

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2014-D-0609]

Draft Guidance for Industry on Drug Supply Chain Security Act Implementation: Identification of Suspect Product and Notification; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled “Drug Supply Chain Security Act Implementation: Identification of Suspect Product and Notification.” The draft guidance addresses new provisions in the Federal Food, Drug, and Cosmetic Act (the FD&C Act), as amended by the Drug Supply Chain Security Act (DSCSA). The draft guidance is intended to aid certain trading partners (manufacturers, repackagers, wholesale distributors, and dispensers) in identifying a suspect product and terminating notifications regarding illegitimate product. This draft guidance identifies specific scenarios that could significantly increase the risk of a suspect product entering the pharmaceutical distribution supply chain; provides recommendations on how trading partners can identify the product and determine whether the product is a suspect product as soon as practicable; and for product that has been determined to be illegitimate, or (for manufacturers) has a high risk of illegitimacy, sets forth the process by which trading partners should notify FDA of illegitimate product and how they must terminate the notifications, in consultation with FDA.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER]. Submit either electronic or written comments concerning the collection of information proposed in the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 2201, Silver Spring, MD 20993-0002; or the Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, suite 200N, Rockville, MD 20852-1448. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

Submit electronic comments on the draft guidance to <http://www.regulations.gov>.

Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Carolyn Becker, Office of Compliance, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993-0002, 301-796-3100, [drugtrackandtrace@fda.hhs.gov](mailto:drugtrackandtrace@fda.hhs.gov).

SUPPLEMENTARY INFORMATION:

## I. Background

FDA is announcing the availability of a draft guidance for industry entitled “Drug Supply Chain Security Act Implementation: Identification of Suspect Product and Notification.” On November 27, 2013, the DSCSA (Title II of Public Law 113-54) was signed into law. Section 202 of the DSCSA adds section 582(h)(2) to the FD&C Act (21 U.S.C. 360eee-1(h)(2)), which requires FDA to issue guidance to aid certain trading partners (manufacturers, repackagers, wholesale distributors, and dispensers) in identifying a suspect product and terminating notifications regarding an illegitimate product. This guidance identifies specific scenarios that could significantly increase the risk of a suspect product entering the pharmaceutical distribution supply chain and provides recommendations on how trading partners can identify the product and determine whether the product is a suspect product as soon as practicable.

Starting January 1, 2015, section 582 of the FD&C Act requires trading partners, upon determining that a product in their possession or control is illegitimate, to notify FDA and all immediate trading partners (that they have reason to believe may have received the illegitimate product) not later than 24 hours after making the determination. Manufacturers are additionally required under section 582(b)(4)(B)(ii)(II) of the FD&C Act to notify FDA and immediate trading partners (that the manufacturer has reason to believe may possess a product manufactured by or purported to be manufactured by the manufacturer) not later than 24 hours after the manufacturer determines or is notified by FDA or a trading partner that there is a high risk that the product is illegitimate. This draft guidance addresses how trading partners should notify FDA using Form FDA 3911. In addition, in accordance with section 582(h)(2) of the FD&C Act, this guidance sets forth the process by which trading partners must terminate the notifications using Form FDA 3911, in consultation with FDA, regarding illegitimate product or,

for a manufacturer, a product with a high risk of illegitimacy, under section 582(b)(4)(B), (c)(4)(B), (d)(4)(B), and (e)(4)(B).

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the Agency's current thinking on identification of suspect product and notification. Guidance documents generally do not create or confer any rights for or on any person and do not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations. For this particular document, section 582 of the FD&C Act gives FDA authority to issue binding guidance on the process for terminating notifications of illegitimate product. Specifically, subsection (h)(2)(A) states that FDA "shall issue a guidance document to aid trading partners in the identification of a suspect product and notification termination. Such guidance document shall...set forth the process by which manufacturers, repackagers, wholesale distributors, and dispensers shall terminate notifications in consultation with the Secretary regarding illegitimate product...." Thus, insofar as section IV.B of this guidance sets forth the process by which trading partners must terminate notifications of illegitimate product in consultation with FDA, it will have binding effect upon finalization.

## II. Paperwork Reduction Act of 1995

This draft guidance contains information collection provisions that are subject to review by the Office of Management and Budget under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The title, description, and respondent description of the information collection are given under this section with an estimate of the reporting and third-party disclosure burdens. Included in the estimate is the time for reviewing instructions, searching existing data

sources, gathering and maintaining the data needed, and completing and reviewing the collection of information.

