

SOPP 8507: Procedures for Responding to an Illegitimate Product Notification and Request for Termination of Notification

Version: 2

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I. Purpose

This Standard Operating Policy and Procedure (SOPP) describes the process that the Center for Biologics Evaluation and Research (CBER) follows after receipt of information of suspect drug products, notifications concerning illegitimate drug products, and requests for termination of notification under Section 582 of the Federal Food, Drug and Cosmetic Act (FD&C Act) as added by the Drug Quality Security Act (DQSA), specifically Title II of the DQSA, the Drug Supply Chain Security Act (DSCSA). Efforts are directed at assessing the potential public health impact of the illegitimate product, and protecting the public health by ensuring adequate notice of the illegitimate product. This SOPP provides the framework for communication within CBER and between appropriate FDA staff and those participants outside the agency.

II. Scope

This SOPP applies to all drug products regulated by CBER that are deemed to be suspect or illegitimate products in accordance with the DSCSA.

III. Background

- A.** On November 27, 2013, the DSCSA (Title II of the DQSA, Public Law 113-54) was signed into law. Starting January 1, 2015, Section 582 of the FD&C Act, as amended by the DSCSA, 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 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.
- B.** Section 582 of the FD&C Act was also amended to allow for the termination of illegitimate product notifications when trading partners determine that a notification made is no longer necessary. FDA must be consulted before issuing a notification termination through the trading partner's submission of a Request for Termination of Notification.

- C. Moreover, the amendments allow FDA to issue information requests to trading partners who must in turn provide certain transaction information for a drug product and verification requests when FDA has determined that product within the possession or control of a trading partner is a suspect product.
- D. Illegitimate drugs may pose significant public health and safety concerns. As a result, patients may be put at risk of serious adverse health consequences. The Office of Compliance and Biologics Quality (OCBQ) coordinates the response to illegitimate product events for CBER. The communications response to an event includes interaction within and outside CBER. The Agency takes very seriously any allegations or information regarding the identification of illegitimate products. As the manufacturing and distribution system has become more global in nature, protecting against illegitimate products has become more challenging.

IV. Definitions

- A. **Counterfeit Drug Product** - Federal law [21 USC 321(g)(2)] defines a counterfeit drug product as a drug sold under a product name, without proper authorization, that is represented, labeled, or packaged in a manner that suggests it is an authentic approved product. **Note:** Counterfeit products may include products without active ingredient (contain only inactive ingredients), products with incorrect ingredients, improper dosages, sub-potent or super-potent ingredients, insufficient quantity of active ingredient, the wrong active ingredient, or products that are contaminated.
- B. **Dispenser** - a retail pharmacy, hospital pharmacy, a group of chain pharmacies under common ownership and control that do not act as a wholesale distributor, or any other person authorized by law to dispense or administer human prescription drugs, and the affiliated warehouses or distribution centers of such entities under common ownership and control that do not act as a wholesale distributor.
- C. **Illegitimate Product** - a drug product for which credible evidence shows that the product:
- is counterfeit, diverted, or stolen;
 - is intentionally adulterated such that the product would result in serious adverse health consequences or death to humans;
 - is the subject of a fraudulent transaction; or
 - appears otherwise unfit for distribution such that the product would be reasonably likely to result in serious adverse health consequences or death to humans.
- D. **Manufacturer** - Manufacturer, with respect to a product, means:
- a person that holds an application approved under section 505 or a license issued under section 351 of the Public Health Service Act for such product, or if such product is not the subject of an approved application or license, the person who manufactured the product;
 - a co-licensed partner of the person described above; or
 - an affiliate of a person described above.

- E. Panorama** - an electronic system maintained by the Center for Drug Evaluation and Research (CDER) used by CBER for the receipt, triage, and close-out of illegitimate product notifications and requests for termination of notifications.
- F. Repackager** - a person who owns or operates an establishment that repacks and relabels a product or package for further sale or distribution without a further transaction.
- G. Suspect Product** - a drug product for which there is reason to believe that the product:
- is potentially counterfeit, diverted, or stolen;
 - is potentially intentionally adulterated such that the product would result in serious adverse health consequences or death to humans;
 - is potentially the subject of a fraudulent transaction; or
 - appears otherwise unfit for distribution such that the product would result in serious adverse health consequences or death to humans.
- H. Trading Partner** - a manufacturer, repackager, wholesale distributor, or dispenser from whom a manufacturer, repackager, wholesale distributor, or dispenser accepts or transfers direct ownership of a product.
- I. Transaction History** - a statement in paper or electronic form, including the transaction information for each prior transaction going back to the manufacturer of the product
- J. Wholesale Distributor** - a person (other than a manufacturer, a manufacturer's co-licensed partner, a third-party logistics provider, or repackager) engaged in wholesale distribution.

