Healthcare Distribution Management Association

August 11, 2014

BY ELECTRONIC FILING

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

Re: Draft Guidance for Industry on Drug Supply Chain Security Act Implementation: Identification of Suspect Product and Notification, 79 Fed. Reg. 33564 (June 11, 2014), Docket No. FDA-2014-D-0609

Dear Docket Officer:

The Healthcare Distribution Management Association (HDMA) thanks you and the Food and Drug Administration (FDA) for the collective efforts to implement Title II of Public Law No. 113-54, the Drug Supply Chain Security Act (DSCSA). As you know, one of the Food and Drug Administration's (FDA) first requirements under the DSCSA is to promulgate draft guidance to aid trading partners in identifying suspect and illegitimate product and in illegitimate product notification termination. *See* new § 582(h)(2) of the Federal Food, Drug and Cosmetic Act (FDC Act), 21 U.S.C. § 360eee-1(h)(2).

In advance of FDA issuing guidance, HDMA provided input on February 24, 2014 and April 18, 2014. We are pleased to offer these comments on the result of that work, the Draft Guidance for Industry on Drug Supply Chain Security Act Implementation: Identification of Suspect Product and Notification, 79 Fed. Reg. 33564 (June 11, 2014), Docket No. FDA-2014-D-0609 (hereinafter "Draft Guidance").

HDMA is the national association representing primary wholesale distributors, the vital link between the nation's pharmaceutical manufacturers and healthcare providers. Each business day, HDMA member companies ensure that 15 million prescription medicines and healthcare products are delivered safely and efficiently to nearly 200,000 pharmacies, hospitals, long-term care facilities, clinics and others nationwide. HDMA and its members work daily to provide value and achieve cost savings, an estimated $42 billion each year to our nation's healthcare system. For more information, visit www.HealthcareDistribution.org.

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HDMA commends FDA for issuing the Draft Guidance in a timely fashion and, in substantive part, we support its provisions. HDMA's comments are organized as follows:

1. HDMA generally supports Section III of the Draft Guidance regarding identification of suspect product.
2. When FDA issues the final Guidance, we ask that the agency clarify certain provisions in Section IV regarding notification of illegitimate product. To avoid multiple notifications which could number in the hundreds or thousands for a single illegitimate product event – we especially urge FDA to specify that only the trading partner that made the determination that a product is illegitimate has the duty to make the illegitimate product notification to the agency.
3. HDMA offers comments on specific language in the Draft Guidance for suggested inclusion in the final Guidance, when it is issued.
4. HDMA offers specific comments on the new proposed Form FDA 3911.
5. We discuss the economic burden analysis presented in the *Federal Register* notice accompanying the Draft Guidance, 79 Fed. Reg. at 33565-67.

1. HDMA Supports the Draft Guidance's Flexible Approach in Section III – Identification of Suspect Product

- **HDMA supports the Draft Guidance's emphasis upon robust Standard Operating Procedures (SOPs) and business processes to aid trading partners in the identification of suspect and illegitimate product.** We agree with FDA that a flexible approach, which avoids prescriptive requirements and checklists, is more likely to capture the variety of situations in which suspect products arise and so may better preserve supply chain security and reduce risks to patient health.

- **Section III.A of the Draft Guidance properly emphasizes the importance of product sourcing and supplier due diligence.** While HDMA believes some clarification is warranted in Section III.A (which we address in page 6 below), we agree with the Draft Guidance's emphasis upon diligent evaluation of product sourcing and suppliers. Draft Guidance at lines 131-161. We stated in our February 24, 2014 letter[1] that supply chain partners should have SOPs in place for assessing such factors as a potential new supplier's corporate history and operational and financial stability before establishing a business relationship; doing business with reliable supply chain partners could aid in reducing the risk of ever acquiring an illegitimate product in the first place. We are pleased to see FDA recognized the importance of this good business practice in the discussion of trading partner and product sourcing and support the inclusion of these principles in the final

[1] Letter to Ilisa B.G. Bernstein, Pharm.D., J.D., Deputy Director, Program Operations, FDA; Re:Draft Guidance Development On Suspect And Illegitimate Product (Title II of Public Law No. 113-54, the Drug Supply Chain Security Act (DSCSA)); From Anita T. Ducca, Vice President Regulatory Affairs, HDMA, February 24, 2014.