We invite comments on these topics: (1) Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Title: Drug Supply Chain Security Act Implementation: Identification of Suspect Product and Notification.

Description: Under section 202 of the DSCSA, manufacturers, repackagers, wholesale distributors, and dispensers (e.g., pharmacies) must: (1) Notify FDA when they have determined that a product in their possession or control is illegitimate, and for manufacturers, when they have determined or been notified by FDA or a trading partner that a product has a high risk of illegitimacy; (2) notify certain immediate trading partners about an illegitimate product that they may have received and, for manufacturers, that a product has a high risk of illegitimacy; (3) terminate notifications regarding illegitimate products, and, for manufacturers, a product with a high risk of illegitimacy, in consultation with FDA when the notifications are no longer necessary; and (4) notify immediate trading partners when the notifications are terminated.

1. Notifications to FDA

Under section 582(b)(4)(B)(ii), (c)(4)(B)(ii), (d)(4)(B)(ii), and (e)(4)(B)(ii) of the FD&C Act, and beginning not later than January 1, 2015, a manufacturer, repackager, wholesale distributor, and dispenser who determines that a product in its possession or control is illegitimate, as defined in section 581 of the FD&C Act (21 U.S.C. 360eee), must notify FDA of that determination not later than 24 hours after the determination is made. In addition, section 582(b)(4)(B)(ii)(II) of the FD&C Act requires manufacturers to notify FDA when a manufacturer determines or is notified by FDA or a trading partner that a product poses a high risk of illegitimacy.

FDA estimates that a total of approximately 5,000 notifications per year will be made by all manufacturers, repackagers, wholesale distributors, and dispensers. This estimate includes the notifications by trading partners who have determined that illegitimate product is in their possession or control, as well as notifications by manufacturers that have determined a product poses a high risk of illegitimacy. This estimate is based on FDA's experience with Field Alert Reports (FARs) (Form FDA 3331) required to be submitted by holders of approved drug applications for certain drug quality issues (21 CFR 314.81(b)(1))<sup>1</sup> and with reports of the falsification of drug sample records, diversion, loss, and known theft of prescription drug samples as currently required under the Prescription Drug Marketing Act (PDMA).<sup>2</sup> Because manufacturers, repackagers, and wholesale distributors are responsible for prescription drugs from the manufacturing through distribution processes, FDA assumes that most notifications of illegitimate products would be made by these three trading partners. FDA is combining the

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<sup>1</sup> FDA review of the number of Field Alert Reports (FARs) received in calendar year 2013 was approximately 5,000. Because FARs are incident and product specific, the estimation does not represent the number of companies that have submitted a FAR to FDA.

<sup>2</sup> FDA cursory review of the number of reports of falsified drug sample records, diversion, loss, or known theft of prescription drug samples under the PDMA in calendar year 2013 was approximately 5,000. This number is being used for estimation purposes only because the DSCSA exempts transactions related to the distribution of product samples by a manufacturer or licensed wholesale distributor in accordance with section 503(d) of the FD&C Act (21 U.S.C. 353(d)).

estimates for manufacturers and repackagers because FDA establishment and drug product listing database indicates that many companies perform activities of both manufacturers and repackagers. While the DSCSA specifically defines dispensers, for estimation purposes, FDA is using estimates for pharmacies in general terms and based on those that must comply with the new requirements under section 582(d) of the FD&C Act. FDA estimates that approximately 50 percent of the notifications will be made by manufacturers and repackagers (2,500), 45 percent by wholesaler distributors (2,250), and 5 percent by pharmacies (250).

FDA estimates that the number of annual notifications will vary from 0-2 for manufacturers/repackagers, as well as from pharmacies, with the vast majority of companies making no notifications. While FDA establishment and drug product listing database currently contains registrations for approximately 6,500 manufacturers and repackagers, we estimate that approximately 2,500 manufacturers/repackagers will notify FDA of illegitimate product an average of one time per year. While FDA estimates approximately 69,000 pharmacy sites in the United States, based on data from the National Association of Chain Drug Stores, the National Community Pharmacists Association, and the American Hospital Association, we estimate that approximately 250 pharmacies will notify FDA of illegitimate product an average of one time per year.<sup>3</sup> Because approximately 30 wholesale distributors are responsible for over 90 percent of drug distributions, based on sales,<sup>4</sup> and because FDA is estimating that over 2,200 small wholesale distributors might be responsible for the remaining 10 percent of drug sales, we

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<sup>3</sup> The estimate of the number of pharmacies in the United States is based on combining estimates of: (a) 41,000 chain pharmacies provided in a National Association of Chain Drug Stores statement for the Senate Budget Committee Conferees (October 29, 2013); (b) 23,000 independent pharmacies represented by the National Community Pharmacist Association (NCPA) according to NCPA's 2014 media kit; and (c) 5,000 U.S. community hospitals in the United States, based on 2012 American Hospital Association Annual Survey and the assumption that each hospital has at least one pharmacy.

