Verification Systems Under the Drug Supply Chain Security Act for Certain Prescription Drugs

Guidance for Industry

DRAFT GUIDANCE

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For questions regarding this draft document, contact the Center for Drug Evaluation and Research (CDER) Office of Compliance at 301-796-3130 or drugtrackandtrace@fda.hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Office of Regulatory Affairs (ORA)

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Procedural

Revision 1

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Guidance for Industry

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Verification Systems Under the Drug Supply Chain Security Act for Certain Prescription Drugs
Guidance for Industry[1]

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION

Section 582 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 360eee-1), as added by the Drug Supply Chain Security Act (DSCSA) (Title II of Public Law 113-54), established requirements to facilitate the tracing and verification[2] of certain prescription drug products through the U.S. pharmaceutical distribution supply chain.

The contents of this document do not have the force and effect of law and are not meant to bind the public in any way, unless specifically incorporated into a contract. This document is intended only to provide clarity to the public regarding existing requirements under the law. FDA guidance documents, including this guidance, should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

Certain trading partners[3] (manufacturers, wholesale distributors, dispensers, and repackagers) are required to have verification systems in place to comply with the requirements under section 582(b)(4), (c)(4), (d)(4), and (e)(4) of the FD&C Act. For the purposes of this guidance, FDA

[1] This guidance has been prepared by the Office of Compliance in the Center for Drug Evaluation and Research in cooperation with the Center for Biologics Evaluation and Research and the Office of Regulatory Affairs at the Food and Drug Administration.

[2] *Verification* or *verify* is defined in section 581(28) of the FD&C Act (21 U.S.C. 360eee(28)):

> The term "verification" or "verify" means determining whether the product identifier affixed to, or imprinted upon, a package or homogeneous case corresponds to the standardized numerical identifier or lot number and expiration date assigned to the product by the manufacturer or the repackager, as applicable in accordance with section 582.

[3] *Trading partner* is defined in section 581(23) of the FD&C Act. Although third-party logistics providers (3PLs) are also considered trading partners under section 581(23)(B), the verification provisions of section 582(b) through (e) do not impose direct requirements on 3PLs. However, 3PLs must have a valid license under State law or section 584(a)(1), in accordance with section 582(a)(7), and must comply with the licensure reporting requirements under section 584(b).

interprets a *system* to mean a coordinated body of processes and procedures that forms an organizational scheme.

Verification system requirements include the quarantine and investigation of suspect products and quarantine and disposition[4] of illegitimate products.[5] In addition, verification system requirements include notification to FDA and certain immediate trading partners of illegitimate product (section 582(b)(4)(B)(ii), (c)(4)(B)(ii), (d)(4)(B)(ii), and (e)(4)(B)(ii) of the FD&C Act). If a suspect product is determined after investigation not to be an illegitimate product, a trading partner is required to notify FDA that the product has been cleared, if applicable, and the product may then be further distributed (section 582(b)(4)(A)(ii), (c)(4)(A)(ii), (d)(4)(A)(iii), and (e)(4)(A)(ii) of the FD&C Act). Trading partners must keep records of the investigation of a suspect product for not less than 6 years after the conclusion of the investigation (section 582(b)(4)(A)(iii), (c)(4)(A)(iii), (d)(4)(A)(iv), and (e)(4)(A)(iii) of the FD&C Act). Records of the disposition of an illegitimate product must also be kept by a trading partner for not less than 6 years after the conclusion of the disposition (section 582(b)(4)(B)(v), (c)(4)(B)(v), (d)(4)(B)(v), and (e)(4)(B)(v) of the FD&C Act).

Section 582(b)(4)(C) and (e)(4)(C) of the FD&C Act also requires manufacturers and repackagers to respond to requests for verification from other trading partners, and section 582(b)(4)(E), (c)(4)(D), and (e)(4)(E) of the FD&C Act requires manufacturers, wholesale distributors, and repackagers to verify certain information before further distribution of the returned product.[6]

FDA is issuing this guidance to describe FDA's interpretation of the requirements of section 582 of the FD&C Act regarding verification systems. This guidance provides recommendations for a robust verification system for the determination, quarantine, and investigation of suspect products, as well as the quarantine, notification, and disposition of illegitimate products. The guidance also addresses the manner in which FDA recommends that trading partners submit cleared product notifications. Finally, this guidance addresses the statutory requirements for verification, including verification of saleable returns, at the package level for product identifiers on packages and homogenous cases intended to be introduced in a transaction into commerce.

This guidance revises the draft guidance for industry *Verification Systems Under the Drug Supply Chain Security Act for Certain Prescription Drugs*, issued in October 2018, including to address comments received from stakeholders. This revised draft guidance:

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[4] *Disposition* is defined in section 581(4) of the FD&C Act:

> The term "disposition," with respect to a product within the possession or control of an entity, means the removal of such product from the pharmaceutical distribution supply chain, which may include disposal or return of the product for disposal or other appropriate handling and other actions, such as retaining a sample of the product for further additional physical examination or laboratory analysis of the product by a manufacturer or regulatory or law enforcement agency.

[5] *Suspect product* is defined in section 581(21) and *illegitimate product* is defined in section 581(8) of the FD&C Act.

[6] These requirements will be phased in over a period of years as outlined in section 582(b)(4)(C) and (E), (c)(4)(D), and (e)(4)(C) and (E) of the FD&C Act.