Guidance when it is issued. (In a few instances we will recommend specific language changes as noted below.)

- **HDMA supports the Draft Guidance's recognition in Section III.B of the importance of trading partner collaboration to resolve product problems.** While HDMA recommends below (pages 4-5) how this section might be clarified, we agree with the overall approach set forth in Section III.B. FDA states, and we concur, that "trading partners should exercise due diligence when conducting business [and] 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." Draft Guidance at lines 218-222. In the experience of wholesale distributors, if a potentially suspect product problem appears between established trading partners during the course of their regular transactions, sound business practices and good communication are likely to resolve the matter quickly.

- **We support FDA's recognition in Section III.B that not every potential product problem merits notification to regulatory authorities and law enforcement.** It is a commercially normal event for some product problems to occasionally arise, such as a broken bottle during an otherwise routine shipment between established trading partners. The Draft Guidance allows supply chain entities the flexibility to develop SOPs that distinguish between the problems that might arise in regular transactions between established trading partners and other types of transactions that do not appear to follow typical business norms.

  On a related point, we note that the definitions of "illegitimate product" and "suspect product" could be very overbroad depending upon how they are applied. The definitions include product that, among other things, "appears otherwise unfit for distribution." *See* § 581(8) (definition of "illegitimate product"); § 581(21) (definition of "suspect product"). A product may technically be "unfit for distribution" because it is, for example, an unsalable return, outdated or nearing expiration, yet *not* be suspect or illegitimate within the meaning of the DSCSA.

  HDMA supports the Draft Guidance's emphasis upon development of SOPs that supply chain entities should implement that aid in distinguishing unsalable product moving between established, authorized trading partners in commercially normal events from suspect and illegitimate products. While the Draft Guidance implicitly recognizes that not all problems merit a "suspect" or "illegitimate" product determination, we believe FDA should clarify that product that is unsuitable for distribution due to factors related to legitimate operations and commercial processes within the supply chain is not considered "suspect" or "illegitimate" under the DSCSA. We also support clarification that it would be acceptable for supply chain members to implement Standard Operating Procedures (SOPs) that aid in distinguishing unsalable product moving between established,

authorized trading partners in commercially normal events from true "suspect" and "illegitimate" products. To do so will avoid burdening legitimate commerce.

2. HDMA Requests FDA Clarify Parts of Section IV

Before illegitimate product notifications begin on January 1, 2015, HDMA respectfully requests that FDA clarify some uncertain issues the Draft Guidance raises regarding notifications to FDA of illegitimate product and termination of those notifications. Even if FDA does not issue a final Guidance before January 1, 2015, we believe clarification of these issues is important if illegitimate product notifications are to occur in an orderly, useful and compliant manner.

- **FDA needs to clarify that the party who makes the illegitimate product determination is also the party who is responsible for making the illegitimate product notification to the agency**. Under sections 582(b)(4)(B)(ii), (c)(4)(B) (ii), (d)(4)(B) (ii), and (e)(4)(B) (ii) of the FDC Act, "[u]pon determining" that a product in its possession or control is illegitimate, the trading partner must make the notification to FDA. We ask that FDA specify that it is the trading partner who determines the product is illegitimate who then has the duty to complete the Form FDA 3911 and notify the agency. Typically, a member of the supply chain who finds a suspect product in inventory immediately contacts the manufacturer because determining whether a product is illegitimate usually requires the manufacturer's knowledge of its own product formulation, manufacturing and packaging. Thus, because such information is proprietary and unavailable to the distributor or dispenser, it is usually only the manufacturer who is in a position to make a determination that a product is illegitimate. If FDA does not clarify that the only entity who notifies the agency is the entity who made the determination that the product is illegitimate, FDA could potentially receive multiple (and even hundreds or thousands) Form FDA 3911 notifications for a single illegitimate product action, which would not advance FDA's response and would result in confusion.