V. Policy

- A.** OCBQ will take the lead in issuance of FDA Information Requests and FDA Verification Requests for CBER regulated products, and will coordinate the review and follow-up of information provided by trading partners.
- B.** FDA may issue an Information Request to a trading partner in the event of a recall or for the purpose of investigating a suspect product or an illegitimate product. The trading partner's response to an Information Request should include the applicable transaction information, transaction history, and transaction statement for the product. Transaction information includes the proprietary or established name or names of the product; the strength and dosage form of the product; the National Drug Code number of the product; the container size; the number of containers; the lot number of the product; the date of the transaction; the date of the shipment, if more than 24 hours after the date of the transaction; the business name and address of the person from whom ownership is being transferred; and the business name and address of the person to whom ownership is being transferred.

- C. A transaction statement can be in paper or electronic form, and states that the entity transferring ownership in a transaction: is authorized as required under the DSCSA; received the product from a person that is authorized as required under the DSCSA; received transaction information and a transaction statement from the prior owner of the product, as required under section 582; did not knowingly ship a suspect or illegitimate product; had systems and processes in place to comply with verification requirements under section 582; did not knowingly provide false transaction information; and did not knowingly alter the transaction history. Trading partners should provide the information within one business day, and not later than 48 hours, after receiving the request, or in other such reasonable time as determined by FDA.
- D. If FDA makes a determination that a product in the possession or control of a trading partner is a suspect product, OCBQ will issue a Verification Request to the trading partner. Upon receiving a Verification Request from OCBQ, a trading partner shall: 1) quarantine such product within the possession or control of the trading partner from product intended for distribution until such product is cleared or dispositioned; and 2) promptly conduct an investigation in coordination with other trading partners, as applicable, to determine whether the product is an illegitimate product, which shall include validating any applicable transaction history and transaction information in the possession of the trading partner and otherwise investigating to determine whether the product is an illegitimate product.
- E. If the trading partner makes the determination that a suspect product is not an illegitimate product, the trading partner shall promptly notify OCBQ of such determination and such product may be further distributed. This notification to OCBQ is known as a **Cleared Product Notification**.
- F. If the trading partner makes the determination that the product subject to the OCBQ Verification Request is an illegitimate product, the trading partner will submit an **Illegitimate Product Notification** to OCBQ and all immediate trading partners.
- G. All Illegitimate Product Notifications and requests for Termination of Notification will be submitted to OCBQ by trading partners using FDA Form 3911. All FDA Form 3911s will be logged into Panorama automatically.
- H. For Illegitimate Product Notifications, trading partners should provide information to OCBQ about: 1) the person or entity initiating the notification; 2) the product determined to be illegitimate or to pose a high risk of illegitimacy that is the subject of the notification to FDA; and 3) a description of the circumstances surrounding the event that prompted the notification.
- I. For requests for Termination of Notification, trading partners should provide information to OCBQ about: 1) the person or entity initiating the request for termination; 2) the illegitimate product or the product with a high risk of illegitimacy, 3) the notification that was issued; and 4) an explanation about what actions have taken place or what information has become available that make the notification no longer necessary to FDA.

- J.** Upon receipt of an Illegitimate Product Notification, OCBQ will coordinate initial review and follow-up to ascertain the potential seriousness of the illegitimate product event. When warranted, an ad hoc internal response team is formed that may include representatives from OCBQ; Office of Communication, Outreach, and Development (OCOD); Office of Regulatory Affairs (ORA), including the Office of Criminal Investigations (OCI), Office of Enforcement and Import Operations (OEIO), and district office(s); the appropriate CBER product Office; Office of Biostatistics and Epidemiology (OBE) and others, as needed, to develop an action plan. Requests for Termination of Notification will be promptly reviewed and OCBQ will notify the submitter of the results of the review.
- K.** This SOPP will be followed by all assigned parties and encompasses all CBER regulated drug products.

