Advances in Drug Supply Chain Security – Focus on Distribution

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REdI Annual Conference – June 2022

Learning Objectives

- Review advances in drug supply chain security, focusing on the distribution of drugs in the U.S. and requirements under the Drug Supply Chain Security Act (DSCSA)
- Describe efforts to better detect counterfeits and other illegitimate product, prevent these products from entering the supply chain, and respond to protect patients from receiving these products

Disclaimer

This presentation is intended only to provide a general overview. It is not intended to be comprehensive, nor does it constitute legal advice. Please refer to appropriate guidelines, regulations, or law for specific information.

Additional Resources

Updates and links to FDA documents or notices summarized in this presentation can be found on FDA's website.

CDER Office of Compliance

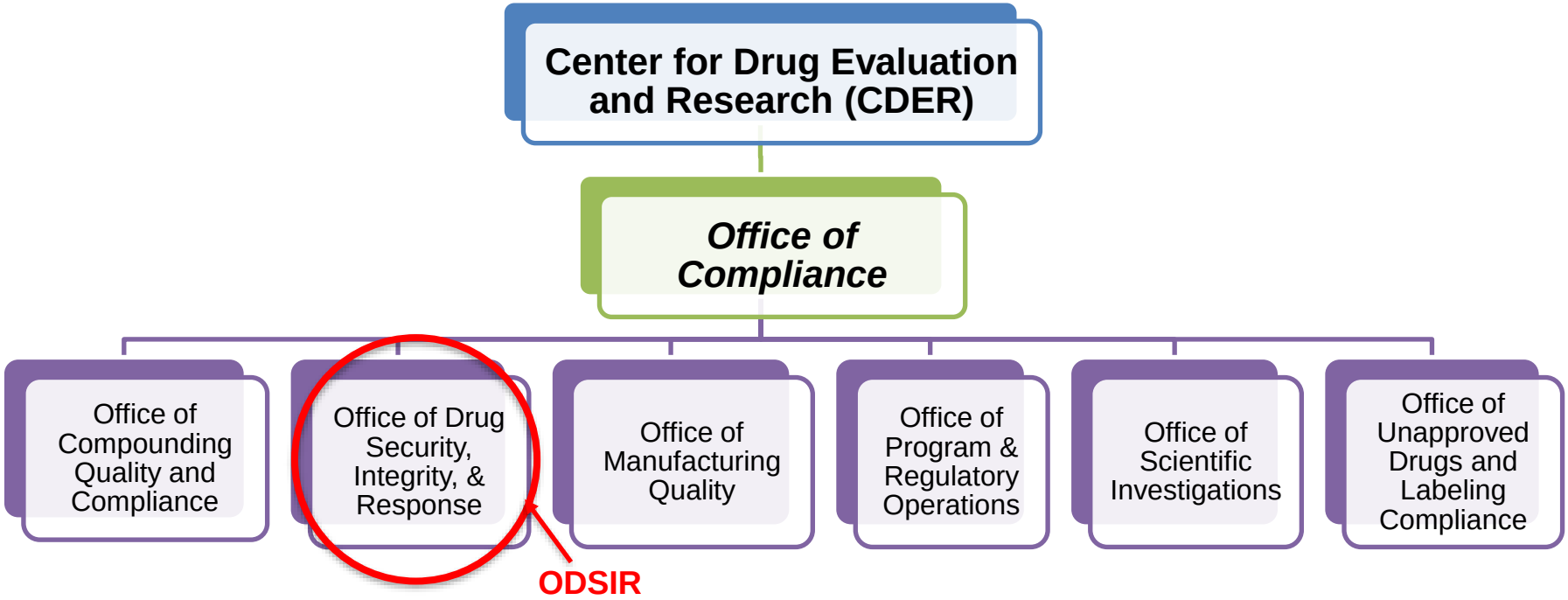
Mission

To shield patients from poor quality, unsafe and ineffective drugs through proactive compliance strategies and risk-based enforcement action.

Vision

To be a model of efficiency, innovation and operational excellence. Guided by law and science, we make strategic and risk-based decisions, communicate clearly to all stakeholders, foster global collaboration, promote voluntary compliance, and take decisive action.

