry explaining how draft and unreleased guidance may or may not be used during application reviews.

DRAFT PROPOSAL 4: In order to foster a more uniform and efficient process, FDA should review existing procedures used to conduct evaluations of importers, or third parties working on behalf of importers, who file information electronically about products offered for import into the United States. This review of the overall process should include what to examine during the evaluation, the error rate classification, the process of discussing the findings with the firm, and the final classification. It should also include the process for handling evaluations of those filers who file entries without being physically located at the port where the product enters the United States.

BIO supports this proposal and efforts to foster a more uniform and efficient process for import activities. A review of existing procedures to evaluate importers should focus on the objective of creating a risk-based approach to import compliance rather than a transaction-based approach. For example, why should a legitimate, known importer that imports the same registered product from the same known supplier have that product repeatedly detained for inspection at the time of entry? With limited resources and growing trade volume, FDA should focus its resources on riskier importers, suppliers, and goods. This would be consistent with FDA intent behind the PREDICT system. This risk-based system should encourage and incentivize importers to file information electronically about products offered for import.

Additional recommendations for consideration include process improvements in the Import for Export (IFE) program to encourage manufacturing in the U.S., clear and timely communication to the importers on the rationale for physical examination of routine commercial shipments that are not subject to an Import Alert, and a defined

timeframe for examination and release of products (the scope of this action would be for products not subject to an Import Alert.)

DRAFT PROPOSAL 5: FDA should initiate a planning process to develop a web-based system that would help importers more easily determine the proper requirements for importation, the correct data codes, and any special requirements. FDA will engage Industry in the planning process.

BIO supports efforts to develop a web-based system that provides information about importing requirements. A web-based tool that clearly identifies the FDA's expectations for the import of different kinds of goods could be very helpful to both FDA and importers. Information related to the documentation and process to follow to clear an import hold should be included in the web-based system. This should include input from the Industry on the FDA flags associated with tariff codes, the addition of products and product types to the FDA Product Code Builder, and the addition of new Affirmation of Compliance (AofC) Codes/qualifiers to clearly differentiate intended uses. This would assure consistency of treatment across the various ports of entry.

III. COMMENTS ON ACTION ITEMS:

ACTION 1: FDA will develop a web-based resource called *FDA Basics for Industry* that will provide basic information online about the regulatory process governing FDA-regulated products, and include information that is frequently requested by Industry.

BIO welcomes the addition of the *FDA Basics for Industry* web site. FDA Basics for Industry is a helpful and instructive tool to help explain FDA's decision-making processes and activities. Not only is such a resource of value to the public and Industry, but also to FDA staff. An improved, consolidated website helps to ensure Agency consistency, transparency, and quality decision-making for the present and future. We note this resource should be updated and maintained on a regular basis to ensure its accuracy. Furthermore, this site should be complementary to and not take the place of the more advanced level online resources.

ACTION 2: FDA will update the Agency organizational charts and senior leadership personnel changes on the FDA Web site on at least a quarterly basis and ensure that the level of detail provided on the organizational charts is consistent across the Agency.

BIO supports this initiative and suggests that FDA update the website on changes in organizational structure, contact information, and personnel in a timely fashion - no more than *30 days* after an official change is made. We suggest that the chart also indicate the date that it was updated.

We note that the proposal recommends that the updated charts "include information down to the office level and include the names of senior leadership in that office." (p. 9) Because most interactions between Industry and the FDA occur at the Division level, we recommend expanding the posting of organizational charts to include Division personnel.

ACTION 3: Each Center has a process for Industry to submit general regulatory questions, and for directing inquiries to individuals with additional expertise, if necessary. Links to these processes will be made available on *FDA Basics for Industry*.

BIO appreciates FDA efforts to consolidate these links and make them widely available.

ACTION 4: If a general question about an existing policy, regulation, or the regulatory process is submitted to any of the email addresses specified below, whenever practicable, FDA should provide a response within 5 business days or acknowledge receipt of the inquiry and provide an approximate timeframe for response. This will be tracked on FDATRACK.

BIO welcomes FDA's initiative to ensure that Industry questions regarding existing policy, regulation, or the regulatory process are acknowledged and responded to in a timely fashion. This, in conjunction with the consolidated links discuss in Proposal #3, will be helpful to drug Sponsors navigating the drug development process.

In both Action Item #4 and #18, we recommend replacing the word "should" with "shall". This leaves the "whenever practicable" condition in place which recognizes that circumstances may not always permit a response in 5 days, but creates a stronger mandate to meet the 5-day time point.

With regard to those situations when it is not practicable for a 5-day reply, we recommend including some upper limit on the projected time for the delayed response. This would bring both predictability and consistency across programs and avoid the long delays common to requests for information through the Freedom of Information Act (FOIA).