- **FDA should identify how to direct questions to the agency regarding illegitimate product notifications**. Trading partners may have substantive questions, such as whether to submit a notification, how to correct an inadvertent error in a notification made, and inquiries about the status of a notification or termination. Technical problems may also arise in the submission process itself, such as in the website interface. We recommend that FDA provide, clearly and in several places, including in the final Guidance and on the agency's website, contact telephone numbers, fax numbers and email addresses where questions about illegitimate product notifications should be directed. Also, we recommend that FDA consider permitting notifications by mail or telephone during extreme disruptions such as natural disasters.

- **The website should be pilot-tested.** The portal for submission of the Form FDA 3911 and updates to it is not yet "live." Supply chain participants would like the opportunity to pilot test the interface and notification process before January 1, 2015.

- **FDA should clarify when illegitimate product notification information should be made public.** FDA does not state when and whether the Form FDA 3911 and/or the information submitted in it will be made publicly available under the Freedom of Information Act. We believe that illegitimate product notifications should not be made public until such time as FDA and/or the trading partner making the notification confirms the product is, in fact, illegitimate. To publicly release information prematurely could cause confusion and have significant and negative repercussions on patient health and the supply chain.

- **Ten business days to respond to requests to terminate notifications may be very burdensome.** FDA states that it intends to respond to a trading partner request to terminate a notification within 10 business days of submission and may extend the response time frame beyond 10 days. While we appreciate that the agency permits the trading partner to describe exigent circumstances necessitating a faster response, we believe that in most instances, 10 business days is far too long. Continuing to quarantine product that the notifying trading partner has determined is, in fact, legitimate, is potentially enormously disruptive and may delay the delivery of safe, effective, life-saving medicines to patients. It is also likely that FDA has already been involved in the investigation and so is well-familiar with the determination that the product is legitimate.

- **HDMA strongly supports the use of existing systems and processes to notify trading partners about illegitimate product.** As discussed in our February 24, 2014 letter, HDMA urged FDA to recognize that trading partners already had in place efficient systems and processes for notifying one another of recalls, market withdrawals and other product problems. Lines 337-341 of the Draft Guidance recognize these existing systems and processes and state that trading partners may use them to notify other trading partners of a termination of an illegitimate product notification. We strongly support this recognition in the Draft Guidance**.**

- **However, the Draft Guidance is silent on how the initial notification to trading partners of the existence of an illegitimate product would be conducted.** HDMA urges FDA to explicitly state that existing systems and processes also may be used for original illegitimate product notifications to trading partners. We also ask that FDA further describe the appropriate procedures when the firm leading the investigation of a suspect product – usually the manufacturer – notifies its trading partners of an illegitimate product situation. We believe this process should be similar to recall communication processes in 21 C.F.R. § 7.49 – the recalling firm (or in this instance, the

firm leading the suspect product investigation) is responsible for notification to FDA and that firm's notification to its direct accounts includes instructions on what the direct accounts should do with the recalled product and whether the direct accounts should, in turn, notify their customers.

3. Recommendations for Specific Changes in the Draft Guidance

Below, HDMA identifies by line in the Draft Guidance specific language that we believe should be deleted (noted by ~~strikeouts~~) and specific language we believe should be added (noted by ***bold italics***).

Lines 121-122: Specific Scenarios That Could Significantly Increase the Risk of a Suspect Product Entering the Pharmaceutical ~~Distribution~~ ***Supply*** Chain

HDMA recommends this title change to clarify that the entire supply chain, and not just distributors, must be vigilant to guard against suspect and illegitimate product problems.

Lines 145-160: Purchasing from a source that a trading partner knows or has reason to believe has transacted business involving suspect products, such as:

- ~~A trading partner that has been involved in business transactions where they sold or delivered suspect or 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.