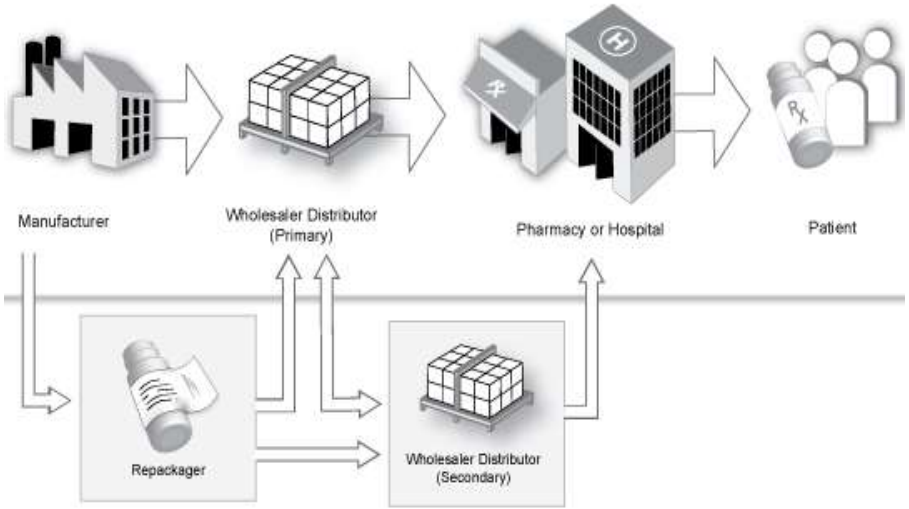
Who We Are


Center for Drug Evaluation and Research (CDER)
Office of Compliance
Office of Compounding Quality and Compliance
Office of Drug Security, Integrity, & Response
Office of Manufacturing Quality
Office of Program & Regulatory Operations
Office of Scientific Investigations
Office of Unapproved Drugs and Labeling Compliance
ODSIR

Supply Chain Challenges

- Recalls
- COVID-19 response
- Internet sellers of unapproved and misbranded drugs
- Counterfeits and other illegitimate products

Threats to the Pharmaceutical Supply Chain



Illegitimate product

Counterfeit, diverted, stolen, intentionally adulterated, subject to a fraudulent transaction, or otherwise unfit for distribution that would result in serious adverse health consequences or death to humans

Unscrupulous players

Distribute illegitimate product

Don't maintain quality of the product

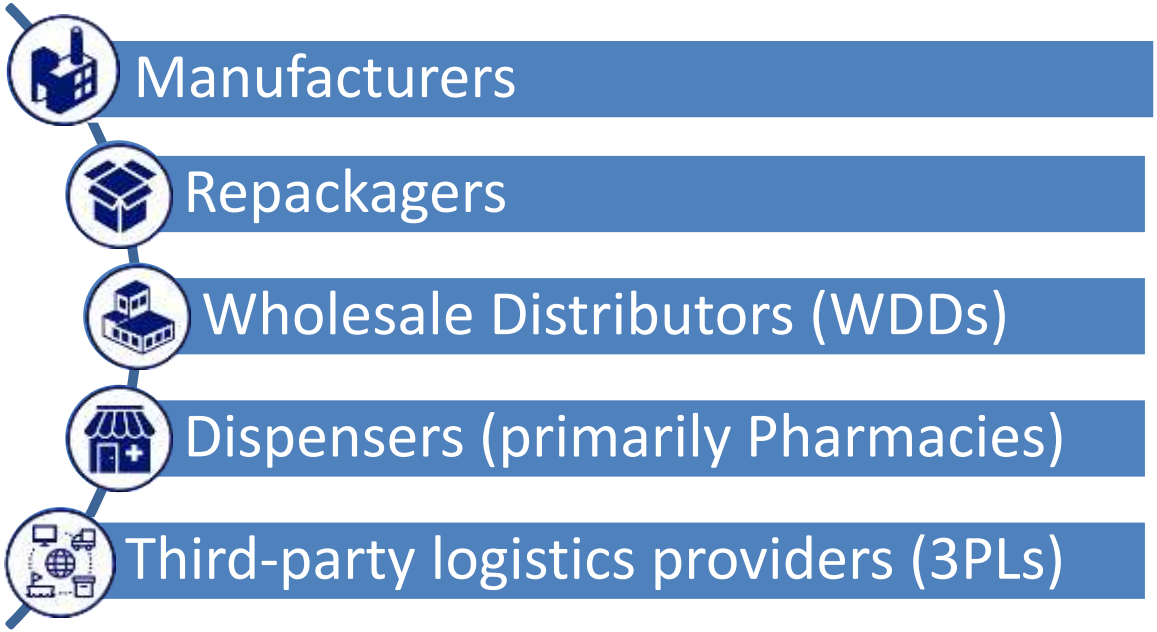
Don't maintain security or integrity of the supply chain (examples: are not authorized or do business with entities that are not authorized)