- Provides FDA's interpretation of what *possession or control* means as used throughout the DSCSA

- Explains that we use the term verification in referring to both the broad set of requirements set forth in paragraphs (b)(4), (c)(4), (d)(4), and (e)(4) of section 582 of the FD&C Act in addition to using the term with the meaning defined in section 581(28) of the FD&C Act, where appropriate to the context

- Recognizes that, in cases where the DSCSA directs trading partners to coordinate with one another during investigations and dispositions of products, certain types of trading partners are typically better suited to handle specific aspects of those statutory requirements

- Clarifies that FDA will make requests for verification if a trading partner is in possession or control of a product that the Agency has determined to be a suspect product

- Clarifies FDA's understanding of what *electronic quarantine* means and when it is an appropriate method of quarantining suspect and illegitimate product.

- Clarifies when samples of illegitimate product should be retained

- Clarifies FDA's expectations for manufacturers and repackagers related to the requirements for responding to requests for verification from authorized trading partners

- Clarifies what information should be communicated among trading partners when determining whether a suspect product is illegitimate

- Informs trading partners of the information that should be included when responding to requests for verification from FDA and other trading partners (where applicable), and verifying saleable returned product

II. BACKGROUND

A. DSCSA Verification Requirements

On November 27, 2013, the DSCSA was signed into law. Section 202 of the DSCSA added section 582 to the FD&C Act, which set forth verification requirements that took effect on January 1, 2015, for manufacturers, wholesale distributors, dispensers, and repackagers of prescription drug products covered by the DSCSA.

Under section 582(b)(4), (c)(4), (d)(4), and (e)(4) of the FD&C Act, trading partners must have systems in place:

- To identify and determine whether a product is a suspect product.

- To quarantine and investigate a product that has been determined to be a suspect product and to coordinate with trading partners, as applicable, in making the determination as to whether that product is illegitimate.

- To clear a product for distribution, as appropriate, if, after investigation, it is determined that the suspect product is not an illegitimate product. The trading partner is required to notify FDA of cleared products, if applicable.

- For products determined to be illegitimate, to complete the following:

  - Further quarantine the illegitimate product.

  - Disposition of the illegitimate product within the trading partner's possession or control.

  - Take reasonable and appropriate steps to assist another trading partner to disposition the illegitimate product.

  - Retain a sample of the illegitimate product if asked to do so by the manufacturer, FDA, or other Federal or State official. These should be retained in an amount sufficient for further physical examination and laboratory analysis by the manufacturer and/or FDA or other appropriate Federal or State official.

  - Provide notification of the illegitimate product to FDA and other trading partners, and upon making a determination, in consultation with FDA, that a notification is no longer necessary, terminate that notification. In addition, a manufacturer must have a system in place for notifying its immediate trading partners and FDA of a product that has a high risk of illegitimacy, as required under section 582(b)(4)(B)(ii)(II) of the FD&C Act.

- That include procedures for taking appropriate action when the trading partner has received an illegitimate product notification or a manufacturer's notification of a high risk of illegitimacy.

- To create and maintain records related to suspect product investigations and the disposition of illegitimate products for a minimum of 6 years as required by section 582 of the FD&C Act.

In addition, manufacturers, wholesale distributors, and repackagers have additional requirements outlined in section 582(b)(4)(C) and (E), (c)(4)(D), and (e)(4)(C) and (E) of the FD&C Act:

- Manufacturers must have systems in place that will allow them to respond to requests from trading partners to confirm that a particular product identifier, including the standardized numerical identifier (SNI), on the product that is the subject of the request corresponds to the product identifier that was affixed to or imprinted upon that product by the manufacturer of that product.

- Repackagers must have systems in place that will allow them to respond to requests from trading partners to confirm that a particular product identifier, including the SNI, on the product that is the subject of the request corresponds to the product identifier that was affixed to or imprinted upon that product by the repackager of that product.

- Manufacturers, wholesale distributors, and repackagers must have systems in place that will allow them, upon receipt of a saleable returned product, to verify the product identifier, including the SNI, for each sealed homogenous case or package before further distribution of such product.

With this guidance, FDA is highlighting that paragraphs (b)(4), (c)(4), (d)(4), and (e)(4) of section 582 of the FD&C Act—which describe the required systems for various trading partners—use the heading *verification*. Certain requirements in these paragraphs meet the definition of *verification* under section 581(28), which is defined to mean the determination of whether the product identifier affixed to or imprinted upon a package or homogenous case corresponds to the SNI or lot number and expiration date assigned to the product by the manufacturer or repackager.[7] However, the paragraphs impose several requirements that fall outside the section 581(28) definition of *verification*. For example, subparagraphs (b)(4)(A)(i)(I), (c)(4)(A)(i)(I), (d)(4)(A)(i)(I), and (e)(4)(A)(i)(I) of section 582 of the FD&C Act require that trading partners quarantine product that has been determined to be suspect. Consistent with this, we use the term *verification* in referring to the broad set of requirements set forth in paragraphs (b)(4), (c)(4), (d)(4), and (e)(4) of section 582 of the FD&C Act in addition to using the term with the meaning defined in section 581(28) of the FD&C Act, where appropriate to the context. In general, the focus of this guidance is on the former (i.e., the broad set of requirements).

B. Scope of This Guidance

This guidance applies to the verification systems that manufacturers, wholesale distributors, dispensers, and repackagers must have in place, as described in section 582(b)(4), (c)(4), (d)(4), and (e)(4) of the FD&C Act.