…

- Transaction information, a transaction statement, and/or transaction history that appears to ***raise concerns that the product is suspect.*** ~~be incomplete or suspicious~~.

Lines 208 - 211

- Finished dosage form that seems ~~suspicious~~ ***suspect*** (e.g., it has a different shape or color from the FDA-approved product …

Questioning a trading partner who has previously been involved with suspect product is unduly conservative. Such a provision inadvertently punishes those trading partners who have excellent controls in place for the detection of suspect product. Nor is there any reason to punish a trading partner where instances of suspect product have been rare, and where the product was cleared.

The term "pedigrees" is no longer appropriate under the DSCSA and so should be deleted.

The data elements of transaction information (TI), transaction history (TH) and the transaction statement (TS) are complex. It is likely, especially in the early periods of DSCSA implementation, that there will be good faith mistakes due to simple confusion and data entry and typographical errors. We do not believe that a product is more likely to be suspect or illegitimate because of errors or omissions in TI, TH or TS, absent other indicia that the product may be suspect.

We also suggest avoiding the term "suspicious" because it has a particular meaning under Drug Enforcement Administration (DEA) regulations. DEA's "suspicious orders" regulation, 21 CFR § 1301.74(b), requires distributors to design and operate a system to disclose to the DEA registrant "suspicious orders" of controlled substances, and to report them to the local DEA office. In this context, a "suspicious order" does not refer to the quality of the product itself. Rather, "suspicious order" indicates there is reason to believe that the individual(s) placing an order with a supplier may be intent on diversion or otherwise may use the product for an illicit purpose.

Thus, it is imperative to avoiding confusion between identification of unusual controlled substance product *orders* and the quality of the *products* themselves. Further, it is equally imperative to avoid any potential confusion about FDA reporting requirements vs. DEA reporting requirements. Steering clear of the identical terminology, *i.e.*, "suspicious," in the FDA final Guidance would help prevent any potential confusion.

Lines 162 -169: 2. Supply, Demand, History and Value of the Product

- ~~Product that is generally in high demand in the U.S. market.~~
- Product that is in higher demand because of its potential or perceived relationship to a public health or other emergency (e.g., antiviral drugs).
- ~~Product that has a high sales volume or price in the United States.~~

While HDMA recognizes that highly profitable pharmaceuticals can provide an incentive to counterfeiters, we believe this section's focus upon high demand, volume and price is too imprecise to aid trading partners in developing SOPs to detect suspicious product. These factors, particularly volume, vary widely across the pharmaceutical supply chain. The second bulleted indicia – product that has potential application in public health and other emergencies – is more useful as it ties the higher demand to a specific risk factor.

Lines 230-257: In the interest of brevity, HDMA does not repeat the entirety of lines 230 to 257 of the Draft Guidance. These lines, however, might be interpreted to suggest that every trading partner should affirmatively examine every individual bottle and package for signs that it may be suspect. Such signs might include changes since the product was last received (lines 234-236), missing product inserts (line 237) and inspecting lot numbers upon receipt (lines 256-257).

It is imperative that FDA clarify as soon as possible that all trading partners are not obligated to visually inspect every individual container that enters their control. In the case of wholesale distributors, who receive thousands of products every day, individual examination of every package of drug product received would have a catastrophic effect upon healthcare operations. The rapid, efficient flow of product entering a wholesale distributor's warehouse would slow to a trickle. Distributors would not be able to perform these manual inspections of every bottle and package received without a cost-prohibitive impact on the entire healthcare system and a dramatic delay in the distribution of drug products.

Moreover, wholesale distributors do not, and cannot, open individual drug cartons and packages to visually inspect the drugs contained within. To disturb a drug's outer package could trigger other regulatory responsibilities and would indicate, erroneously, to the subsequent, downstream trading partner, that the drug had been tampered with. Even when labeling such as the package insert appears to be missing, in the experience of wholesale distributors, this is not a reliable indicia of suspect product.