Weakness in the drug supply chain can be anywhere

The Drug Supply Chain Security Act DSCSA

- Enacted November 27, 2013
- Outlines steps to achieve interoperable, electronic tracing of product at the package level to identify and trace certain prescription drugs as they are distributed in the U.S.
- Enhances ability to help protect consumers from exposure to drugs that may be counterfeit, stolen, contaminated, or otherwise harmful
- Improves detection and removal of potentially dangerous drugs from the drug supply chain
- Establishes national licensure standards for wholesale drug distributors and third-party logistics providers (3PLs)

Trading partners need to comply with DSCSA



Products

- What's covered:
  - Prescription drug in finished dosage form for administration to a patient without further manufacturing (such as capsules, tablets, lyophilized products before reconstitution)
- What's not covered:
  - Blood or blood components intended for transfusion
  - Radioactive drugs or biologics
  - Imaging drugs
  - Certain IV products
  - Medical gas
  - Homeopathic drugs
  - Lawfully compounded drugs

Refer to the definition for "product" in section 581(13) of the FD&C Act for specific information regarding exceptions.

Transactions

- Involve transfers of product where a *change of ownership* occurs
- Excludes:
  - Intracompany distributions
  - Distribution among hospitals under common control
  - Public health emergencies
  - Dispensed pursuant to a prescription
  - Product sample distribution
  - Blood and blood components for transfusion
  - Minimal quantities by a licensed pharmacy to a licensed practitioner
  - Certain activities by charitable organizations
  - Distributions pursuant to a merger or sale
  - Certain combination products
  - Certain medical kits
  - Certain IV products
  - Medical gas distribution
  - Approved animal drugs

Refer to the definition for "transaction" in section 581(24) of the FD&C Act for specific information regarding exclusions.

DSCSA Implementation

2015
Authorized Trading Partners

- Manufacturers and Repackagers: valid registration with FDA
- WDDs & 3PLs: valid State or Federal license and compliance with reporting requirements
- Dispensers: valid State license

2015
Product Tracing

- Lot-level
- Provide and receive transaction documentation with each sale
- Respond to request for information
- Store records
- Paper and electronic formats

2015
Verification

- Quarantine and investigate suspect product
- Investigation illegitimate product
- Notify FDA and trading partners of illegitimate product
- Response to verification requests
- Store records

The requirements under section 582 of the FD&C Act apply to manufacturers, repackagers, wholesale distributors, and dispensers (pharmacies).

Product Tracing Information

Transaction Information (TI):

- Proprietary or established name or names of the product;
- Strength and dosage form of the product;
- National Drug Code number of the product;
- Container size;
- Number of containers;
- **Lot number of the product;**
- Date of the transaction;
- Date of the shipment, if more than 24 hours after the date of the transaction; and
- Business name and address of the person from whom and to whom ownership is being transferred.

Transaction History (TH): A statement in paper or electronic form, including the transaction information for each prior transaction going back to the manufacturer of the product

Transaction Statement (TS): A statement, in paper or electronic form, that the--

- Entity transferring ownership in a transaction is authorized as required under DSCSA;
- Received the product from a person that is authorized as required under DSCSA;
- Received transaction information and a transaction statement from the prior owner of the product, as required under the law;
- Did not knowingly ship a suspect or illegitimate product;
- Had systems and processes in place to comply with verification requirements under the law;
- Did not knowingly provide false transaction information; and
- Did not knowingly alter the transaction

Product Tracing Information

Transaction Information (TI):

- Proprietary or established name or names of the product;
- Strength and dosage form of the product;
- National Drug Code number of the product;
- Container size;
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- nowingly provide false transaction
  on; and
- owingly alter the transaction

November 27, 2023
TI changes
TH sunsets
Electronic

Investigate and properly handle suspect and illegitimate products

Suspect Product: ***reason to believe*** that product potentially is:

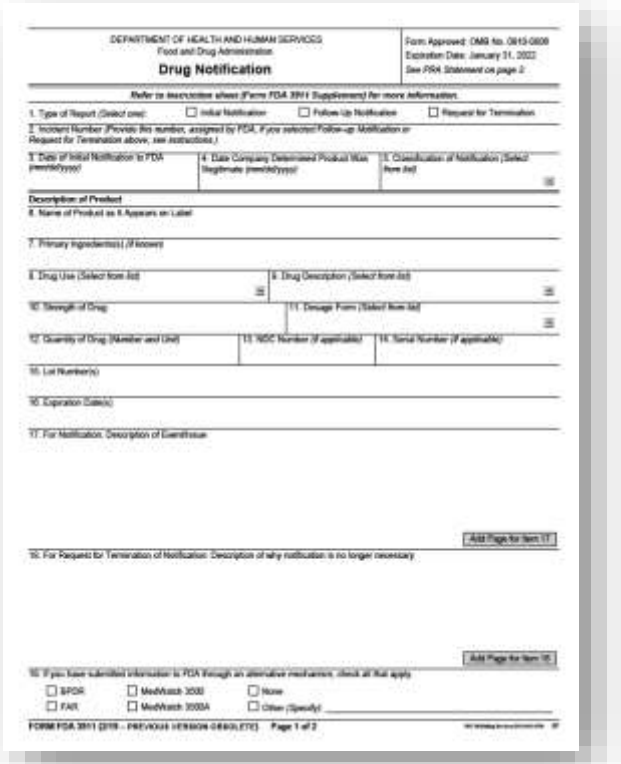
- counterfeit, diverted, stolen
- subject of fraudulent transaction
- intentionally adulterated or appears otherwise unfit for distribution such that the product would result in serious adverse health consequences or death to humans

Illegitimate Product: ***credible evidence*** shows that the product is:

- counterfeit, diverted, stolen
- subject of fraudulent transaction
- intentionally adulterated or appears otherwise unfit for distribution such that the product would result in serious adverse health consequences or death to humans

Notify FDA of Illegitimate Product within 24 hours (Form FDA 3911) and other trading partners within 24 hours

Drug Notifications to FDA – Illegitimate Product



DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Drug Notification

Form Approved: OMB No. 0910-0806
Expiration Date: January 31, 2022
See PRA Statement on page 2.

Refer to instruction sheet (Form FDA 3911 Supplement) for more information.

1. Type of Report (Select one): ☐ Initial Notification ☐ Follow-Up Notification ☐ Request for Termination

2. Incident Number (Provide this number, assigned by FDA, if you selected Follow-up Notification or Request for Termination above, see instructions.)

3. Date of Initial Notification to FDA (mm/dd/yyyy) | 4. Date Company Determined Product Was Illegitimate (mm/dd/yyyy) | 5. Classification of Notification (Select from list)

Description of Product

6. Name of Product as It Appears on Label

7. Primary Ingredient(s) (If known)

8. Drug Use (Select from list) | 9. Drug Description (Select from list)

10. Strength of Drug | 11. Dosage Form (Select from list)

12. Quantity of Drug (Number and Unit) | 13. NDC Number (If applicable) | 14. Serial Number (If applicable)

15. Lot Number(s)

16. Expiration Date(s)

17. For Notification, Description of Event/Issue

Add Page for Item 17

18. For Request for Termination of Notification: Description of why notification is no longer necessary

Add Page for Item 18

19. If you have submitted information to FDA through an alternative mechanism, check all that apply

☐ EPDR ☐ MedWatch 3500 ☐ None
☐ FAR ☐ MedWatch 3500A ☐ Other (Specify) _____

FORM FDA 3911 (2019) – PREVIOUS VERSION OBSOLETE) Page 1 of 2

Notify FDA within 24 hours using Form FDA 3911

Notify other trading partners within 24 hours

Request notification termination using Form FDA 3911

DSCSA Implementation

2018

Product Identification (Serialization)

Manufacturers & repackagers encode product identifiers on prescription drug packages on the smallest individual saleable unit

Product Identifier
National Drug Code (NDC), Serial Number, Lot, Expiration Date)

2018+

Verification

- Serialized product can be verified down to the package level using the product identifier
- Saleable returns
- Compliance policies issued that provide additional time

2023+

Enhanced Drug Distribution Security Requirements

- All electronic
- Enhanced product tracing at the package level (i.e., includes product identifier)
- Enhanced verification

The requirements under section 582 of the FD&C Act apply to manufacturers, repackagers, wholesale distributors, and dispensers (pharmacies).

Challenge Question #1

Which DSCSA requirements help to improve supply chain integrity?