This guidance is intended to provide assistance to industry in understanding the verification system requirements under section 582 of the FD&C Act and to provide guidance on what should be included in these systems. This guidance serves to inform trading partners of the information that should be reviewed and communicated with other trading partners when

[7] Section 582(b)(4)(A)(i)(II), (C), and (E); (c)(4)(A)(i)(II) and (D); (d)(4)(A)(ii); and (e)(4)(A)(i)(II), (C), and (E) of the FD&C Act obligates trading partners to verify products at the package level, including the SNI.

verifying whether a suspect product is illegitimate. This guidance also serves to inform trading partners of the information that should be included in responding to requests for verification from FDA and other trading partners, where applicable, and in verifying saleable returned product. This guidance does not address all of the provisions in section 582 of the FD&C Act related to verification. For example, the Agency previously issued a guidance on the identification of suspect products and notification of illegitimate products that includes processes by which notifications to FDA and other trading partners of illegitimate product are made, as well as the termination of those notifications, as described in section 582(h)(2)(A)(iii) of the FD&C Act.[8]

When designing and implementing the verification systems required under the DSCSA, trading partners are cautioned that although section 582 of the FD&C Act may not require that a product be withheld or removed from the U.S. pharmaceutical distribution supply chain because it does not fit within the definition of *suspect product* or *illegitimate product*, trading partners have other obligations under the FD&C Act and the Public Health Service Act regarding the introduction of products into interstate commerce. Violation of those requirements may result in enforcement actions, regardless of a trading partner's compliance with section 582 of the FD&C Act. For example, an adulterated product may not be a suspect product because it is not within the definition in section 581(21) of the FD&C Act, but it is a prohibited act to introduce or deliver for introduction into interstate commerce an adulterated drug under section 301(a) of the FD&C Act (21 U.S.C 331(a)).

III. VERIFICATION SYSTEMS UNDER SECTION 582 OF THE FD&C ACT

Section 582 of the FD&C Act requires manufacturers, wholesale distributors, dispensers, and repackagers to have "systems in place to enable [them] to comply" with certain verification requirements relating to the identification and handling of suspect and illegitimate products. Specific requirements include the quarantine and investigation of a product determined to be a suspect product and the quarantine, disposition, and notification of a product determined to be an illegitimate product.[9]

To satisfy the requirements under section 582(b)(4), (c)(4), (d)(4), and (e)(4) of the FD&C Act, these verification systems may be based on existing standard operating procedures (SOPs) or processes, new SOPs or processes, or a combination of both. These systems may include the use of a secure electronic database, as provided under section 582(b)(4)(D), (c)(4)(C), (d)(4)(C), and (e)(4)(D) of the FD&C Act.

A. Systems To Determine That a Product Is Suspect

[8] FDA guidance for industry *Drug Supply Chain Security Act Implementation: Identification of Suspect Product and Notification* (June 2021) (hereafter referred to as the Suspect Product and Notification Guidance).

[9] See section 582(b)(4)(A) and (B), (c)(4)(A) and (B), (d)(4)(A) and (B), and (e)(4)(A) and (B) of the FD&C Act.

Trading partners must have systems in place to determine whether a product is a suspect product.[10] These systems should ensure that, when appropriate, a trading partner makes a consistent, effective, and timely determination that a product is suspect. The determination that a product is suspect triggers obligations to quarantine and investigate the suspect product under sections 582(b)(4)(A)(i), (c)(4)(A)(i), (d)(4)(A)(i), and (e)(4)(A)(i) of the FD&C Act. In order to help ensure patient safety, it is essential that this system be well-designed to detect and assess suspect product. Trading partners should focus on drugs that potentially fall into one of the categories of drugs listed in the definition of suspect product in section 581(21) of the FD&C Act: product that may be counterfeit, diverted, stolen, intentionally adulterated, the subject of a fraudulent transaction, or unfit for distribution. In the draft guidance for industry *Definitions of Suspect Product and Illegitimate Product for Verification Obligations Under the Drug Supply Chain Security Act* (June 2021), FDA clarified its interpretation of the following terms listed in the definition of suspect product in section 581(21) of the FD&C Act: counterfeit, fraudulent transaction, unfit for distribution, stolen and diverted.[11]

In particular, trading partners should consider the risk of such product entering the U.S. pharmaceutical distribution supply chain and the scenarios that could significantly increase such risk. The Suspect Product and Notification Guidance provides recommendations on how trading partners can identify a suspect product and determine whether the product is a suspect product as soon as practicable. The list of scenarios and recommendations in that guidance are not all-inclusive, and trading partners should always exercise due diligence to ensure that a suspect product is identified.

FDA may make a request for verification to a trading partner when FDA has determined that the trading partner has a suspect product within its possession or control.[12] For purposes of determining compliance with the DSCSA's verification requirements, FDA interprets the phrase *possession or control* to include physical custody of the product, or ownership of the product. Upon receipt of a request for verification from FDA, trading partners must proceed as directed by section 582(b)(4)(A)(i), (c)(4)(A)(i), (d)(4)(A)(i), and (e)(4)(A)(i) of the FD&C Act (see section III.B below). Notifications to FDA of product determined *not* to be illegitimate product are discussed in section III.C below, and notifications to FDA of product determined to be illegitimate are discussed in section III.E below.