HDMA has previously addressed a similar point in its comments[2] to FDA in response to the FDA's Public Workshop on Standards for the Interoperable Exchange of Information for Tracing of Human, Finished, Prescription Drugs, in Paper or Electronic Format, 79 Fed. Reg. 18562 (Apr. 2, 2014) [Docket No. FDA-2014-N-0337]. As we explained in that comment, in the DSCSA, Congress specified precisely what a trading partner must do in order to accept a prescription drug product from another trading partner. The DSCSA merely prohibits acceptance of ownership of a product unless the previous owner provides the TI, TH and TS as required. *See* § 582(c)(1)(A)(i). Further, a wholesale distributor must have systems in place to enable it to: determine if it is in possession of suspect product; respond to verification requests made by FDA; notify FDA that suspect product subject to an agency verification request is not illegitimate; and, determine, in coordination with the manufacturer that a product is illegitimate. *See* § 582(c)(4). The DSCSA says nothing of, and does not require, wholesale distributors (or any other supply chain member) to routinely inspect every product received.

Where individual product must be inspected, the statute so states. For instance, beginning six years after the date of enactment of the DSCSA, "upon receipt of a returned product that the wholesale distributor intends to further distribute, before further distributing such product, the wholesale distributor shall verify the product identifier, including the standardized numerical identifier" for sealed homogeneous cases or each package if not sealed in a homogeneous case. *See* § 582(c)(4)(D). If Congress expected wholesale

[2] Letter to Connie T. Jung, RPh, PhD, Associate Director for Policy and Communication, Office of Compliance, FDA; Re: Notice; establishment of docket; request for comments: Standards for the Interoperable Exchange of Information for Tracing of Human, Finished, Prescription Drugs, in Paper or Electronic Format, 79 Fed. Reg. 18562 (Apr. 2, 2014), Docket No. FDA-2014-N-0337; From Anita T. Ducca, Vice President Regulatory Affairs, HDMA, June 9, 2014.

distributors to physically evaluate each of the thousands of products it receives from manufacturers and ships to dispensers every day, it would have so stated in the DSCSA. It did not.

4. Recommendations for Specific Changes to the New Proposed Form FDA 3911

Title of the Form: The form is identified by a number and with the title "Drug Notification". To clarify that this form is intended only for "illegitimate" product notifications and/or terminations, and is not intended for other drug-related notifications such as adverse event reporting, we suggest a more descriptive title such as "*Illegitimate Product Notification, Follow-up Notification or Termination Notification*". Additionally, FDA could consider including an introductory statement in the directions accompanying the form that the form is only intended for illegitimate product notifications as required under the DSCSA.

Fields 5 and 6: "Generic Name" and "Trade Name (if applicable)": The inclusion of the words "if applicable" after "Trade Name" creates an ambiguity we believe should be clarified. It suggests that if the illegitimate product being reported is a generic drug, the Trade Name is not "applicable" and should be omitted. This would be logical and indeed would prevent uncertainty as to whether the notification is applicable to a brand drug or its generic drug. However, neither the form nor the directions indicate when both the trade and generic names are to be entered. We suggest that FDA specifically explain how and when these fields should be completed.

Field 7: Drug Use: The directions state: "Provide the primary approved use of the drug (i.e., human use)." We recommend deletion of this field as the DSCSA only applies to drugs intended for human use and is not applicable to veterinary products. *See* § 581(12) (definition of "prescription drug").

Field 8: Drug Description: The directions state: "Select the appropriate description of the drug (i.e., finished)". HDMA also recommends FDA eliminate this field. We recommend deletion of this field as the DSCSA only applies to drugs in their final finished form. *See* § 581(13) (definition of "product").

Field 19: Company Name & Address: The instructions state that this field should be completed with "name and address information for the company that is responsible for the product or for the notification" but then also states under "Company Name," "Provide the name of the company that is responsible for the notification." Insertion of the concept of "responsibility" confuses the notification process and we request that FDA clarify these instructions.