A. Trading partners must be authorized (valid FDA registration or licensure, as applicable).

B. Product tracing information (transaction information, history, and statement) is exchanged with each transaction of product between trading partners.

C. Verification requirements, which include notifications of illegitimate product within 24 hours of determination, allow FDA and trading partners to better respond when illegitimate product is found in the supply chain.

D. Manufacturers and repackagers are required to encode product identifiers (national drug code (NDC), serial number, lot, expiration date) on prescription drug packages on the smallest individual saleable unit.

E. All of the above

2023 Enhanced Drug Distribution Security Effective 11/27/2023

Section 582(g) Enhanced Drug Distribution Security -

(1) In general.--On the date that is 10 years after the date of enactment of the Drug Supply Chain Security Act, the following interoperable, electronic tracing of product at the package level requirements shall go into effect:

(A) The transaction information and the transaction statements as required under this section shall be exchanged in a secure, interoperable, electronic manner in accordance with the standards established under the guidance issued pursuant to paragraphs (3) and (4) of subsection (h), including any revision of such guidance issued in accordance with paragraph (5) of such subsection.

(B) The transaction information required under this section shall include the product identifier at the package level for each package included in the transaction.

(C) Systems and processes for verification of product at the package level, including the standardized numerical identifier, shall be required in accordance with the standards established under the guidance issued pursuant to subsection (a)(2) and the guidances issued pursuant to paragraphs (2), (3), and (4) of subsection (h), including any revision of such guidances issued in accordance with paragraph (5) of such subsection, which may include the use of aggregation and inference as necessary.

(D) The systems and processes necessary to promptly respond with the transaction information and transaction statement for a product upon a request by the Secretary (or other appropriate Federal or State official) in the event of a recall or for the purposes of investigating a suspect product or an illegitimate product shall be required.

(E) The systems and processes necessary to promptly facilitate gathering the information necessary to produce the transaction information for each transaction going back to the manufacturer, as applicable, shall be required-

(i) in the event of a request by the Secretary (or other appropriate Federal or State official), on account of a recall or for the purposes of investigating a suspect product or an illegitimate product; or

(ii) in the event of a request by an authorized trading partner, in a secure manner that ensures the protection of confidential commercial information and trade secrets, for purposes of investigating a suspect product or assisting the Secretary (or other appropriate Federal or State official) with a request described in clause (i).

(F) Each person accepting a saleable return shall have systems and processes in place to allow acceptance of such product and may accept saleable returns only if such person can associate the saleable return product with the transaction information and transaction statement associated with that product.

2023 Enhanced Drug Distribution Security Effective 11/27/2023

2023+

Enhanced Drug Distribution Security Requirements

- All electronic
- Enhanced product tracing at the package level (i.e., includes product identifier)
- Enhanced verification

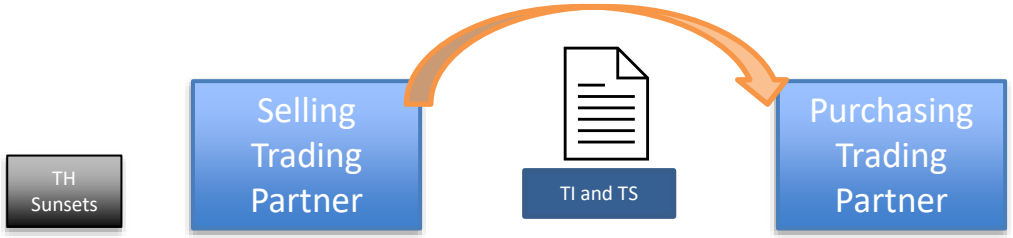
Enhanced Product Tracing

- Exchange of transaction information (TI) and transaction statement (TS)
- Serialized TI
- Gathering of relevant product tracing information in response to requests…

Enhanced Verification

- Package-level
- Saleable Returns

Enhanced Product Tracing:
Exchange of Transaction Information & Statement



Beginning 11/27/2023 –

- Transaction information (TI) and the transaction statements (TS)…shall be exchanged in a secure, interoperable, electronic manner… [section 582(g)(1)(A) of the FD&C Act]
- Promptly facilitate gathering the information necessary to produce the transaction information for each transaction going back to the manufacturer, as applicable… [section 582(g)(1)(E) of the FD&C Act]

Enhanced Product Tracing:
Serialized Transaction Information

Under section 582(g)(1)(B) of the FD&C Act, transaction information…shall include the product identifier at the package level for each package included in the transaction.