<sup>4</sup> The estimate of the number of wholesale drug distributors is based on the Healthcare Distribution Management Association number of members and estimation of the percentage of all prescription drugs sold in the United States by these entities provided in Congressional testimony before the U.S. House of Representatives, Committee on Energy and Commerce (April 25, 2013).

estimate that each distributor will make about an average of 1 notification per year to account for the estimated 2,250 notifications FDA will receive regarding illegitimate product.

FDA intends to make available Form FDA 3911 on its Web page for notifying FDA. Each notification should include information about the person or entity initiating the notification, the product determined to be illegitimate, and a description of the circumstances surrounding the event that prompted the notification. FDA estimates that each notification will take about 1 hour. The estimated total annual burden hours for making notifications to FDA is approximately 5,000 hours annually (table 1).

## 2. Notifications to Trading Partners of an Illegitimate Product

Under section 582(b)(4)(B)(ii), (c)(4)(B)(ii), (d)(4)(B)(ii), and (e)(4)(B)(ii) of the FD&C Act, a trading partner who determines that a product in its possession is illegitimate must also notify all immediate trading partners that the trading partner has reason to believe may have received such illegitimate product of that determination not later than 24 hours after the determination is made. In addition, a manufacturer is required, under section 582(b)(4)(B)(ii)(II) of the FD&C Act, to notify all immediate trading partners that the manufacturer has reason to believe may possess a product manufactured by or purported to be manufactured by the manufacturer not later than 24 hours after the manufacturer has determined or been notified by FDA or a trading partner that the product has a high risk of illegitimacy.

Because the extent of distribution of any illegitimate product is likely to vary from one situation to another, FDA is using estimates that assume wide distribution of each illegitimate product. FDA estimates that for each notification made by a manufacturer or repackager to FDA, approximately 30 trading partners (based on the number of distributors) will also be notified. This results in approximately 75,000 notifications annually to trading partners of

manufacturers/repackagers. This estimate includes the notifications by manufacturers and repackagers who have determined that illegitimate product is in their possession or control, as well as notifications by manufacturers that have determined that a product poses a high risk of illegitimacy.

FDA estimates that a large wholesale distributor might have up to 4,500 trading partners, but a small wholesale distributor might have 200 trading partners, for an average of approximately 2,350. A wholesale distributor would notify 2,350 trading partners for each of the 2,250 illegitimate products identified, resulting in approximately 5,287,500 notifications annually to wholesale distributors' trading partners.

FDA estimates that a pharmacy purchases prescription drugs from an average of two wholesale distributors. Therefore, a pharmacy would notify 2 trading partners for each of the 250 illegitimate products identified, resulting in approximately 500 notifications annually to pharmacy trading partners.

Manufacturers/repackagers, wholesale distributors, and pharmacies might notify their trading partners using existing systems and processes used for similar types of communications, which might include, but is not limited to, posting of notifications on a company Web site, sending an email, or mailing or faxing a letter or notification. The information contained in the notification to the immediate trading partner should be the same as or based on the notification that was already submitted to FDA. FDA estimates that for all trading partners, each notification of immediate trading partners will take approximately 0.2 hours. The estimated total burden hours of making notifications to trading partners is approximately 1,072,600 hours annually (table 2).

### 3. Consultation with FDA and Termination of Notification

Section 582(b)(4)(B)(iv), (c)(4)(B)(iv), (d)(4)(B)(iv), and (e)(4)(B)(iv) of the FD&C Act require that a trading partner, who determines in consultation with FDA that a notification made under section 582(b)(4)(B)(ii), (c)(4)(B)(ii), (d)(4)(B)(ii), or (e)(4)(B)(ii) is no longer necessary, must terminate the notification. The draft guidance sets forth the process by which trading partners must consult with FDA to terminate notifications that are no longer necessary.

