Biotechnology Industry Organization

August 8, 2014

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. FDA-2014-D-0609: Draft Guidance for Industry on the Drug Supply Chain Security Act Implementation: Identification of Suspect Product and Notification

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Organization (BIO) thanks the Food and Drug Administration (FDA) for the opportunity to submit comments on the "Draft Guidance for Industry on the Drug Supply Chain Security Act Implementation: Identification of Suspect Product and Notification."

BIO represents more than 1,000 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:

This Draft Guidance is related to the Drug Supply Chain Security Act (DSCSA), and is intended to aid trading partners in identifying a suspect product, to provide information on how to notify trading partners and FDA about illegitimate product, and to delineate the process to subsequently terminate those notifications. Due to the critical nature of supply chain security as well as the high impact of DSCSA and this Draft Guidance on industry, it is essential that the Final Guidance be clear, practical, and represent best practice based on regulator and industry experience.

The intent of DSCSA is to minimize the risk of illegitimate product reaching patients. While no measures can completely prevent introduction of counterfeit product into the supply chain, it is crucial that both industry and regulators take all appropriate measures to protect the supply chain and assure patient safety. The Draft Guidance provides insight into potentially problematic situations and product characteristics to aid industry in identifying suspect product and scenarios where heightened surveillance may be appropriate. To be effective, this Guidance must offer viable measures to identify suspect product without unintended impact on the ability of legitimate entities to carry out their business.

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A. Additional Clarification Needed

We are concerned with FDA's use of the term "heightened vigilance". How FDA defines this term will have a major impact on suspect product reporting per DSCSA. As required in this legislation, products with a high risk of illegitimacy must be reported. High risk is defined to include "a specific high risk that could increase the likelihood that illegitimate product will enter the pharmaceutical distribution supply chain and other high risks as determined by the Secretary in guidance". It could be interpreted based on this definition of high risk that all products which possess the "heightened vigilance" characteristics described in this Draft Guidance, such as high price or high volume, would be considered at a high risk of illegitimacy and therefore must be reported to FDA. Reporting all product shipments that meet any of these broad categories of risk factors would result in over-reporting, which would have a deleterious effect on the end goal: removal of illegitimate product from the market. In the Final Guidance, for risk factors or combinations of risk factors that FDA deems require heightened vigilance, FDA should clarify regulatory expectations for procedures and documentation.

B. Trading Partners and Sourcing

FDA should clarify that the listed scenarios regarding trading partners and sourcing are intended to be guidelines and should be evaluated in the full context of the trade relationship. Although the examples listed in the Draft Guidance may, in some cases, be risk factors for potentially unethical trading partners, each of these factors alone is not sufficient to require additional controls. Qualification and selection of trading partners is already effectively addressed by internal company procedures. As written, the identified trading partner characteristics would negatively impact many companies operating in the pharmaceutical supply chain. For example:

- Requiring heightened surveillance for all new sources would adversely affect the ability of small or recently launched companies to compete in the marketplace.
- Even the most vigilant company could be the victim of a fraudulent transaction and inadvertently sell or deliver suspect product. Singling out these companies as requiring heightened vigilance could be a strong disincentive for reporting suspect product.

For several other criteria listed, specific measures are already required by DSCSA:

- Per DSCSA, manufacturers, wholesale distributors, and dispensers will trade only with authorized trading partners. The intent of this provision is to ensure that all trading partners are known to FDA, preventing trading with unknown and potentially fraudulent sources.
- DSCSA specifically requires trading partners to not accept ownership of material without appropriate transaction information, and therefore the cited absent or erroneous transaction information, transaction history, or transaction statement would be identified as a standard business practice.

Although the examples listed in the Draft Guidance are a helpful review of risk factors, internal business processes are sufficient to address all of the identified scenarios regarding trading partners and product sourcing without heightened regulatory vigilance.

C. Supply, Demand, History and Value of the Product

The identification of market-driven characteristics of products, such as high price, high sales volume, or high demand as a basis for heightened vigilance is particularly problematic. Without clear guidance on the criteria for defining high price, high sales volume, or high demand, implementation of these recommendations will be inequitable across the industry. In addition, although the characteristics listed may increase the likelihood that fraud will be attempted, these factors alone do not indicate that fraud has occurred. It is important that FDA clarify that these inherent product characteristics are individual risk factors that should be considered as part of a broader product risk assessment. It is also unclear how identification as an at-risk product will affect FDA's expectations for product monitoring or reporting.

D. Appearance of the Product

It would be helpful to clarify that Section 3, line 191, refers to "Unexpected" Appearance of the Product. Some products may be labeled in both English and other languages as a matter of course, and therefore should not be considered suspect. In addition, not all products use holograms, color shifting ink, or watermarks, so lack of these characteristics would not be considered suspect for these products. It should also be made clear that this list, as well as the list in lines 230 through 257, are provided as helpful guides for evaluating product identified as potentially suspect and are not intended as a checklist for receipt of product.