Pre-November 2023

Transaction Information:

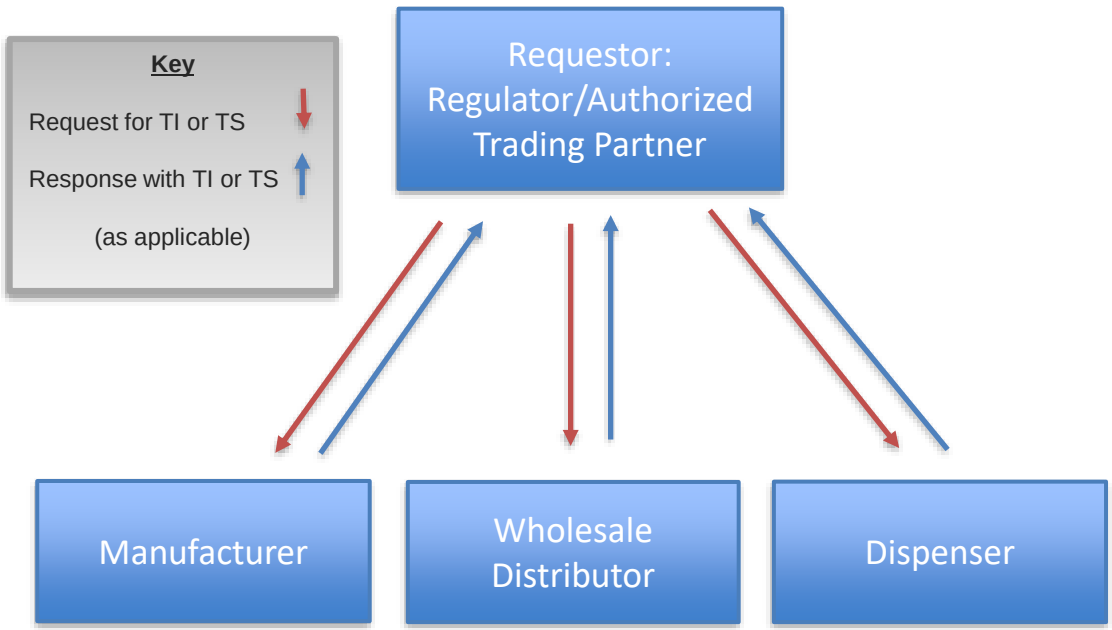
- Proprietary or established name or names of the product
- Strength and dosage form of the product
- National Drug Code number of the product
- Container size
- Number of containers
- Lot number of the product
- Date of the transaction
- Date of the shipment, if more than 24 hours after the date of the transaction
- Business name and address of the person from whom and to whom ownership is being transferred

November 2023+

Transaction Information:

- Proprietary or established name or names of the product
- Strength and dosage form of the product
- National Drug Code number of the product
- Container size
- Number of containers
- Lot number of the product
- Date of the transaction
- Date of the shipment, if more than 24 hours after the date of the transaction
- Business name and address of the person from whom and to whom ownership is being transferred
- Serial number
- Expiration date

Gathering of Relevant Product Tracing Information

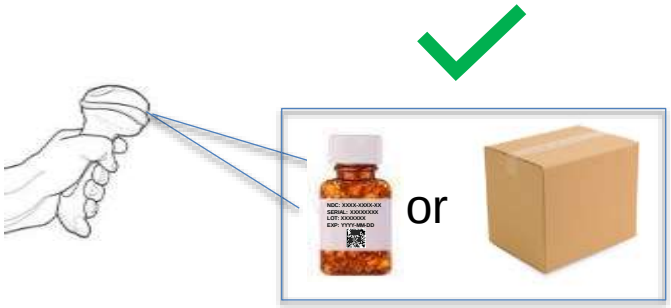


Under sections 582(g)(1)(D) and (E) of the FD&C Act:
...promptly respond with the TI and TS...upon a request by the Secretary (or other appropriate Federal or State official) in the event of a recall or for the purposes of investigating a suspect product or an illegitimate product shall be required...

and

...promptly facilitate gathering the information necessary to produce the TI for each transaction going back to the manufacturer... (i) in the event of a request by the Secretary (or other appropriate Federal or State official), on account of a recall or for the purposes of investigating a suspect product or an illegitimate product; or (ii) in the event of a request by an authorized trading partner, in a secure manner that ensures the protection of confidential commercial information and trade secrets, for purposes of investigating a suspect product or assisting the Secretary (or other appropriate Federal or State official) with a request described in clause (i).

