



Healthcare Distribution Alliance

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Ilisa B.G. Bernstein, Pharm.D., J.D.
Deputy Director
Office of Compliance
Food and Drug Administration
Room 4268, White Oak Office Building 51
10903 New Hampshire Avenue
Silver Spring, MD 20993
ilisa.bernstein@fda.hhs.gov

Connie T. Jung, R.Ph., PhD
Senior Advisor for Policy
Office of Drug Security, Integrity, and Recalls
Office of Compliance
Food and Drug Administration
Room 2242, White Oak Office Building 51
10903 New Hampshire Avenue
Silver Spring, MD 20993
connie.jung@fda.hhs.gov

Daniel G. Bellingham
Office of Drug Security, Integrity, and Recalls
Office of Compliance
Food and Drug Administration
Room 4285, White Oak Office Building 51
10903 New Hampshire Avenue
Silver Spring, MD 20993
Daniel.Bellingham@fda.hhs.gov

RE: Drug Supply Chain Security Act Implementation: Identification of Suspect Product and Notification; Guidance for Industry; Availability, 81 Fed. Reg. 89112 (Dec. 9, 2016), Dkt. No. FDA-2014-D-0609

Dear Doctor Bernstein, Doctor Jung, and Mr. Bellingham:

The Healthcare Distribution Alliance (HDA) appreciates this opportunity to provide public comments to the Food and Drug Administration (FDA) regarding the *Drug Supply Chain Security Act (DSCSA) Implementation: Identification of Suspect Product and Notification; Guidance for Industry; Availability*, 81 Fed. Reg. 89112 (Dec. 9, 2016) (Final Guidance).

HDA represents the nation's primary, full-service healthcare distributors. Our members are large national companies and regional, family-owned and small businesses. HDA member companies deliver nine million healthcare products to more than 200,000 pharmacies, hospitals, nursing homes, physician offices, and clinics across the United States. This essential function is provided with little public recognition or visibility, and at great savings to the healthcare system. HDA members serve as the central link in a sophisticated national supply chain. HDA members take this mission very

seriously, and we support manufacturers, healthcare providers and the government in ongoing efforts to ensure the U.S. medicine supply remains secure, efficient and highly regulated.

HDA commented upon the draft version of this Final Guidance in 2014; we thank FDA for issuance of the Final Guidance and the many respects in which the Agency addressed the concerns HDA raised about the 2014 Draft Guidance. Pursuant to the *Federal Register* notice announcing the release of the Final Guidance and FDA's Good Guidance Practices, 21 C.F.R. § 10.115, interested parties may submit comments on final guidances at any time.

HDA offers comments on six issues raised in the Final Guidance. Where we show changes or recommendations for additional changes, the relevant bullet point is reprinted below, with the Final Guidance's new language in *blue italics*, the final guidance's (and HDA's recommended) omitted language in ~~red and striken~~, and HDA's recommended revised or additional language in *black italics*. At the conclusion of the discussion of the Final Guidance, we briefly comment upon section III.C., which FDA issued in draft form.

1. Section III.A.1. *Trading Partners and Product Sourcing*, pages 5-6.

In Section III.A.1., page 5, the Final Guidance significantly revises the Draft Guidance.

- Purchasing from a source that a trading partner knows or has reason to believe has *engaged in questionable or suspicious business practices that could increase the risk of suspect product entering the supply chain, ~~transacted business involving suspect products~~*, such as:
 - A trading partner that has been involved in business transactions where they sold or delivered illegitimate product.
 - A trading partner that has a history of problematic or potentially false transaction histories or pedigrees, such as those that contain misspelled words or incomplete information.
 - A trading partner that is reluctant to provide a transaction history associated with the product being purchased, or does not do so in a timely manner.
 - A trading partner that provides transaction information, a transaction statement, and/or transaction history that appears to be incomplete or suspicious.

HDA supports this revision from the draft to Final Guidance and thanks FDA for the change. The Draft Guidance appeared to penalize a trading partner that had excellent controls in place and so had been able to detect suspect and illegitimate product in the past. The language in the Final Guidance suitably places the emphasis upon appropriate due diligence and vetting of sources.

