BIOTECHNOLOGY INDUSTRY ORGANIZATION

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April 13, 2009

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

Re: Docket No. FDA-2009-D-0675, OC 20091.

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Industry Organization (BIO) thanks the Food and Drug Administration (FDA) for the opportunity to submit comments on the Draft Guidance for Industry on Good Importer Practices. This guidance provides a useful quality systems framework for importers across all FDA-regulated industries to promote the safety of imported products. Biotechnology companies are currently leading significant efforts to further enhance the safety and security of biopharmaceuticals at every step of the supply chain and we encourage the FDA to minimize the potential for divergence between this guidance and current drug and biologic Good Manufacturing Practices regulations.

BIO represents more than 1,200 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.

BIOTECHNOLOGY COMPANIES ARE LEADERS IN ONGOING EFFORTS TO FURTHER SECURE THE SUPPLY CHAIN:

BIO and its member companies work closely with the FDA to ensure that the United States' drug supply is safe, secure, and reliable, and that Americans can be confident that when they use an FDA-approved prescription drug or biologic, the medicine will be safe

and effective. In fact, FDA's regulatory standards for biopharmaceutical current Good Manufacturing Practices (cGMP) are among the most rigorous in the world. BIO member companies routinely exceed those standards. Our members' facilities that manufacture prescription drugs and biologics for the U.S. market must comply with cGMP requirements to ensure that their prescription drugs and biologics can be produced consistently and in accordance with U.S. laws and regulations. Manufacturers of finished dosages that use imported ingredients test and monitor the safety, purity, and consistency of those ingredients that they use in the manufacture of their products, and facilities are periodically inspected by FDA to ensure compliance with regulation. Under current regulations and best practices, many biotechnology companies routinely develop and deploy quality systems and controls to better understand their products, trading partners, and potential hazards that may arise during the product's lifecycle. The proposed multi-industry Good Importer Practices document reinforces many of the concepts that the biotechnology industry has embraced and continues to implement in everyday practice.

Furthermore, many biotechnology companies are currently spearheading industry initiatives to further strengthen the biopharmaceutical supply chain beyond what is required by regulation. For example, Rx360 (www.rx-360.org) is a new international pharmaceutical supply chain consortium being launched by several BIO member companies. The mission of Rx360 is to create and monitor a global quality system that meets the expectations of industry and regulators, and assures patient safety by guaranteeing product quality and authenticity throughout the supply chain. The consortium is developing novel approaches to ingredient supplier auditing, endorsing best practices for supply chain management, encouraging the development of new supply chain technologies, and surveying the global marketplace for potential vulnerabilities.

Another promising initiative is the Qualified Trusted Importer Program (QTIP), a proposed voluntary certification program for highly compliant importers. The proposed program would assess the applicant's internal processes and controls with respect to product quality, supply chain security and trade compliance. Upon review, companies that qualify as "trusted importers" would be afforded interagency green lane status and certain other benefits. Such a program would complement existing U.S. Government efforts to further secure the supply chain and would build additional safety into the supply chain by incentivizing medical product manufacturers and importers to adopt best practices. BIO encourages the FDA to consider endorsing the QTIP proposal as part of the U.S. Government's overall efforts to continually enhance import safety.

GOOD IMPORTER PRACTICES SHOULD BE FULLY HARMONIZED WITH PHARMACEUTICAL cGMPs:

BIO recognizes that the draft guidance applies to all FDA-regulated industries – from drugs and biologics to food and cosmetics. As noted in the guidance, "Because of the wide variety of products and their production processes, the regulatory systems that apply to particular products, and the range of product and importer relationships, it is difficult to develop a set of detailed recommendations that fits every product." (p.5) Due to those limitations, the guidance is drafted from a high-level perspective and cannot be expected to address the specific and unique security considerations inherent in importing

biopharmaceutical products, intermediates and raw materials. As a result, the document as written may not have enough detail for biopharmaceutical importers to develop specific practices that can prevent or detect potential problems at critical points along the product's life cycle. Due to the high level nature of the guidance, key stakeholders in the biopharmaceutical supply chain will need to continue to rely on cGMPs, current GMP guidances, and other best practices in order to deliver on the major objectives of draft Good Importer Practices guidance document.

While many of the proposed actions in the guidance are consistent with current pharmaceutical regulations, we are concerned that in some areas it seems the document is intending to add requirements for safety and security of drugs beyond the current regulations. For example, there is the potential for additional business process changes and resource implications related to the need for inbound route monitoring noting any changes to routes and/or ports; stricter controls over material inspection upon receipt (physical examination of product packaging and labeling); and risk based product sampling and testing by the importer or an independent third party to authenticate the product. These activities may sometimes provide value in the biopharmaceutical supply chain, but we request that it be made clear these proposed actions are recommendations, not requirements, and that the proposed actions be framed within the context of existing pharmaceutical cGMP regulations.