Enhanced Verification: Package-Level



Requestor: FDA/Authorized Trading Partner

Key

Request for verification of the product identifier (including the NDC and serial number)

Response to verification request

Authorized Trading Partner

Under section 582(g)(1)(C) of the FD&C Act: systems and processes for verification of product at the package level, including the standardized numerical identifier shall be required in accordance with the standards established under the guidance issued pursuant to subsection (a)(2) and the guidances issued pursuant to paragraphs (2), (3), and (4) of subsection (h)...which may include the use of aggregation and inference as necessary.

Enhanced Verification: Saleable Returns

Under Section 582(g)(1)(F) of the FD&C Act: Each person accepting a saleable return shall have systems and processes in place to allow acceptance of such product and may accept saleable returns only if such person can associate the saleable return product with the transaction information and transaction statement associated with that product.

FDA DSCSA Guidances

Wholesale Distributor Definitions

Wholesale Distributor

(Section 581(29) of the FD&C Act)

A person (other than a manufacturer, a manufacturer's co-licensed partner, a third-party logistics provider, or repackager) engaged in wholesale distribution (as defined in section 503(e)(4) of the FD&C Act, as amended by the DSCSA)

Wholesale Distribution

(Section 503(e)(4) of the FD&C Act)

"…distribution of a drug subject to [503(b)] … to a person other than a consumer or patient, or receipt of a drug subject to [503(b)] by a person other than the consumer or patient"

3PL Definitions

Third-Party Logistics Provider (3PL)

(Section 581(22) of the FD&C Act)

"…an entity that *provides or coordinates warehousing, or other logistics services* of a product in interstate commerce on behalf of a manufacturer, wholesale distributor, or dispenser of a product, *but does not take ownership of the product*, nor have responsibility to direct the sale or disposition of the product."

Other Logistics Services

(Section 503(e)(4) of the FD&C Act)

See proposed 21 CFR 205.3(i):

Other logistics services include services provided by entities that accept or transfer direct possession of products from that entity's facility within the United States and its territories on behalf of a trading partner (e.g., manufacturer, wholesale distributor, dispenser) but that do not take ownership of the product nor have the responsibility to direct a product's sale or disposition.

National Standards for the Licensure of Wholesale Drug Distributors and Third-Party Logistics Providers Proposed Regulations – 21 Part 205

Section 583 of the FD&C Act - National Standards for Prescription Drug Wholesale Distributors

Section 583(a) of the FD&C Act, as amended by DSCSA, requires that FDA "establish by regulation the standards for the licensing of persons under section 503(e)(1)… including the revocation, reissuance, and renewal of such license."

Section 584 of the FD&C Act – National Standards for Third-Party Logistics Providers

Section 584(d) of FD&C Act, as amended by DSCSA, requires that FDA "issue regulations regarding the standards for licensing under subsection (a), including the revocation and reissuance of such license, to third-party logistics providers under this section."

The proposed rule, when finalized, will establish the national standards for the licensure of WDDs and 3PLs required under sections 583 and 584 of the FD&C Act, as amended by the DSCSA.

Need for Regulation

- Provide certainty and clarity to regulated industry
- Harmonize requirements and standards for licensure across State lines
- Reduce product diversion
- Minimize threats to the legitimate supply chain

Proposed Effective Dates for National Licensing Standards

	DSCSA Effective Dates	National Licensing Standards Proposed Implementation Dates
WDD	2 years after the regulation is finalized	2 years after the regulation is finalized
3PLs	1 year after the regulation is finalized	FDA does not intend to enforce requirements with respect to the national standards for licensure of 3PLs until 2 years after the regulation is finalized

Preemption

- FDA interprets section 585(b)(1) of the FD&C Act as preempting States and localities from establishing or continuing requirements for 3PL or WDD licensure that are different from the standards and requirements applicable under the regulations promulgated under sections 584 and amended 503(e) of the FD&C Act.
- State and local licensure requirements which are inconsistent with the federal requirements (as reflected in this regulation) will be preempted only once this regulation, when finalized, takes effect; until such time, current State and local licensing of WDDs and 3PLs may continue.