B. System for Suspect Product Quarantine and Investigation

Upon determining that a product is suspect, or upon receiving a request for verification from FDA (following a determination by the Agency that a product within the possession or control of the trading partner is a suspect product), a trading partner is required to quarantine the product, and to conduct an investigation in coordination with other trading partners, as applicable, to

[10] See section 582(b)(4), (c)(4), (d)(4), and (e)(4) of the FD&C Act.

[11] When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[12] See section 582(b)(4)(A)(i), (c)(4)(A)(i), (d)(4)(A)(i), and (e)(4)(A)(i) of the FD&C Act.

determine whether it is an illegitimate product.[13] Trading partners must have systems in place to enable such quarantines and investigations of suspect product.[14]

1. Quarantine

Quarantine of a suspect product may be accomplished using physical separation and/or other procedures.[15] FDA interprets "other procedures" to include electronic means when a trading partner lacks physical possession of the product. FDA encourages trading partners to use both physical and electronic quarantine when possible to ensure accurate record keeping. FDA understands *quarantine by electronic means* (or *electronic quarantine*) to be an electronic system or process that designates specific products as being quarantined to prevent the sale and further distribution of the product. For example, if a trading partner places a product in quarantine using electronic means, the trading partner's system should designate the product as quarantined so that information retrieved from the system about that product would indicate that the product is currently quarantined and should not be sold or further distributed.

The system for quarantine should be robust enough to ensure that the suspect product is not inadvertently distributed. The authority to terminate a quarantine of suspect product and to release the product for further distribution should be assigned to an appropriate person(s) in the trading partner's organization. For example, a member of the Quality Control Unit for a manufacturer or repackager, a facility manager or responsible person identified by a wholesale distributor, or a pharmacist-in-charge for a dispenser may be an appropriate person to exercise such authority.

2. Components of a Robust Investigation

Trading partners are required to promptly conduct an investigation, in coordination with other trading partners, as applicable, into whether a suspect product is an illegitimate product.[16] Such investigations must include validation of any applicable transaction history and transaction information in the trading partner's possession.[17] In addition, such investigations should include:

- Active communication and coordination of the investigation with the manufacturer, repackager, and/or other trading partners, as appropriate, to ensure that the investigation is thorough and the conclusions are accurate.

[13] See section 582(b)(4), (c)(4), (d)(4), and (e)(4) of the FD&C Act.
[14] See section 582(b)(4)(A), (c)(4)(A), (d)(4)(A), and (e)(4)(A) of the FD&C Act.
[15] See section 581(15).
[16] See section 582(b)(4)(A)(i)(II), (c)(4)(A)(i)(II), (d)(4)(A)(i)(II), and (e)(4)(A)(i)(II) of the FD&C Act.
[17] See section 582(b)(4)(A)(i)(II), (c)(4)(A)(i)(II), (d)(4)(A)(ii)(III), and (e)(4)(A)(i)(II) of the FD&C Act.

- Use of appropriate laboratory standards, controls, and techniques in situations where laboratory testing of suspect product is necessary to determine whether the product is an illegitimate product.[18]

- An analysis by the trading partner of how the product came to be in its possession or control when the trading partner determines that a suspect product is an illegitimate product, and of how to help prevent a similar situation in the future.

As noted above, all trading partners are required to conduct suspect product investigations in coordination with other trading partners, as appropriate. FDA therefore considers it appropriate for trading partners participating in a coordinated investigation with the product's manufacturer or repackager to rely on the results of the investigation conducted by that manufacturer or repackager. FDA expects manufacturers and repackagers to share the results of their investigations with their trading partners with whom they are conducting the investigation because doing so would be consistent with their obligation under section 582 of the FD&C Act to conduct investigations in coordination with their trading partners.[19]

In addition, investigations into whether a suspect product is an illegitimate product must include verifying the product at the package level.[20] The verification steps required under applicable provisions of the statute vary, depending on the trading partner making the verification.

For manufacturers, verification systems for suspect product must enable manufacturers to validate any applicable transaction history and transaction information in their possession.[21] FDA interprets this provision to include the requirement that the manufacturer confirm that the National Drug Code (NDC) and lot number reported in the manufacturer's internal records for the transaction information made at the time of the transaction corresponds to the information assigned to the suspect product.[22] The manufacturer must then verify that the NDC, serial number, lot number and expiration date of the product identifier imprinted upon or affixed to the package or homogenous case of the suspect product corresponds to the information originally assigned to the product by the manufacturer.[23, 24] Similarly, the suspect product verification

[18] FDA expects that the product's manufacturer will conduct most laboratory analyses carried out as part of a coordinated investigation.

[19] See section 582(b)(4)(A)(i)(II) and (e)(4)(A)(i)(II) of the FD&C Act.

[20] Section 582(b)(4)(A)(i)(II), (c)(4)(A)(i)(II), (d)(4)(A)(ii)(II), and (e)(4)(A)(i)(II) of the FD&C Act.

[21] See section 582(b)(4)(A)(i)(II) of the FD&C Act.

[22] See section 581(26) of the FD&C Act. The transaction information includes the NDC and lot number of a product. Under the 2023 enhanced drug distribution security system described in section 582(g) of the FD&C Act, the transaction information will then include the product identifier at the package level for each package included in the transaction (section 582(g)(1)(B)).

[23] See section 582(b)(4)(A)(i)(II) of the FD&C Act.