We remind the Agency that in 2023, when requirements regarding passing and maintenance of transaction history (TH) sunset (§ 582(k)(1) of the Federal Food, Drug and

Cosmetic Act (FDC Act), the TH language in the Final Guidance in the last two subpoints shown above, and in other sections, will need to be removed.

2. Section III.B., *Recommendations on how trading partners might identify suspect product and determine whether the product is a suspect product as soon as practicable, pages 6-7.*

FDA made several important revisions to this section, including the following:

...If a trading partner receives a product in a secured transport container or sealed homogenous case, trading partners should examine the appearance of that container as recommended below. If trading partners observe anything suspicious, they should take steps to ascertain whether the product inside the transport container is suspect. Strategies to identify suspect product include, but are not limited to, the following recommendations:

...

- Closely examine the package and the transport container (such as the case or tote):
 - To look for signs that it has been compromised (e.g., opened, broken seal, damaged, repaired, or otherwise altered). *If a trading partner receives a product in a secured transport container or sealed homogenous case, trading partners should examine the appearance of that container to see if anything about that appearance seems suspicious, such as shrink wrap that has unexpected markings, or a seal that is broken, torn, or repaired.*
 - To see if *the package or the transport container* ~~it~~ has changed since *the last shipment of the same product type* ~~it~~ was ~~last~~ received for an unexplained reason (e.g., a notification about the change from the manufacturer has not been received).
 - To see if product inserts are missing, do not correspond to the product, or are suspicious in some way.
 - For shipping addresses, postmarks, or other materials indicating that the product came from an unexpected foreign entity or source.

Final Guidance at 7.

HDA appreciates FDA's changes in the Final Guidance to clarify that trading partners, specifically wholesale distributors, are not obligated to visually inspect every individual container that enters their control. As HDA explained in its comments on the Draft Guidance, wholesale distributors receive thousands of products every day in sealed cases and cartons and they cannot and do not open each one to inspect the individual units within.

HDA agrees with and supports the Final Guidance's instruction that further steps should be taken to inspect individual units within a secured transport container or sealed homogenous

case when anything questionable is observed, as described in the first subpoint, such as “shrink wrap with unexpected markings or broken, torn, or repaired seals.” Final Guidance at 7.¹

However, HDA does not support the above language’s second and third subpoints in two respects.

First, we disagree with the suggestion that strategies for identifying suspect product should include “see[ing] if the package or the transport container has changed since the last shipment of the same product type was received.” Final Guidance at 7. It is not realistic for employees in busy, complex wholesale distribution warehouses to compare whether each of the thousands of homogenous cases received in one shipment are different from those received in a different shipment. Outer shipping packaging/containers can change for many reasons, at any time, frequently without notice and there is no efficient or meaningful way to capture what a shipping container *is* at point of receipt in order to distinguish it from what it *was*. Nor do wholesale distributors believe that changes to outer transport containers are a useful indicator of suspect product given that containers, even for the same product, from the same manufacturer, can vary from shipment to shipment as manufacturers may use different third-party logistics providers and have different shipping points.

Second, as noted in our original comment on the Draft Guidance, it is not feasible, efficient, or proper for a wholesale distributor to be checking to “see if product inserts are missing, do not correspond to the product, or are suspicious in some way.” Final Guidance at 7. Wholesale distributors leave package inserts intact and undisturbed to comply with the FDC Act and so that they will be available for the healthcare professional and/or patient who may need and use them. Inserts may not be visible unless multiple layers of product packaging are breached. In the experience of wholesale distributors, even the absence of a package insert affixed to an outer drug container is not a reliable indicator of suspect product.

We believe that the two indicators identified above – problems with package inserts and changes to packages or containers – should be triggering further investigations only if something about the “secured transport container or sealed homogenous case” is suspect in the first instance, “such as shrink wrap that has unexpected markings, or a seal that is broken, torn, or repaired.”