VI. Responsibilities

A. OCBQ:

- 1.** Serves as the focal point within CBER for issuance of FDA Information Requests and FDA Verification Requests regarding Illegitimate Product Notifications; responds to Illegitimate Product Notifications and requests for Termination of Notifications.
- 2.** Communicates with the notification submitter and the manufacturer regarding the event to obtain relevant information.
- 3.** Assesses the public health aspects, in close collaboration with the appropriate Product Office.
- 4.** Coordinates with ORA (OCI, OEIO and district offices and laboratories) to investigate the report.
- 5.** Reviews the illegitimate product information provided to CBER.
- 6.** Organizes, reports, and tracks information, including the manufacturer's review of its adverse experience/event information.
- 7.** Coordinates the interpretation of the data with the ad hoc response team focal points.
- 8.** Provides guidance to the manufacturer on regulatory submissions that may be needed to support implementation of changes to prevent further illegitimate product events (e.g., changes to packaging systems to introduce anti-counterfeiting or tamper-evident measures).
- 9.** Notifies the appropriate FDA contacts, including the Emergency Operations Center (EOC), as necessary.

B. OCOD:

- 1.** Obtains relevant information in consultation with OCBQ and articulates the Center's public information.
- 2.** Receives and responds to incoming calls from consumers, healthcare providers, and others.

3. Distributes incoming, relevant information to appropriate ad hoc response team focal points.
4. Coordinates with manufacturers to post any needed notices to the medical community and the public on the FDA website, with a link to the manufacturer's website. CBER expects manufacturers to cooperate with the agency in efforts to notify healthcare providers, patients, and other public health officials.
5. Develops a Question & Answer (Q&A) or other document, as appropriate and in conjunction with OCBQ and the Product office, for handling calls from consumers and healthcare providers and/or for posting on the FDA website.

C. Product Office:

1. Provides OCBQ with an assessment of health hazard and patient specific concerns that may be associated with the illegitimate product.
2. Provides input concerning requests for Termination of Notification.

D. OBE:

1. Reviews adverse event reports for the illegitimate product.
2. Provides this information to the product Offices and OCBQ.

VII. Procedures

1. FDA Information Requests

- a. Contact OCBQ/DCM when an Office believes a FDA Information Request is needed for a product. [**CBER Offices**]
- b. Coordinate the issuance of the Information Request. [**OCBQ/DCM**]
- c. Coordinate review of the transaction information received. [**OCBQ/DCM**]

2. FDA Verification Requests

- a. Contact OCBQ/DCM when an Office believes a FDA Verification Request should be issued for a product. [**CBER Offices**]
- b. Coordinate the issuance of a Verification Request when CBER determines that product in possession of a trading partner is a suspect product. [**OCBQ/DCM**]
- c. Ensure that for each FDA Verification Request issued, the trading partner submits a Cleared Product Notification or Illegitimate Product Notification. [**OCBQ/DCM**]
- d. Coordinate review of the trading partner's response. [**OCBQ/DCM**]

3. Triage of initial notifications and requests for terminations
 - a. Review Panorama at least once each business day to check for submission of new Form 3911s. **[OCBQ/DCM]**
 - b. Determine appropriate review Center, in conjunction with CDER, for all new Form 3911 submissions, based on Center product jurisdiction; assign appropriate submissions to CBER. **[OCBQ/DCM]**
 - c. Execute report to confirm correct assignment of recent Form 3911 submissions. **[OCBQ/DCM]**
 - d. Initiate review of all Form 3911 submissions assigned to CBER. **[OCBQ/DCM]**
4. Initial assessment of submissions
 - a. Perform an initial assessment of all Illegitimate Product Notifications for CBER regulated products, in consult with the notification submitter, manufacturer, product Office, and other FDA components as needed. **[OCBQ/DCM, Product Office]**
 - b. Confirm the purported identity and manufacturer of the illegitimate product (based on the product's labeling) as part of the initial assessment. **[OCBQ/DCM, Product Office]**
 - c. Notify the submitter if the initial assessment determines that the product included in the notification does not meet the definition of an illegitimate product, and, if needed, advises the submitter of the appropriate notification method (e.g., Biological Product Deviation Report (BPDR), adverse event report) for the event. **[OCBQ/DCM]**
 - d. Communicate with the Director and Deputy Director, OCBQ, if the initial assessment confirms the existence of an illegitimate product event. **[OCBQ/DCM]**
 - e. Serve as the focal point within CBER to coordinate the response to the illegitimate product event. **[OCBQ/DCM]**
 - f. Schedule internal meeting with the Director and Deputy Director, OCBQ; the Director, Division of Case Management (DCM); and the Associate Director for Policy, OCBQ, to discuss the available information. **[OCBQ/DCM]**
 - g. Notify appropriate units within and outside the Center via phone and/or electronic mail (e.g., product manufacturer, product Office, OBE, OCOD, ORA, OCI, OC (EOC)). **[OCBQ/DCM]**