[24] Trading partners must *verify* suspect product (sections 582(b)(4)(A)(i)(II), (c)(4)(A)(i)(II), (d)(4)(A)(i)(II), and (e)(4)(A)(i)(II)). This includes determining whether the product identifier affixed to, or imprinted upon, the package or homogeneous case of product corresponds to the information assigned by the manufacturer or repackager. The product identifier includes the standardized numerical identifier (SNI), lot number and expiration date of the product. The SNI includes the products National Drug Code (NDC) and serial number. See sections 581(14), (20), and (28) of the FD&C Act for the definitions of *product identifier*, *standardized numerical identifier*, and *verify*.

systems of repackagers must enable repackagers to validate any applicable transaction history and transaction information in its possession.[25] FDA interprets this provision to include the requirement that the repackager confirm that the NDC and lot number reported in the repackager's internal records for the transaction information made at the time of the transaction corresponds to the information assigned to the suspect product. The repackager must then verify that the NDC, serial number, lot number and expiration date of the product identifier imprinted upon or affixed to the package or homogenous case of the suspect product corresponds to the information originally assigned to the product by the repackager.[26]

As of November 27, 2019, wholesale distributors, and, beginning on November 27, 2020, dispensers, must have systems in place to enable them to comply with a number of verification requirements for determining whether a suspect product is an illegitimate product.[27] A wholesale distributor must validate any applicable transaction history and transaction information in its possession.[28] FDA interprets this provision to include the requirement that the wholesale distributor confirm that the NDC and lot number in the wholesale distributor's internal records for the transaction information corresponds to the information assigned to the product that the wholesale distributor received from the manufacturer, repackager, or other wholesale distributor of such product. In addition, the wholesale distributor must also verify with the respective manufacturer or repackager that the NDC, serial number, lot number and expiration date of the product identifier imprinted upon or affixed to the package or homogenous case corresponds to the information assigned to the product by the respective manufacturer or repackager.[29]

Like the other trading partners, dispensers must validate any applicable transaction history and transaction information in its possession.[30] FDA interprets this provision to include the requirement that the dispenser confirm that the NDC and lot number in the dispenser's internal records for the transaction information corresponds to the information assigned to the product that the dispenser received from the manufacturer, repackager, or wholesale distributor of such product. Dispensers must also verify with the respective manufacturer or repackager that the NDC, serial number, lot number and expiration date of the product identifier imprinted upon or affixed to the package or homogeneous case corresponds with the product identifier assigned to

[25] See section 582(e)(4)(A)(i)(II) of the FD&C Act.

[26] Id.

[27] In October 2020, FDA published *Wholesale Distributor Verification Requirement for Saleable Returned Drug Product and Dispenser Verification Requirements When Investigating a Suspect or Illegitimate Product - Compliance Policies*. This guidance explains FDA's intent to extend the delay in enforcement of the DSCSA provisions requiring wholesale distributors to verify the product identifier prior to further distributing returned product beginning on November 27, 2019. (FDA's intent to delay enforcement of this provision was originally described in the guidance entitled *Wholesale Distributor Verification Requirement for Saleable Returned Drug Product - Compliance Policy* (September 2019).) In addition, this guidance announces FDA's intended enforcement policy with respect to the DSCSA provisions requiring dispensers to verify the product identifier for suspect or illegitimate product in the dispenser's possession or control beginning on November 27, 2020. For these wholesale distributor and dispenser provisions, FDA will delay enforcement until November 27, 2023.

[28] See section 582(c)(4)(A)(i)(II) of the FD&C Act.

[29] Id.

[30] See section 582(d)(4)(A)(ii)(III) of the FD&C Act.

the product by the respective manufacturer or repackager.[31] The product identifier must be verified for at least 3 packages or 10 percent of such suspect product, whichever is greater, or all packages if there are fewer than 3.[32] Therefore, the verification requirement for dispensers differs from that of other trading partners when there are more than three packages of suspect product. In addition, dispensers have the additional requirement to verify that the lot number corresponds with the lot number assigned to the product by the respective manufacturer or repackager.[33] To do this, a dispenser may consult the transaction information and transaction history to verify the product lot number and if neither contains the required information, contact the manufacturer or repackager of the product.

FDA encourages trading partners to periodically evaluate their systems for conducting investigations to identify opportunities for improvement and to ensure that the systems are compliant with the applicable verification requirements.

C. System for Cleared Product Notification Regarding Suspect Products

Trading partners must have systems in place to enable them to promptly notify FDA when suspect product is determined not to be illegitimate.[34] Under section 582 of the FD&C Act, trading partners must promptly notify FDA, if applicable, if they determine after investigation that a suspect product is not an illegitimate product and is therefore a cleared product.[35] This notification is considered a *cleared product notification*. FDA expects trading partners to inform the Agency about cleared product only if the suspect product is the subject of an FDA request for verification; where FDA has made no request for verification, a trading partner is not expected to submit a cleared product notification to the Agency. Cleared product notifications should be made before the product is further distributed or dispensed. Trading partners should be advised that once a product has been cleared, they must still ensure compliance with the other applicable provisions of the FD&C Act before the product may be further distributed.