BIO believes that the guidance should make every attempt not to deviate from or contradict the cGMP regulations, and this should be further clarified throughout the document. We recommend that either:

1. The guidance (or an appendix to the guidance) specifically cross-reference the Good Importer Practice recommendations against the pharmaceutical cGMP regulations. This type of comparison between this guidance and specific cGMP guidances and regulations would avoid redundancy and burden to FDA and the pharmaceutical industry where appropriate controls and oversight currently exist. This comparison should also clearly state any new recommendations in this guidance document that may supersede cGMPs.

<u>or</u>

2. Pharmaceuticals, biologics, and devices be specifically removed from the scope of the guidance since many areas of the draft guidance provide a level of detail that is generally captured within existing laws, regulations and guidance applicable to the pharmaceutical industry. A separate cGMP guidance could be issued to address more detailed good importer practices for drugs and biologics.

IMPLEMENTATION & COMPLIANCE:

BIO welcomes additional clarification around several issues that will help companies to implement the general recommendations of the guidance and continue to comply with cGMP regulations.

First, we request that FDA confirm that companies can utilize certifications from existing government programs, such as the U.S. Customs and Border Protection's Trade Partnership Against Terrorism (C-TPAT) and Importer Self-Assessment (ISA) programs, or the Transportation Security Administration's Certified Cargo Screening Program (CCSP), to demonstrate compliance with the proposed guidelines.

Second, we request that FDA establish a process to affirm that existing pharmaceutical quality systems currently implemented comply with the intent of the guidance.

Finally, we request the FDA establish a timeframe for complying with the proposed recommendation that manufacturers obtain certification and evidence of compliance from suppliers (p.11). Without an adequate timeframe for implementation, this provision may lead to manufacturers to "renegotiate" supplier contracts outside of the standard budgeting and business cycles, which may lead to difficulties establishing new contracts. An established time period in the guidance would help companies appropriately comply with this recommendation.

We have provided Specific Comments in Appendix 1.

CONCLUSION:

BIO appreciates this opportunity to comment on the Draft Guidance for Industry on Good Importer Practices. We would be pleased to provide further input or clarification of our comments, as needed.

Sincerely,

/S/

Andrew J. Emmett
Director for Science and Regulatory Affairs

APPENDIX 1: SPECIFIC COMMENTS:

BIO is pleased to offer the following specific comments on the guidance.

SECTION	ISSUE	PROPOSED CHANGE
Lines 57-87 and 135-178	Within the Introduction and Scope sections of the document, it is not clear what specifically is intended by the terms "safety" and "security" as well as what constitutes risk. Is the term safety intended to cover how to maintain product quality throughout the supply chain or simply to cover how to ensure products are not contaminated or counterfeited via the supply chain?	Please clarify terms and scope.
Lines 98-101	This reference to the Strategic Framework states that it will "require a paradigm shift from an intervention, border-focused strategy to a life-cycle approach that stresses a risk-based approach to prevention with verification that identifies high risk segments of the product life cycle and verifies the safety of products at those important phases."	We request that FDA provide more information about how and which segments of the product life cycle will be classified as "high-risk". For example, importing drug product from a company's foreign contract manufacturer should not be considered "high risk".
Line 138	Does the term "foreign sourced product" refer to a finished product for sale or is a raw material or component also in scope? This is not clear as discussed in the Scope section.	Please clarify the scope in regards to "product". We recommend adding a glossary to the document that includes definitions to be used with this guidance. Terms like "product" should be clearly defined.
Line 160	"Appropriate steps" is vague and may be widely and differently defined.	Please clarify by providing examples of what is considered to be "appropriate steps".

Lines 175-178	An additional vulnerability of the supply chain is supply chain temperature storage requirements, particularly with respect to biologic products.	We recommend adding "temperature excursion" to "…known vulnerabilities, such as microbiological contamination, temperature excursion and product defects…"
Line 177	It would be very helpful to understand the agency's thoughts on appropriate monitoring processes for detecting counterfeiting and intentional contamination.	Please provide examples of good monitoring processes for detecting counterfeiting and intentional contamination.
Lines 187-189	This provision states that "Not all recommendations are appropriate or feasible for every product, and for every importer, but we suggest that importers identify and understand potential risks before deciding to import a particular product." What is the profile of a qualifying product subject to the scope of the guidance? Is it one that you have assessed to meet importation requirements per U.S. regulations and exporting country regulations and have performed a risk analysis on the key critical elements for entry to U.S.?	Please provide a definition (in an added glossary as mentioned in comment above) of "qualifying product".
Line 208	This guidance is advocating processes and procedures that are the responsibility of supply chain and import functions within a company, but the term "Product safety program" for a manufacturer also includes the clinical aspects of product safety. We recommend that the focus should be directed to import safety functions.	Please change reference of Product Safety Management to "Import Safety Management".
Lines 225-254	Testing is part of the lifecycle process and a manufacturer could have a testing as an element of the product import safety program.	We recommend adding a bullet point explicitly mentioning product testing as a potential element of the product safety management program.