- As discussed in page 4, HDMA recommends that FDA make very clear that the trading partner who made the determination that a product is illegitimate is the party who also should make the notification to the agency, and is the only party who should do so to avoid hundreds and even thousands of notifications being submitted for the same illegitimate product situation. To that end, FDA should also align the Form FDA 3911 and its instructions with this illegitimate product determination and reporting duty. We recommend that the Form FDA 3911 clarify that the reporting party is the entity that made the determination that the product is illegitimate.

- Identification of the company "that is responsible for the product" is confusing as it could mean: the party responsible for creating the illegitimate product; the party that possesses or controls the illegitimate product (which could include multiple wholesalers and hundreds or thousands of dispensers); the party that discovered the illegitimate product; or the party who determined the product was illegitimate and made the report. Under the FDC Act, the entity "responsible" for the drug is the one identified on the product labeling which, if the product is counterfeit, would be falsified. HDMA suggests that FDA modify this language to indicate that Field 19 should include the name and address of the company making the notification to FDA.

- We note further that the party "responsible" for the illegitimate product might very well be an unknown and/or unlawful actor and so unlikely to be identified on the Form FDA 3911.

Field 20: Unique Facility Identifier: We note in the instructions to Field 20 that FDA states that the reporting entity should provide its D-U-N-S number and should obtain a D-U-N-S number if it does not have one. The D-U-N-S number is a corporate identifier, not a facility identifier as the title suggests. FDA should clarify that it is asking for the unique "Corporate" and not "Facility" identifier.

Other issues with Form FDA 3911: We suggest adding a liability statement to the Form FDA 3911 that is similar to that found in the MedWatch form. The MedWatch form states that submission of a report does not constitute an admission that the medical personnel, user facility, importer, distributor, manufacturer or product caused or contributed to the event being reported. We believe similar language is appropriate for illegitimate product notification.

5. The Federal Register Notice and Annual Paperwork Burden Estimates

HDMA believes FDA's estimates of expected annual notifications may be high. FDA estimates that there will be 5,000 illegitimate product notifications to the agency per year, of which 2,500 would be made by wholesale distributors. 79 Fed. Reg. at 33565. As wholesale

distributors report receiving typically two or three alerts a year through the Counterfeit Alert Network, 5,000 notifications appears to be overly generous and we similarly believe it unlikely that wholesale distributors would need to file 2,500 illegitimate product reports to the agency in a single year. We recognize, however, that FDA created these estimates based upon reports submitted through other means not available to wholesale distributors, such as manufacturer's Field Alert Reports and reported thefts of prescription drug samples.

Nevertheless, as discussed on page 4, typically, determining if a product is illegitimate will require the manufacturer's expertise. HDMA believes that while wholesale distributors will be assisting a manufacturer in its investigation, they will not have the product knowledge to actually make the illegitimate determination. We believe that as the manufacturer will usually be the party making the illegitimate determination, it will also usually be the party making the notification.

The agency also notes that under sections 582(b)(4)(B)(ii), (c)(4)(B)(ii), (d)(4)(B)(ii), and (e)(4)(B)(ii) of the FDC Act, a trading partner who determines it is in possession of illegitimate product must also notify its immediate trading partners who it has reason to believe may have received that illegitimate product. 79 Fed. Reg. at 33566. Extrapolating 2,500 illegitimate product notifications from manufacturers, and wide distribution to approximately 30 trading partners, who in turn distribute to an average 2,350 trading partners, FDA estimates approximately 75,000 notifications by manufacturers to wholesale distributors and approximately 5,287,500 notifications by wholesale distributors to their trading partners. Id. Based upon our members' experience with past notifications of illegitimate products, we also believe – and hope – that these estimates are very high.

HDMA and its members are committed to improving these illegitimate product burden and cost estimates as the supply chain begins implementation of the DSCSA.

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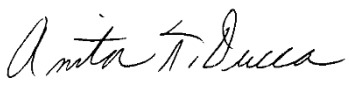
HDMA thanks you for this opportunity to comment on the Draft Guidance. If you have any questions, please contact me at 703-885-0240 or at aducca@hdmanet.org.

Sincerely,



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