However, we note that the Task Force excluded from this process any matters related to scientific issues or particular products. As we note in our general comments, it is important to facilitate these types of informal scientific discussions so that issues can be resolved in a timely manner to the benefit of FDA, the Sponsor, and ultimately patients.

ACTION 5: In September 2010, FDA issued its "Strategic Priorities FY 2011-2015" in draft form for public comment. FDA will issue a final version of the "Strategic Priorities FY 2011-2015" by March 2011.

BIO supports finalization of the Strategic Priorities document and asks the Agency to also issue final versions of FDA work plans so the translation of strategic priorities to actual implementation is apparent.

ACTION 6: FDA will post on the FDA Web site slide presentations that are delivered by FDA employees to external audiences at events Sponsored by, or co-sponsored by, the Agency.

See comments under Draft Proposal #1.

ACTION 7: FDA will compile all FDA Center guidance and standard operating procedures on FDA employees meeting with Sponsors about product applications on the web-based resource, *FDA Basics for Industry*.

We appreciate the compiled list of Center Guidances and Standard Operating Procedures (SOP) on *FDA Basics for Industry*, but we ask that FDA also include CDRH application review SOPs.

ACTION 8: As part of the *FDA Basics for Industry* web-based resource, FDA will describe the types of notifications it provides to Industry (e.g., letter acknowledging receipt of the application, mid-cycle review meetings) associated with the product application review process. FDA will explain its practice of providing the Sponsor with the name and contact information of the individual who should be contacted with questions about the product application. FDA will provide an overview of the processes used to strive for consistency of product application review.

BIO supports this action and recommends that the description of the notification type include a reference to the level of authority for the notification. For example, approval orders are specified in the *Food, Drug, and Cosmetics Act,* mid-cycle review meetings are specified in the regulations, and acknowledgement of receipt is specified in the guidance/operating procedures.

ACTION 9: FDA will communicate on the web-based resource, *FDA Basics for Industry,* general expectations about the circumstances, if any, under which it is appropriate to use secure email between FDA and a manufacturer when there is a question involving the manufacturer's product.

BIO appreciates FDA's willingness to explore the use secure email between FDA and a manufacturer when there is a question involving the manufacturer's product or regulatory action. Today, many FDA regulatory actions are currently being conducted via paper and the Agency is not consistently providing rapid communication of action letters to

applicants. In certain review areas, FDA staff is not willing to fax or email a copy of a signed action letter to the applicant before processing the letter through regular mail, and additionally refuse to inform the applicant of the outcome until the letter arrives in the mail. It can often take one week or more for the applicant to receive the action letter through regular mail. Technology exists to avoid these delays in communication and the time and effort required to provide this rapid notification via email is minimal and seems justified.

ACTION 10: FDA will explain via the *FDA Basics for Industry* web-based resource how a Sponsor is informed about whether the review of its product application is on track to meet the target date for FDA action on the application. FDA is also willing to hold further discussions with Industry about application tracking systems, and explore the feasibility of implementing such a system at FDA.

BIO supports this action and is willing to participate in further discussions with the Agency about application tracking systems and the feasibility of implementing such a system at FDA. It will be beneficial, particularly to companies without prior experience in working with FDA, to have a central location to learn about FDA's provisions to obtain information on the status of application review. We strongly recommend development of a web-based tracking system similar to that offered by Health Canada. We believe that this capability may provide the greatest value to Sponsors if the tracking system is set up in such a way that it allows companies to monitor the status of the review as it moves through the GRMP milestones established under the *21st Century Review Program.*

We recognize that an initial resource investment will be required to create an automated tracking system but we believe, based on experience with the Health Canada system, that the resource savings for Industry and FDA once the system is in place would be considerable. We note that FDA representatives conferred with Health Canada officials about the Canadian application tracking system and reached the initial conclusion that the system "did not provide a significant increase in the amount or quality of information available to a Sponsor or applicant regarding their submission." Although the information FDA is able to share with Sponsors is similar, the FDA process requires direct contact with Agency staff. Industry encounters considerable difficulty in this regard (*i.e.*, "telephone tag," need to send repeated e-mail inquiries) which frequently places availability of timely information on the status of applications out of reach. Because FDA staff cannot be expected to have the requested information on the status of applications at their fingertips, such inquiries usually require a return phone call after checking Agency records. Therefore, while the same information is theoretically available, the process is cumbersome and can be time consuming for everyone involved. Our experience with the Health Canada system has been extremely positive.