- h. Assemble an ad hoc internal response team. The team will always include members of OCBQ, OCOD, and the product Office, and may include other FDA components (e.g., OBE, ORA) as needed. **[OCBQ/DCM]**
 - i. Follow procedures in *SMG 9002.1: FDA's Response to Cargo Thefts* if an illegitimate product event is related to cargo theft. In addition, if the illegitimate product event includes potential criminal activity, notify OCI in accordance with *SMG 9111: Sharing of Information Related to Criminal Violations*. **[OCBQ/DCM]**
5. Further review of initial notifications
- a. Lead the ad hoc internal response team in developing an action plan for the illegitimate product event. **[OCBQ/DCM]**
 - b. Develop the action plan. **[Internal Response Team]**
 - i. Considerations for action plans will should include:
 - a) the adequacy of efforts to identify and quarantine the illegitimate product and whether FDA action is needed to ensure control of the product;
 - b) for illegitimate product from foreign sources, the need to restrict further importation of the product;
 - c) whether the event could result in a product shortage; and
 - d) the timing and need for an Information Advisory and/or other communications (e.g. talking points).
 - c. Communicate with the notification submitter and the product manufacturer regarding the event in a timely fashion, as appropriate, to obtain information about the incident, including complaints and adverse events reported for the subject product. Other members of the ad hoc internal response team may participate in communications with the manufacturer as appropriate. **[Internal Response Team]**
 - d. Coordinate with the submitter and manufacturer to post on the FDA website notice to the medical community, and the public, if determined to be necessary by FDA. **[OCOD]**
 - e. Analyze information provided to CBER by consumers, and others, in conjunction with appropriate ad hoc internal response team focal points; **[OCBQ/DCM]** and:
 - i. organizes reports and tracks information related to the illegitimate product provided to the agency, including the firm's adverse experience/event information, if appropriate;

- ii. coordinates the interpretation of the data with the ad hoc response team focal points; and
- iii. updates senior CBER management (Center Director, Deputy Center Directors, Associate Center Directors, or Office Directors), as necessary, on the progress of the investigation.

6. Review of notification termination requests

- a. Review requests for Termination of Notification and the rationale provided for terminating the notification. **[OCBQ/DCM]**
- b. Consult with the appropriate members of the ad hoc internal response team. **[OCBQ/DCM]**
- c. Provide the submitter with FDA’s expert views and advice on the proposed termination, and whether FDA agrees that the notification should be terminated. **[OCBQ/DCM]**
- d. Respond to the submitter of the request for Termination of Notification within 10 business days of submission, or notify the submitter if additional time is needed to respond to the request. **[OCBQ/DCM]**

7. Close out of submissions

- a. Enter a short statement in the record’s comment field that briefly describes the outcome of the review (e.g., determined to not meet definition of illegitimate product, all product recalled, termination request accepted, etc.) at the time of close out. **[OCBQ/DCM]**
- b. Prepare a memorandum to the file detailing the actions taken in response to the event if the notification or termination request concerns a product that was confirmed to be illegitimate based on the initial assessment. **[OCBQ/DCM]**
- c. Upload the memorandum into Panorama. **[OCBQ/DCM]**
- d. Ensure that the Panorama record is closed out for every Illegitimate Product Notification and request for Termination of Notification for CBER regulated products. **[OCBQ/DCM]**

VIII. Appendix

N/A

IX. References

- A. The Drug Quality and Security Act (DQSA), signed into law November 27, 2013
<http://www.fda.gov/Drugs/DrugSafety/DrugIntegrityandSupplyChainSecurity/DrugSupplyChainSecurityAct/default.htm>
- B. Draft Guidance for Industry: Drug Supply Chain Security Act Implementation: Identification of Suspect Product and Notification
<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM400470>
- C. Staff Manual Guide 9002.1, FDA’s Response to Cargo Thefts, dated March 23, 2012
<http://www.fda.gov/AboutFDA/ReportsManualsForms/StaffManualGuides/ucm297206.htm>
- D. Staff Manual Guide 9111, Sharing of Information Related to Criminal Violations, dated August 20, 2010
<http://www.fda.gov/AboutFDA/ReportsManualsForms/StaffManualGuides/ucm212504.htm>

X. History

Written/Revised	Approved By	Approval Date	Version Number	Comment
Tom Adams and CBER OCBQ WG	Chris Joneckis, PhD	Jan 18, 2016	2	Updated for DSCSA illegitimate product notifications
CBER OCBQ	Robert Yetter, PhD	March 9, 2004	1	Original