1. Cleared Product Notifications To Be Submitted to FDA

If, after investigating a suspect product that is the subject of an FDA request for verification, a trading partner determines that the product is not an illegitimate product, the trading partner must promptly submit a cleared product notification to FDA documenting its determination.[36] Only the trading partner to whom FDA made its request for verification need submit a cleared product notification. The cleared product notification should be submitted to ***drugnotifications@fda.hhs.gov***.[37]

[31] See section 582(d)(4)(A)(ii)(II) of the FD&C Act.
[32] Id.
[33] See section 582(d)(4)(A)(ii)(I) of the FD&C Act.
[34] See section 582(b)(4), (c)(4), (d)(4), and (e)(4) of the FD&C Act.
[35] See section 582(b)(4)(A)(ii), (c)(4)(A)(ii), (d)(4)(A)(iii), and (e)(4)(A)(ii) of the FD&C Act.
[36] Id.
[37] Cleared product notifications should not be submitted using the FDA Form 3911 because it is for notifying FDA of illegitimate product and products with a high risk if illegitimacy.

2. Components of Cleared Product Notifications

Cleared product notifications should include:

- A subject line that states, "Cleared Product Notification."

- The identity of the product that was determined to be a suspect product but has now been determined, after investigation, not to be an illegitimate product. The product should be identified by the:

  - Proprietary or established name of the product[38]
  - Strength and dosage form of the product
  - NDC of the product[39]
  - Lot number
  - Expiration date
  - Serial number(s) of the product(s) (if available)[40]
  - Container size
  - Number of containers

- The date of the FDA request for verification to which the cleared product notification applies and the name of the FDA office and/or employee who made the request for verification.

- The reason why the product was determined to be suspect and a summary of the investigation that led to the trading partner's determination that the product was not an illegitimate product.

- The date the product was cleared.

- The name and official position of the employee or officer representing the trading partner who cleared the suspect product.

3. Recordkeeping of Suspect Product Investigations Resulting in Cleared Product

[38] The *proper name* should be used for biological products. See 21 CFR 600.3(k).

[39] If an alternatively formatted NDC is approved for use in accordance with 21 CFR 207.33(b)(4), the alternatively formatted NDC should be used to identify the product.

[40] When a product identifier must be affixed to or imprinted upon a product per section 582(b)(2) and (e)(2) of the FD&C Act, trading partners should include the serial number along with the NDC, lot number, and expiration date as the product identifier of the product package(s) or sealed homogenous case of product (see section 581(14) and (20) of the FD&C Act). Also, a product might not have a serial number if it was packaged or repackaged before November 27, 2018 (considered as "grandfathered"), or if it received a waiver, exception, or exemption from the product identifier requirement under section 582(a)(3) of the FD&C Act.

Records of suspect product investigations, including all cleared product notifications, must be maintained for a period of at least 6 years after the conclusion of the investigation.[41] This recordkeeping requirement also includes maintaining records about cleared product when no notification is made to FDA because the suspect product was not the subject of an FDA request for verification. The investigative record should also clearly explain how the trading partner reached the decision that a suspect product was not illegitimate.

D. System for Illegitimate Product Quarantine and Disposition

Trading partners must meet certain requirements for the quarantine and disposition of illegitimate product, including coordination with other trading partners, as applicable. [42] In making the determination that a product is illegitimate, trading partners are required to coordinate with the manufacturer.[43] In addition, FDA recognizes that a situation may arise where a trading partner is not able to physically quarantine, disposition, or collect a sample of illegitimate product that the trading partner owns because that product has been stolen and is no longer in the trading partner's physical custody.

1. Quarantine

Upon determining that a product in the possession or control of a manufacturer, repackager, or wholesale distributor is an illegitimate product, such trading partner must quarantine such product within its possession or control from product intended for distribution until such product is dispositioned.[44] Upon receipt of a notification from FDA or a trading partner that a determination has been made that a product is an illegitimate product, a manufacturer, repackager, wholesale distributor, or dispenser must identify all illegitimate product subject to such notification that is in its possession or control, including any illegitimate product that is subsequently received by that trading partner, and quarantine and investigate such product, pursuant to section 582(b)(4)(A), (c)(4)(A), (d)(4)(A), and (e)(4)(A) of the FD&C Act, respectively.[45] Quarantine of an illegitimate product may be accomplished using physical separation and/or other procedures.[46] As explained above in section III.B.I, "other procedures" may include electronic means, when a trading partner lacks physical possession of the product. FDA encourages trading partner to use both physical and electronic quarantine when possible to ensure accurate record keeping.

FDA also suggests that a system be able to alert the trading partner if it receives product that has the same product information (e.g., having the same transaction information or the same data elements in its product identifier, particularly the serial number) that the trading partner has

[41] Section 582(b)(4)(A)(iii), (c)(4)(A)(iii), (d)(4)(A)(iv), and (e)(4)(A)(iii) of the FD&C Act.
[42] Section 582(b)(4)(B), (c)(4)(B), (d)(4)(B), and (e)(4)(B) of the FD&C Act.
[43] Id.
[44] Section 582(b)(4)(B)(i)(I), (c)(4)(B)(i)(I), and (e)(4)(B)(i)(I) of the FD&C Act. Section 582(d)(4)(B)(iii) of the FD&C Act requires dispensers to quarantine product for which they receive a notice of illegitimacy. Dispensers should also quarantine product they determine to be illegitimate.
[45] Section 582(b)(4)(B)(iii), (c)(4)(B)(iii), (d)(4)(B)(iii), and (e)(4)(B)(iii) of the FD&C Act.
[46] See section 582(15) of the FD&C Act.

already identified as illegitimate in the system so the received product may be properly quarantined and dispositioned. The system for quarantine should be robust enough to ensure that an illegitimate product is not inadvertently distributed. Authority to release the illegitimate product from quarantine should only be exercised by appropriate people in the organization who are expressly authorized to terminate quarantine for the illegitimate product. For example, a member of the Quality Control Unit for a manufacturer or repackager, a facility manager or responsible person for a wholesale distributor, or a pharmacist-in-charge for a dispenser may be an appropriate person to exercise such authority.