Line 236	This line may be inconsistent with Scope section. The mention of control responsibilities for finished product raw materials or other in-process components seems to conflict with the Scope of the guidance which is applicable to finished product.	We suggest either amending the Scope to include raw materials or revising line 238 to indicate "finished product only."
Line 275-276	As noted previously, supply chain storage requirements are important for maintenance of product safety.	We recommend adding "storage requirements" to "…product composition, specifications, safety concerns, storage requirements, etc."
Lines 314-318	Not all foreign government agencies will hand out inspection information about firms, and firms may be hesitant to hand out information in regards to inspections, inspection results, and the severity of the findings. It may be possible to address this by asking the firm to provide a certified attestation listing any previously identified violations.	We suggest adding: "…Alternatively or in addition, request a certified attestation from the supplier listing any previously identified violations relating to product safety."
Lines 353-354	With respect to the recommendation to "Know, if possible, whether the product was or could have been exposed to pesticides, other chemicals, or contaminants", it is not practical or necessary to evaluate every product for every type of potential exposure.	We request that FDA clarify that potential exposure to the conditions listed should be assessed in accordance with risk evaluation.
Lines 393-394	States that the importer's responsibility could continue after the product has moved into distribution within the U.S.	We recommend that this expanded responsibility of the importer be clarified to recognize that ownership change may negate the ability of the importer to continue to control product safety and security.

Lines 397-400	It may be possible that there is a situation where an external supplier is the importer of record and a different organization is the manufacturer. In that case, who would be responsible for what?	Please clarify the distinction between a manufacturer's responsibility vs. an importer's responsibility.
Lines 403-406	States that the importer should share information where appropriate to inform others when a problem is uncovered. It references informing both the public and private sector.	We request this be clarified to state that such notification might be appropriate when a problem that has been uncovered has public health implications.
Line 420	Due diligence should include an understanding of the firm's financial health and any recent change in ownership. These factors may impact business risk.	Please insert bullet point: "Evaluate the financial profile of the firm and understand any recent ownership changes as part of this due diligence."
Line 428	We suggest that the verbiage be consistent with quality system procedures for risk management.	Please change "…effective product safety program…" to "…effective product risk management plans…"
Line 432	In the context of this document, it is important to have a clear understanding of what types of information the FDA defines as "potentially significant or questionable."	Please clarify or provide examples of what "potentially significant or questionable" information means.
Line 458	Due to the number of suppliers and inherent costs of auditing or having personnel on site, etc., it would seem that a risk-based approach to a firm's supplier inspection program would also be appropriate.	We suggest adding in a risk-based approach to auditing of suppliers: "Periodically inspect the foreign firm where appropriate and feasible <u>or develop a risk-based approach to auditing of suppliers.</u> The importer could conduct inspections either through periodic visits or…."
Lines 518-527	This section proposes criteria for a risk based monitoring program. The provision recommends "Risk-based product sampling and testing by the importer or an independent third party, to ensure the product is	It is important for this language to be general enough to allow for the importer to utilize controls beyond testing at receipt to ensure product safety.

	authentic, and meets company specifications and U.S. requirements. Importers should use appropriately accredited laboratories".	Additionally, risk-based testing can be an important element of an effective import safety monitoring system, but we request clarification regarding FDA's thoughts on the conditions in which import testing would be considered essential. We recommend exclusion of pharmaceutical products manufactured under contract to a U.S. company where regulatory audit and surveillance programs are in place.
Lines 535	This provision recommends that importers "Conduct or have an appropriate third party conduct licensed custom house broker audits".	BIO believes that shared audits, such as across industry groups and regulatory agencies, would increase quality assurance.
Lines 561-563	With respect to the term "violative product", we again note that it is not clear what definition of "product" is being used, and thus what types of product fall under the scope of this guidance. We request clarification of the scope of the guidance in order to ensure that that sponsors can comply with it.	As we have also requested above, please clarify the scope of this guidance. What is the definition of "product" throughout the document?