Therefore, we strongly urge FDA to initiate steps to develop a web-based application tracking system similar to that employed by Health Canada with due consideration to protection of confidential information. Given the importance of protecting competitive and confidential commercial information, it is imperative that such a system provide

access only to the Sponsor and be operated under strict security guidelines. The implementation of any such system could be conditioned on (1) the existence, and FDA's acquisition of, appropriate technology with all necessary firewalls; (2) an extensive public workshop and comment process; (3) the execution of a thorough and well-designed pilot program; and/or (4) FDA agreeing to assist in bringing all available sanctions in the case of any such breach.

ACTION 11: To examine suggestions for improving the guidance process, the Commissioner has formed a cross-Agency working group under the leadership of the Office of Policy. This working group is examining the current process and will identify best practices for improving the Agency's work on guidance. Topics include streamlining guidance development, reducing the time between issuance of draft and final guidance, and making it easier to find guidance documents on the FDA Web site.

The formation of the cross Agency group is positive and BIO applauds FDA for taking this step. Regulatory transparency and clear articulation of FDA's policies and expectations through development and timely publication of guidance documents can help to foster innovation. Yet it takes the Agency long periods of time—often several years—to finalize policy under FDA's guidance development process. The time-consuming and burdensome process also creates a disincentive for FDA to develop guidance in key areas where FDA direction is sorely needed. This creates significant uncertainty for Sponsors, leaving companies to ascertain FDA policy by interpreting Agency's regulatory decisions and enforcement actions, which is a less efficient way for Industry to understand and meet the Agency's expectations. BIO supports the working group's efforts to Agency review the FDA guidance development process to ensure that there is regulatory transparency, consistency, and predictability to help stakeholders better understand the Agency's expectations.

In the spirit of transparency, we encourage the FDA to share its findings with stakeholders and engage in dialogue to improve the process. We ask the Agency to consider the following actions.

- Seek input on the working group recommendations prior to implementation; and
- The streamlined process should include sufficient time for notice and comment;
- Establish metrics to assess and improve the guidance development process.

Additionally, to advance public health, FDA should target high-priority disease areas that may be lagging in medical product development and commit to production of guidances following workshop or public meeting sessions to further understand hurdles and concerns.

ACTION 12: FDA will describe the ways in which interested individuals can provide input to the Agency about guidance development as part of the web-based resource, *FDA Basics for Industry*. Links that provide Industry with a list of guidance documents that have been withdrawn during the past year as well as possible topics for future guidance development or revision also will be made accessible in one location via *FDA Basics for Industry*.

BIO thanks FDA for inviting public input on guidance topics and content. FDA guidance should be informed by the best available science, which is often available outside of the Agency. 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 increased 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 should continue and build upon this type of public dialogue.

ACTION 13: After FDA issues a final rule, FDA will conduct outreach to the affected stakeholders as part of implementing the final rule if the rule imposes substantial new obligations.

BIO supports this action and asks the Agency to clearly articulate transition timelines and expectations.

We also suggest that public outreach should be part of the guidance implementation process, not just final rules. It is 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.

ACTION 14: FDA, working with the Department of Health and Human Services and the Office of Management and Budget, will improve the accuracy of the timetables included in the Agency's regulatory agenda published as part of the *Unified Agenda*.

BIO thanks FDA for this action to more consistently and strategically utilize the *Unified Agenda*. The guidance agenda issued annually is a very useful tool when employed strategically by the Agency. Unfortunately, in the past many guidance documents did not develop beyond the agenda listing (*e.g.*, draft guidance regarding requirements for post-approval change in a risk-based environment). As discussed previously, additional public consultation regarding the guidance development process may help to prioritize which guidances should be developed.

ACTION 15: FDA will publish on the FDA Web site contact information for each Import Program Manager and update that list on a regular basis.

No comments

ACTION 16: FDA will allow interested members of the public to receive email notifications when an Import Alert is posted on the FDA Web site, or an existing Import Alert is updated.

No comments

ACTION 17: As part of FDA's efforts to implement the forthcoming Strategic Import Plan, FDA will develop and execute a project to promote more uniform processes and procedures across districts, when appropriate, and inform Industry of district and port-specific practices and procedures. This project will be tracked on FDA-TRACK.

No comments

ACTION 18: If a general question about the import process or existing policy is submitted to the Division of Import Operations and Policy (DIOP) in the Office of Regulatory Affairs (ORA) or to a FDA field office, DIOP or the field office should provide a response, if practicable, within 5 business days or acknowledge receipt of the inquiry and provide an estimated time frame for response. DIOP will compile a list of answers to questions frequently asked by Industry and post this information on the FDA Web site.

Please see comments under Action Item #4.

ACTION 19: FDA will work with Customs and Border Protection to explore developing a process by which brokers and filers can correct inadvertent data errors submitted about imported products and FDA should post that process online.

No comments

CONCLUSION:

BIO appreciates this opportunity to comment on improving FDA transparency towards regulated industry. 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)