Ultimately, one of the best defenses against illegitimate product is clear communication among trading partners and with FDA. As the manufacturer has the most specific knowledge on the origin and appearance of legitimate product, the manufacturer should be consulted early in the process of identifying potentially suspect product. A simple request for verification or notification of damage during shipping should not be reportable; only if the concern rises to the level of suspect product should a report to FDA or product quarantine be required. Resolved issues following a request for verification should be maintained in internal records.

E. Notification of Illegitimate Product

It is imperative that communication be both accurate and timely. Manufacturers are required to notify FDA regarding product determined to be illegitimate. Based on context in the Guidance and DSCSA, it is understood that the determination that a product is illegitimate follows an initial investigation. We believe that it would be beneficial for FDA to clarify expectations regarding reporting following an initial notification or request for verification. Reporting to FDA only after an initial investigation determines that the product has a high risk of illegitimacy or is indeed illegitimate maintains supply chain security and prevents over-reporting.

Based on the DSCSA notification requirements, there may be multiple notifications made to FDA for the same event. For example, a dispenser, a wholesale distributor, and a manufacturer would all be required to notify FDA once they determined a product was illegitimate. If there are multiple notifications to FDA from multiple supply chain trading partners, it will be difficult for FDA to link these events and ensure that the event is closed uniformly. If, as suggested earlier in this document, supply chain partners are required to contact the manufacturer early in the verification process, a manufacturer's event identification number could be used to link the reports. It is possible that following discussions between supply chain trading partners, trading partners may disagree on whether a specific product is illegitimate even after close collaboration. In the Final Guidance, FDA should clarify who makes the final determination on whether a product is illegitimate.

Accurate and timely communication includes termination of notifications in consultation with FDA. It is appreciated that FDA has included a mechanism for requesting an expedited response in the event that the 10 business day target FDA response could result in a drug shortage. It will also be important to expedite the review in cases of upcoming or short expiry periods to prevent undue loss of marketable product. However, even in cases that would not result in a drug shortage or immediate loss of product, a 10 business day response period could have serious unintended business impact. As most termination requests should be straightforward (*i.e.,* after investigation the product was not, in fact, illegitimate, or all illegitimate product inventory has been identified and reconciled), a 3 business day FDA response is reasonable. For cases that require additional review, a request within 3 days from FDA for more information would automatically extend the consultation period.

It is important to clarify that Form 3911 is not intended for reports of damage during shipping. Technically, cracked vials or other types of product damage could be considered to meet the requirements of 581(8)(D) of the FD&C Act, "appears otherwise unfit for distribution such that the product would be reasonably likely to result in serious adverse health consequences or death to humans." Without additional clarification, this requirement would result in drastically increased reporting without additional patient benefit, as damaged product would be removed from the supply chain upon inspection.

F. Form 3911

Several adjustments should be made to Form 3911 to improve its utility, as noted below:

- Box 2: Date of initial notification should be described in the instructions as the initial notification by the reporter, since multiple members of the supply chain may report the same suspect product.
- This form should include a checkbox for "High Risk of Illegitimacy" as noted in DSCSA. Not all suspect products will have been confirmed as illegitimate at the time of reporting. Note that for product reported due to a high risk of illegitimacy, there will be no date illegitimate product was determined (Box 3), as the product will be under investigation.

- Box 4: DSCSA 582(b)(4)(B)(ii)(II) does not limit the requirement for manufacturers to report all product with a high risk of illegitimacy to FDA to product in the manufacturer's possession or control. Therefore, in some cases none of the descriptions may apply. It may be helpful to add a box, "Product in the possession of" with a checkbox for "reporter" or "other (specify)", as shown below. This would also enable firms to identify an additional trading partner that possesses a portion of the same illegitimate product, for example when a portion of a lot has been sold before the seller identifies the product as illegitimate.

    5. Product in the possession of (select all that apply)
        - Reporter
        - Other (specify)
            - (Free text box)

- An additional box should be added to indicate if this event, to the reporter's knowledge, has been reported by another member of the supply chain (as in the MedWatch form).
- An additional box should be added to allow input of the manufacturer's report # (as in the MedWatch form) to allow for greater traceability.

G. Additional Issues

We note that a majority of suspect counterfeit cases stem from U.S. Immigration and Customs Enforcement (ICE) seizures that are outside of the supply chain. As such, we ask FDA to clarify whether these individual cases require reporting under the DSCSA provisions.

Additionally, we ask FDA to clarify whether under DSCSA a company is required to report information regarding a potentially diverted product being in the U.S. (*e.g.,* a product that is approved in the U.S., but inventory of the product is made for another country).

CONCLUSION:

The entire pharmaceutical industry shares FDA's mission to eliminate patient risk due to illegitimate product. This Draft Guidance is an excellent first step in clarifying FDA's expectations for implementation of select DSCSA provisions. We appreciate the opportunity to provide comments on this Draft Guidance, and look forward to continuing to work with FDA to develop the most practical and effective tools to protect the supply chain based on our collective experience.

Sincerely,

/S/

Andrew J. Emmett
Managing Director, Science and Regulatory Affairs
Biotechnology Industry Organization (BIO)