FDA is making available to trading partners Form FDA 3911 on its Web page to request a termination of notification. Each request for termination of notification must include information about the person or entity initiating the request for termination, the illegitimate product or product with a high risk of illegitimacy, the notification that was issued, and an explanation about what actions have taken place or what information has become available that make the notification no longer necessary. The request for a termination will be viewed as the request for consultation with FDA. FDA estimates that the same amount of time will be required to provide the information necessary to request termination as is required to make the notification. The time required to investigate and resolve an illegitimate product notification will vary, but FDA assumes that each notification will eventually be terminated at some point. FDA assumes that the number of requests for termination of a notification per year will be the same as the original number of notifications for a given year. The estimated total burden hours of making requests for termination of notifications to FDA is approximately 5,000 hours annually (table 3).

### 4. Notifications to Trading Partners that a Notification Has Been Terminated

Section 582(b)(4)(B)(iv), (c)(4)(B)(iv), (d)(4)(B)(iv), and (e)(4)(B)(iv) of the FD&C Act require that a trading partner who, in consultation with FDA, terminates a notification made

under section 582(b)(4)(B)(ii), (c)(4)(B)(ii), (d)(4)(B)(ii), or (e)(4)(B)(ii) must also promptly notify immediate trading partners that the notification has been terminated.

FDA estimates that the burden for notifying trading partners of an illegitimate product and the number of trading partners notified will be the same as the estimates for notification of termination. The estimated total burden hours of notifying trading partners that the notification is terminated is approximately 1,072,600 hours annually (table 4).

Description of Respondents: Respondents are drug manufacturers, repackagers, wholesale distributors, and dispensers and might include small businesses in these categories.

Table 1.--Estimated Annual Reporting Burden<sup>1</sup>

Notifications to FDA	No. of Respondents	No of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Manufacturers and Repackagers	2,500	1	2,500	1 hour	2,500
Wholesale Distributors	2,250	1	2,250	1 hour	2,250
Dispensers	250	1	250	1 hour	250
Total					5,000

<sup>1</sup> There are no capital costs or operating and maintenance costs associated with this collection of information.

Table 2.--Estimated Annual Reporting Burden<sup>1</sup>

Consultation With FDA and Termination of Notification	No. of Respondents	No of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Manufacturers and Repackagers	2,500	1	2,500	1 hour	2,500
Wholesale Distributors	2,250	1	2,250	1 hour	2,250
Dispensers	250	1	250	1 hour	250
Total					5,000

<sup>1</sup> There are no capital costs or operating and maintenance costs associated with this collection of information.

Table 3.--Estimated Annual Third-Party Disclosure Burden<sup>1</sup>

Notifications to Trading Partners of an Illegitimate Product	No. of Respondents	No. of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours
Manufacturers and Repackagers	2,500	30	75,000	.20 (12 minutes)	15,000
Wholesale Distributors	2,250	2,350	5,287,500	.20 (12 minutes)	1,057,500
Dispensers	250	2	500	.20 (12 minutes)	100
Total					1,072,600

<sup>1</sup>There are no capital costs or operating and maintenance costs associated with this collection of information.

Table 4.--Estimated Annual Third-Party Disclosure Burden<sup>1</sup>

Notifications to Trading Partners of Termination	No. of Respondents	No. of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours
Manufacturers and Repackagers	2,500	30	75,000	.20 (12 minutes)	15,000
Wholesale Distributors	2,250	2,350	5,287,500	.20 (12 minutes)	1,057,500
Dispensers	250	2	500	.20 (12 minutes)	100
Total					1,072,600

<sup>1</sup>There are no capital costs or operating and maintenance costs associated with this collection of information.

## 5. Capital Costs

There are no capital costs associated with this collection of information. For notifications to FDA, manufacturers, repackagers, wholesale distributors, and dispensers will be accessing and using a system controlled by FDA. For notifications of immediate trading partners, manufacturers, repackagers, wholesale distributors, and dispensers will be using current mechanisms, which might include, but are not limited to, posting of notifications on a company Web site, sending an email, or mailing or faxing a letter or notification.

## III. Comments

Interested persons may submit either electronic comments regarding this document to <http://www.regulations.gov> or written comments to the Division of Dockets Management (see ADDRESSES). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at <http://www.regulations.gov>.

## IV. Electronic Access

Persons with access to the Internet may obtain the document at <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>,

<http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>, or <http://www.regulations.gov>.

Dated: June 4, 2014.

Leslie Kux,

Assistant Commissioner for Policy.

4160-01-P

[FR Doc. 2014-13544 Filed 06/10/2014 at 8:45 am; Publication Date: 06/11/2014]