2. Disposition

Disposition involves the removal of product from the pharmaceutical distribution supply chain.[47] The method of disposition of an illegitimate product should ensure that the public health hazards associated with that product are appropriately controlled. A trading partner should have SOPs detailing its systems and processes for the disposition of illegitimate product that is within its possession or control.[48] Each trading partner is also required to maintain systems to assist in the disposition of illegitimate product not in its own possession or control, but, instead, in the possession or control of one of its trading partners.[49]

3. Records

Records of the disposition of an illegitimate product must be maintained by trading partners for not less than 6 years after the conclusion of the disposition.[50] This should include records about contractors hired to disposition the illegitimate product and sample retention.

4. Retention of Samples

Trading partners must retain a sample of the illegitimate product for further physical examination or laboratory analysis by the manufacturer or FDA (or other appropriate Federal or State official) upon request by the manufacturer or FDA (or other appropriate Federal or State official).[51] Such samples are illegitimate product and should be appropriately quarantined. Consistent with the manufacturers' responsibility to assist trading partners in the disposition of illegitimate product,[52] FDA expects manufacturers to inform trading partners in a timely manner about whether a sample is needed for further physical examination or laboratory analysis before the investigation can be completed. FDA also intends to inform trading partners in a timely manner if the collection of samples is necessary for further physical examination or laboratory analysis by the Agency.

Samples should be:

[47] Section 581(4) of the FD&C Act.
[48] Section 582(b)(4)(B)(i)(II), (c)(4)(B)(i)(II), (d)(4)(B)(i)(I), and (e)(4)(B)(i)(II) of the FD&C Act.
[49] Section 582(b)(4)(B)(i)(III), (c)(4)(B)(i)(III), (d)(4)(B)(i)(II), and (e)(4)(B)(i)(III) of the FD&C Act.
[50] Section 582(b)(4)(B)(v), (c)(4)(B)(v), (d)(4)(B)(v), and (e)(4)(B)(v) of the FD&C Act.
[51] Section 582(b)(4)(B)(i)(IV), (c)(4)(B)(i)(IV), (d)(4)(B)(i)(III), and (e)(4)(B)(i)(IV) of the FD&C Act.
[52] Section 582(b)(4)(B)(i)(III).

- Representative of the illegitimate product.

- Of an amount/quantity sufficient for analysis if available, to permit proper laboratory examination by the entity or entities requesting that a sample be retained.

- Maintained and appropriately stored so that the condition of the product will be preserved until it is collected.

- Appropriately labeled and stored to preserve the identity of the sample. For example, a product should be identified and labeled as a retained sample of illegitimate product for a specific investigation, and a log identifying each person who handled the product, identifying the date they handled it and describing the manner in which they handled it, should be maintained, and should accompany the sample when it is submitted for testing.

E. System for Illegitimate/High Risk of Illegitimacy Product Notifications

Trading partners must have systems in place for notifying FDA and immediate trading partners of an illegitimate product and, for manufacturers, products with a high risk of illegitimacy.[53] In accordance with section 582(b)(4)(B)(ii)(II), *high risk* may 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 FDA in guidance.[54, 55] Upon receipt of an illegitimate product notification from a trading partner or a notification from FDA that a product has been determined to be an illegitimate product, a trading partner must identify all illegitimate products subject to such notification in its possession or control, including any product that is subsequently received, and conduct the activities required for suspect product, as applicable, described in section 582(b)(4)(A), (c)(4)(A), (d)(4)(A), and (e)(4)(A) of the FD&C Act.[56] Trading partners should follow these same procedures upon receipt of a notification from a manufacturer that a product has a high risk of illegitimacy. The Suspect Product and Notification Guidance referenced above sets forth in more detail the process by which trading partners should notify FDA of the illegitimate product or products with a high risk of illegitimacy and the process they must use to terminate notifications, in consultation with FDA.[57] Refer to that guidance for specific information related to these notifications.

F. System for Responding to Requests for Verification From Authorized Trading Partners

[53] Section 582(b)(4)(B)(ii)(I) and (II), (c)(4)(B)(ii), (d)(4)(B)(ii), and (e)(4)(B)(ii) of the FD&C Act.
[54] Section 582(b)(4)(B)(ii)(II) of the FD&C Act.
[55] See Suspect Product and Notification Guidance.
[56] Section 582(b)(4)(B)(iii), (c)(4)(B)(iii), (d)(4)(B)(iii), and (e)(4)(B)(iii) of the FD&C Act.
[57] For terminating notification requirements, see section 582(b)(4)(B)(iv), (c)(4)(B)(iv), (d)(4)(B)(iv), and (e)(4)(B)(iv) of the FD&C Act.

Manufacturers and repackagers must have systems in place to respond to requests for verification from an authorized trading partner[58] that is in possession or control of a product that they believe to be manufactured or repackaged by the respective manufacturer or repackager not later than 24 hours after receiving such request or in "other such reasonable time" as determined by FDA, based on the circumstances of the request.[59] The systems must allow the manufacturer or repackager to respond to the trading partner inquiring whether the product identifier, including the SNI, that is the subject of the request corresponds to the product identifier affixed or imprinted by that manufacturer or repackager.[60] FDA also suggests that systems for verification allow for the manufacturer or repackager to include other pertinent information, such as whether the product has been the subject of a recall or is known to be illegitimate.