National Standards for the Licensure of Wholesale Drug Distributors and Third-Party Logistics Providers Proposed Regulations – 21 Part 205

21 CFR § 205.4 – 205.19 Third-Party Logistics Providers Licensure Standards
Provisions include: application requirements, federal licensure process, expiry and renewal, licensure denial, suspension, reinstatement, revocation and voluntary termination, good storage practices, personal requirements, recordkeeping, annual reporting to FDA, inspections, approved third-party organizations…

21 CFR § 205.20 – 205.33 Wholesale Distributors Licensure Standards
Provisions include: surety bond requirement, application requirements, federal licensure process, qualifications for key personnel, national standards for storage and handling of prescription drugs, maintenance of records of distribution, inspections, annual reporting to FDA, licensure denial, suspension, reinstatement, revocation and voluntary termination, approved third-party organizations…

Webinar on the Proposed Rule: National Standards for the Licensure of Wholesale Drug Distributors and Third-Party Logistics Providers

Submit comments to the public docket:
closes Sept. 6, 2022

https://www.fda.gov/drugs/news-events-human-drugs/proposed-rule-national-standards-licensure-wholesale-drug-distributors-and-third-party-logistics

Challenge Question #2

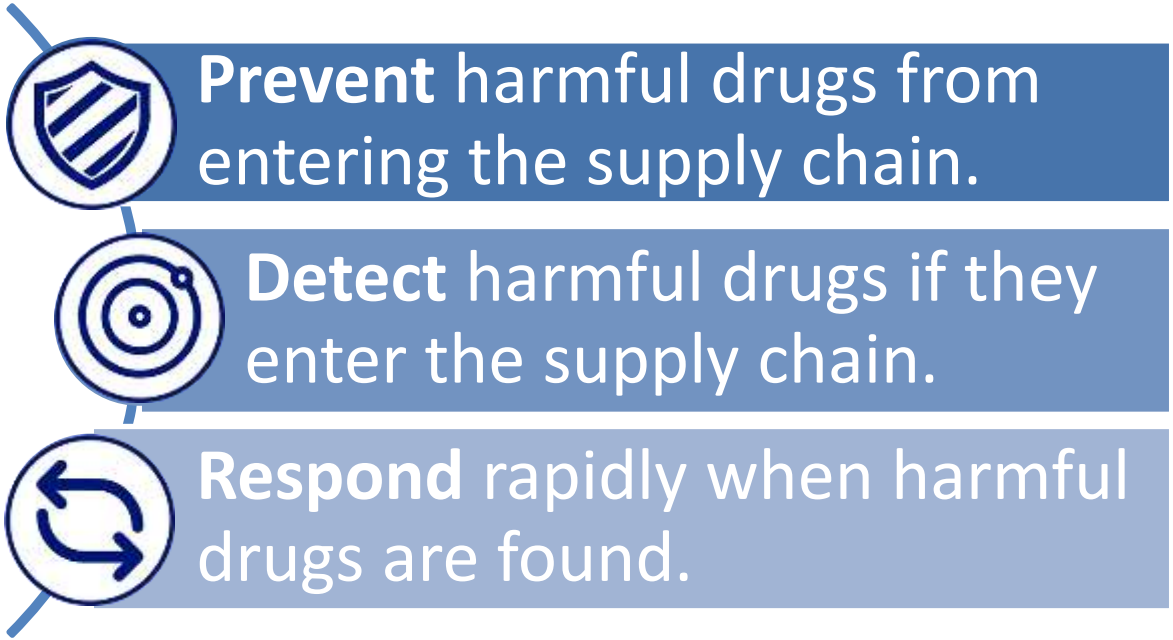
Is the following statement true or false?

National standards for licensure for wholesale distributors and third-party logistics providers will harmonize requirements and standards for licensure across State lines.

A. True

B. False

Protecting Patients



FDA Resources

- DSCSA main webpage

  https://www.fda.gov/Drugs/DrugSafety/DrugIntegrityandSupplyChainSecurity/DrugSupplyChainSecurityAct/default.htm

- DSCSA regulatory documents (i.e., regulations, guidances, federal register notices, pilot programs)

  https://www.fda.gov/Drugs/DrugSafety/DrugIntegrityandSupplyChainSecurity/DrugSupplyChainSecurityAct/ucm424963.htm

- Proposed Rule: National Standards for the Licensure of Wholesale Drug Distributors and Third-Party Logistics Providers

  https://www.fda.gov/drugs/drug-supply-chain-security-act-dscsa/fda-announces-proposed-rule-national-standards-licensure-wholesale-drug-distributors-and-third-party

U.S. FOOD & DRUG ADMINISTRATION

Questions?

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CDER | US FDA


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