We believe that the two sub-points, (“Seeing if the package or the transport container...” and “Seeing if product inserts ...”) should be indented further under the immediately previous bullet point to clarify that these subsequent actions would be triggered by a suspicion that a homogenous case or transport container appears opened, damaged, repaired, or altered, or

¹ We add, however, it is our preference for the Agency to use the term “suspect” rather than “suspicious” here and throughout the guidance. As we noted on our comments to the Draft Guidance, the term “suspicious” is used in Drug Enforcement Administration (DEA) regulations [21 C.F.R. § 1301.74(b)] which requires reporting of “suspicious orders”. For the sake of clarity in explaining our views on the Final Guidance, we have not corrected each instance where we found the use of the term “suspicious.” However, we urge FDA to make the conversion from the term “suspicious” to “suspect” throughout as revisions are undertaken. We believe doing so will help reduce the potential confusion between the two terms, including when reporting to each Agency is indicated.

otherwise questionable. We suggest that FDA clarify this section of the guidance as follows, with HDA's suggested additions in **black bolded italics**, and HDA recommended ~~strikeouts in red~~.

...If a trading partner receives a product in a secured transport container or sealed homogenous case, trading partners should examine the appearance of that container as recommended below. If trading partners observe anything suspicious, they should take steps to ascertain whether the product inside the transport container is suspect. Strategies to identify suspect product include, but are not limited to, the following recommendations:

...

- Closely examine the package and the transport container (such as the case or tote):
 - To look for signs that it has been compromised (e.g., opened, broken seal, damaged, repaired, or otherwise altered). If a trading partner receives a product in a secured transport container or sealed homogenous case, trading partners should examine the appearance of that container to see if anything about that appearance seems ~~suspicious~~ **suspect**, such as shrink wrap that has unexpected markings, or a seal that is broken, torn, or repaired. **Such examination may include:**
 - **Seeing ~~To see~~** if the package or the transport container has changed since the last shipment of the same product type was received for an unexplained reason (e.g., a notification about the change from the manufacturer has not been received).
 - **Seeing ~~To see~~** if product inserts are missing, do not correspond to the product, or are ~~suspicious~~ **suspect** in some way.
 - For shipping addresses, postmarks, or other materials indicating that the product came from an unexpected foreign entity or source.

Sub-bullets change from - to a ■ to indicate change to sub-sub bullet status

3. The Final Guidance should be revised to explicitly instruct trading partners to coordinate illegitimate product determinations with the relevant manufacturer.

Section III.B. contains helpful additions that HDA supports (the Final Guidance's new language in *blue italics*):

The following are recommendations for trading partners on ways that they can expeditiously identify suspect product and determine whether the product is suspect (*and, after investigation, whether it is illegitimate*). In general, trading partners should exercise due diligence when conducting business *and should confirm that all trading partners are authorized*. Trading partners should discuss with each other any observations, questions, or concerns they have related to the status of a drug as a suspect product to aid them in determining whether the drug

should be considered a suspect product. Trading partners should also contact regulatory authorities, law enforcement, *the drug's manufacturer*, or other available resources to aid in that determination when additional expertise is called for to make an accurate assessment of the status of a drug as a suspect product.

Final Guidance at 6.

HDA specifically supports the new language instructing trading partners to contact the drug's manufacturer. However, we do not believe this language goes far enough.

HDA supported the comments on the Draft Guidance submitted by the Pharmaceutical Distribution Security Alliance (PDSA) which stated on page 4:

Furthermore, we believe that all trading partners should engage and coordinate with the relevant manufacturer prior to determining that a product is suspect product. The manufacturer is best positioned to assess the authenticity and quality of the product under consideration. Coordination with the manufacturer will avoid unnecessary and incorrect determinations that a product is suspect and the related disruption such determinations cause throughout the distribution chain.

HDA similarly stated in its comments on the Draft Guidance on page 4 that typically only manufacturers possess the requisite knowledge and expertise to definitely determine whether a particular product is, in fact, suspect and/or illegitimate. Because of the importance of the manufacturer's involvement, HDA suggests the following addition to Section III.B:

Because a product's manufacturer is usually best able to assess the authenticity and quality of a product, a trading partner should immediately consult with the manufacturer when conducting any investigation into whether a product may be suspect and/or illegitimate.

As set forth in our comments on the Draft Guidance, HDA again asks that FDA clarify that the party who makes the illegitimate product determination – which will usually be the manufacturer – is also the party who is responsible for making the illegitimate product notification to the Agency. We continue to believe that otherwise FDA would receive multiple (and even hundreds or thousands) of Form FDA 3911 notifications for a single illegitimate product action, which we do not believe would aid FDA's investigation and response. These multiple notifications would result in confusion, for both FDA and the supply chain. For example, would the multiple reports mean that a single illegitimate product event occurred that happens to involve multiple reporting entities finding the same reason for designating the product as illegitimate? Or, do they represent multiple events with different types of potential illegitimacy that happen to involve the same product?