To avoid a public health risk, if a trading partner does not receive a response from a manufacturer or repackager within 24 hours of making a request for verification, the product should be considered to be suspect product and should not be further distributed or dispensed. In addition, on a case-by-case basis, FDA may consider "other such reasonable time" for responding to requests for verification under limited circumstances, such as in the event of a large infrastructure failure because of a natural disaster. In those situations, the trading partner making the request for verification should also wait until the manufacturer or repackager is able to verify the product identifier before the product is further distributed or dispensed, if appropriate.

These systems should allow the manufacturer or repackager to respond to the request within the required timeframe with a clear statement as to whether the product identifier has been verified. In addition, these systems should be integrated with SOPs and business practices used to identify suspect product and illegitimate product. If the manufacturer or repackager has reason to believe that the product is illegitimate, it must indicate as much in its response to a request for verification from a trading partner and should inform the trading partner why it believes that the product is illegitimate.[61,62]

As discussed in section III.B.2 regarding suspect product investigations, when a manufacturer or repackager receives a verification request from an authorized trading partner, the manufacturer or repackager must verify that the product identifier, which includes the NDC and serial number, imprinted upon or affixed to the package or homogenous case corresponds to the information assigned to the product by that manufacturer or repackager.[63]

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[58] A manufacturer or repackager could confirm that an indirect trading partner is an authorized trading partner if the trading partner provides the transaction information and transaction history of the product, or explains how it obtained the product if not through a transaction, as defined by section 581(24) of the FD&C Act, as amended by DSCSA.

[59] See section 582(b)(4)(C) and (e)(4)(C) of the FD&C Act.

[60] Id.

[61] Id.

[62] In addition, section III.E above describes the recommendation for a system to notify FDA and all immediate trading partners when an illegitimate product is identified (and, for manufacturers, when products with a high risk of illegitimacy are identified).

[63] Section 582(b)(4)(C) and (e)(4)(C) of the FD&C Act.

G. System for Processing Saleable Returns

Manufacturers, wholesale distributors, and repackagers must have systems in place that will allow them to process saleable return products that they intend to further distribute.[64, 65, 66] These systems must allow the trading partners to verify the product identifier, including the SNI, on each sealed homogeneous case of saleable returned product or, if such product is not in a sealed homogeneous case, on each package of saleable returned product.[67] A saleable returned product may not be further distributed until the product identifier has been verified.[68] If the product identifier is not successfully verified, the product should be handled as a suspect product (i.e., it must be quarantined and investigated).[69] Because the systems and processes for verification of saleable returns are similar to those used for verifying suspect product at the package level as required by sections 582(b)(4)(A)(i)(II), (c)(4)(A)(i)(II), and (e)(4)(A)(i)(II), FDA anticipates that some trading partners may use the same system for both requirements.

When a manufacturer or repackager receives returned product that it intends to further distribute, before further distributing such product, the manufacturer or repackager must verify the product identifier for each sealed homogeneous case of such product or, if such product is not in a sealed homogeneous case, verify the product identifier on each package, as explained above in sections III.B.2 and III.F.[70] Before a wholesale distributor may further distribute returned product, it must first verify that the product identifier imprinted upon or affixed to the package or homogenous case corresponds to the information assigned to the product the wholesale distributor received from the manufacturer or repackager of such product, as explained above in section III.B.2.[71] Until November 27, 2023, a dispenser may return product to the trading partner it purchased the product from without providing the related transaction history, transaction information, and transaction statement.[72]

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[64] See section 582(b)(4)(E), (c)(4)(D), and (e)(4)(E) of the FD&C Act.

[65] Under the statute, these systems must be in place by November 27, 2017, for manufacturers; by November 27, 2018, for repackagers; and by November 27, 2019, for wholesale distributors. However, in *Wholesale Distributor Verification Requirement for Saleable Returned Drug Product and Dispenser Verification Requirements When Investigating a Suspect or Illegitimate Product - Compliance Policies* (October 2020), FDA explained that we do not intend to take action against wholesale distributors who do not, before November 27, 2023, verify a product identifier before further distribution of returned product, as required under section 582(c)(4)(D) of the FD&C Act.

[66] *Return* is defined in section 581(17) of the FD&C Act.

[67] Section 582(b)(4)(E), (c)(4)(D), and (e)(4)(E) of the FD&C Act.

[68] Id.

[69] For how these trading partners must handle suspect product, see section 582(b)(4)(A)(i), (c)(4)(A)(i), and (e)(4)(A)(i) of the FD&C Act.

[70] See section 582(b)(4)(E) and (e)(4)(E) of the FD&C Act.

[71] See section 582(c)(4)(D) of the FD&C Act. FDA does not intend to take action against wholesale distributors who do not, before November 27, 2023, verify a product identifier before further distribution of returned product, as required under section 582(c)(4)(D) of the FD&C Act. See FDA guidance for industry *Wholesale Distributor Verification Requirement for Saleable Returned Drug Product and Dispenser Verification Requirements When Investigating a Suspect or Illegitimate Product - Compliance Policies (October 2020)*.

[72] See section 582(d)(1)(C)(i) and (k)(2) of the FD&C Act.