4. The Final Guidance should be revised to clarify which party makes the illegitimate product notification to the agency.

Both HDA and PDSA expressed concerns with the Draft Guidance's process for making illegitimate product notifications to the Agency. HDA stated that only the entity that makes the illegitimate determination should notify the Agency to avoid multiple notifications regarding a single product action. PDSA similarly stated that disparate individual notifications from every trading partner with possession or control of the illegitimate product could lead to the reporting of redundant, confusing and even inconsistent information. HDA reiterates the request that FDA more clearly establish a process "that minimizes the operational challenges and burdens of excessive notification and maximizes the usability and reliability of the related information." See PDSA Comment on Draft Guidance at 9.

5. The Final Guidance should be revised to terminate notifications in fewer than 10 days.

Both HDA and others representing supply chain trading partners urged FDA to commit to terminating illegitimate product notifications in fewer than 10 days. We believe that once the Agency has cleared product, it is imperative that it be permitted to move out of quarantine and forward to patients and healthcare providers as quickly as possible. While we recognize the potential administrative burdens to the Agency, we believe that prompt resumption of distribution is critical to patient health and to minimizing the costs to the supply chain. We ask that FDA commit to terminating illegitimate product notifications within three business days.

6. The Final Guidance should be revised to clarify that all trading partners must be authorized.

In footnote 4 of the Final Guidance, FDA reiterates that trading partners "must be authorized as defined in FD&C Act section 581(2) and required under FD&C Act section 582(b)(3), (c)(3), (d)(3) and (e)(3)." Final Guidance at 1 n.4 (emphasis supplied). However, elsewhere in the Final Guidance, the statutory requirement appears more equivocal: "In general, trading partners should exercise due diligence when conducting business and should confirm that all trading partners are authorized." Final Guidance at 6. We believe it is equivocal because, the term "should" in an FDA guidance "means that something is suggested or recommended, but not required." Final Guidance at 2. Using "should" on page 6 of the Final Guidance with respect to dealing with authorized trading partners could lead to the conclusion this is only an FDA recommendation, and not a DSCSA mandate.

We recommend revising the above sentence to reflect that the requirement for doing business only with those who are "authorized" is mandatory in the DSCSA. We also believe that including references to, or the actual DSCSA language spelling out, the definition of "authorized" in § 581(2) would be appropriate so that there is no ambiguity as to the meaning of these terms and a trading partner obligations. Our suggested revision would read as follows:

In general, trading partners should exercise due diligence *and develop mechanisms to help ensure they comply with the DSCSA's specifications for* conducting business *only with* authorized *trading partners*.

7. Proposed Section III.C. appears to be vague and overbroad.

The new proposed Section III.C. of the Final Guidance provides information on how to identify product that poses a “high risk of illegitimacy” and the notifications manufacturers make to FDA and to trading partners. We are concerned that the Guidance’s proposed language does not seem to adequately differentiate products that are a high risk of illegitimacy from products that are merely suspect products and do not require notifications. Further, the Guidance states that FDA “recommends” manufacturers make certain notifications to trading partners. We find this language to be vague, particularly because Section III.C. does not clearly distinguish between suspect product and that which poses a high risk of illegitimacy. One likely result is that wholesale distributors and other trading partners may receive multiple, burdensome notifications that are either “false alarms,” or concern a product that, even if illegitimate, is highly unlikely to ever enter into wholesale distribution. We are concerned that wholesale distributors will have to unnecessarily dedicate considerable time and resources to sort through many notifications based on little real evidence that the product poses any risks.

HDA understands that manufacturers, manufacturing trade associations, and other organizations representing them intend to provide public comments on the Draft Guidance, including suggestions for modifications to further clarify how to identify products with a “high risk of illegitimacy.” HDA, therefore, defers to the recommendations of these organizations as we believe their collective expertise places them in a strong position to offer this type of input.

* * *

HDA thanks FDA for the opportunity to provide input on potential revisions to the Final Guidance. Should you have any questions about these comments, please feel free to contact me at 703-885-0240 or aducca@hda.org.

Sincerely,



Anita T. Ducca
Senior Vice President, Regulatory Affairs