Guidance for Industry on Drug Supply Chain Security Act Implementation:
Identification of Suspect Product and Notification
0910-NEW
Supporting Statement

Terms of Clearance: None.

A. Justification

1. Circumstances Making the Collection of Information Necessary

On November 27, 2013, the Drug Supply Chain Security Act (DSCSA) (Title II of Public Law 113-54) was signed into law. Section 203 of the DSCSA adds new section 582(h)(2) to the Federal Food, Drug, and Cosmetic Act (the FD&C Act), which requires FDA to issue guidance to aid trading partners in identifying a suspect product and terminating a notification regarding an illegitimate product and, for a manufacturer, a product with a high risk of illegitimacy. "Suspect product" is defined in section 581(21) of the FD&C Act as a product for which there is reason to believe it: (A) is potentially counterfeit, diverted, or stolen; (B) is potentially intentionally adulterated such that the product would result in serious adverse health consequences or death to humans; (C) is potentially the subject of a fraudulent transaction; or (D) appears otherwise unfit for distribution such that the product would result in serious adverse health consequences or death to humans. Beginning January 1, 2015, section 582 of the FD&C Act requires certain trading partners, upon determining that a product in their possession or control is a suspect product, to quarantine the product while they promptly conduct an investigation to determine whether the product is an illegitimate product. "Illegitimate product" is defined in section 581(8) of the FD&C Act as a product for which credible evidence shows that it is: (A) counterfeit, diverted, or stolen; (B) intentionally adulterated such that the product would result in serious adverse health consequences or death to humans; (C) is the subject of a

fraudulent transaction; or (D) appears otherwise unfit for distribution such that the product would be reasonably likely to result in serious adverse health consequences or death to humans. Beginning January 1, 2015, section 582 of the FD&C Act requires trading partners, upon determining that a product in their possession or control is illegitimate, to notify FDA and all immediate trading partners, that they have reason to believe may have received the illegitimate product, not later than 24 hours after making the determination. Manufacturers are additionally required under section 582(b)(4)(B)(ii)(II) 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.

2. Purpose and Use of the Information Collection

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

The purpose and use of this information is to minimize the likelihood that illegitimate products or products with a high risk of illegitimacy will be widely disseminated in the U.S. supply chain. Information about an illegitimate product is required to be sent to all trading

partners that could possess the product in addition to the FDA. This will allow FDA to work with the entity making the notification to alert consumers about the product, if necessary.

3. Use of Improved Information Technology and Burden Reduction

FDA developed the Form FDA 3911 as an efficient way to standardize and collect the needed information from the various trading partners about an illegitimate product or product with a high risk of illegitimacy. FDA is developing a fillable version of Form FDA 3911 to simplify the process and provide for more efficient notification by trading partners.

4. Efforts to Identify Duplication and Use of Similar Information

The FDA does not know to what extent there may be duplication of submitted information under the DSCSA with existing required submissions. Wholesale distributors and dispensers currently have no reporting requirements regarding drug products. A field has been added to the Form FDA 3911 to capture whether other submissions have been made to the FDA related to the same incident. FDA will monitor for duplicate submissions.

5. Impact on Small Businesses or Other Small Entities

The notification of FDA and other trading partners is only required when an illegitimate product is identified by a manufacturer, repackager, wholesale distributor, or dispenser or by a manufacturer when a product is found to have a high risk of illegitimacy. There are small businesses in the four categories of trading partners. However, they will only be impacted if they find illegitimate product in their possession or control. Small manufacturers would have to notify FDA and immediate trading partners if they become aware of a product with a high risk of illegitimacy.

6. Consequences of Collecting the Information Less Frequently

The DSCSA requires manufacturers, repackagers, wholesale distributors, and dispensers to notify FDA within 24 hours of making the determination that a product in their possession or control is illegitimate. In addition, manufacturers are required to notify FDA within 24 hours of determining that a product has a high risk of illegitimacy. The collection of information only occurs when a product is determined to be illegitimate or to have a high risk of illegitimacy. Notifications are not routine submissions. It is not possible to collect this information any less frequently than when it actually occurs.

7. Special Circumstances Relating to the Guidelines in 5 CFR 1320.5

There are no special circumstances relating to this information collection. (The submission of proprietary, trade secret, or other confidential information is addressed under section 10 below).

8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

In accordance with 5 CFR 1320.8(d), FDA published a 60 day notice for public comment in the FEDERAL REGISTER notice of June 11, 2014, (79 FR 33564). FDA received comments on the draft guidance from 20 different organizations, companies, and individuals. The draft guidance provided scenarios that could increase the risk of a suspect product entering the supply chain and recommendations on how trading partners may identify products that may be suspect. The draft guidance also provided the process for notifying FDA and immediate trading partners when a trading partner has determined that a product is illegitimate product or a manufacturer has determined that a product has a high risk of illegitimacy and the process for terminating those notifications in consultation with FDA. Many of the comments requested information about parts of the DSCSA that were not specifically covered by, nor intended to be covered by, the draft guidance, such as cleared product notifications, suspect product

investigation, illegitimate product determinations, quarantine, and verifications, which FDA intends to address in other guidance or public means.

Several commenters raised issues pertaining to the information collection provisions in the draft guidance and the Form FDA 3911. FDA has clarified the process for making notifications and requests for termination to the FDA in the final guidance. FDA also clarified several fields on Form FDA 3911 and the instructions for using the Form FDA 3911 in response to comments received to the draft guidance. The issues raised by the commenters are addressed below.

Scope-related Issues:

Issue One: Several comments were received requesting clarification about the scope of what is considered to be an illegitimate product or what constitutes a high risk of illegitimacy. For example, commenters requested clarification that a product may be determined to be illegitimate only as a result of fraud and not due solely to quality issues. Commenters also asked for a definition of high risk of illegitimacy.

FDA Response to Issue One: The purpose of this guidance, relative to notifications, is to provide a process for trading partners to submit notifications to FDA and immediate trading partners after the determination of illegitimacy or high risk of illegitimacy has been made and to submit requests for consultation to FDA to terminate a notification. To determine the scope of illegitimate products, trading partners should refer to the definition of illegitimate product, which does not exempt quality issues. The current guidance has been amended to add scenarios to help clarify what manufacturers may consider when determining if a product has a high risk of illegitimacy.

Issue Two: Is it necessary to send a notification to FDA when an illegitimate product or product with high risk of illegitimacy can be dispositioned or contained quickly?

FDA Response to Issue Two: Yes, provisions of the DSCSA requires trading partners to notify FDA when a determination has been made that a product is illegitimate, or for manufacturers, that a product has a high risk of illegitimacy. The amount of time it takes for a firm to control the product or manage the situation is not a factor in determining when a notification to FDA and other trading partners should take place, i.e. not later than 24 hours after the determination is made that a product is illegitimate or has a high risk of illegitimacy.

Issue Three: Many commenters asked if the FDA was going to make either the Form FDA 3911 or information about the notifications public.

FDA Response to Issue Three: The notifications and requests for termination will be handled according to Agency regulations, the Freedom of Information Act, and other applicable disclosure law. In some cases, FDA may coordinate with the notifying person or entity and issue agency public health alerts to protect the public health based on information received through drug notifications received under sections 582(b)(4)(B)(ii), (c)(4)(B)(ii), (d)(4)(B)(ii), and (e)(4)(B)(ii) of the FD&C Act.

Form FDA 3911- and Instruction-related Issues:

Several commenters requested clarification of the instructions for filling out existing fields on Form FDA 3911 or requested additional information be added to the Form FDA 3911 including additional fields.

Issue Four: Commenters requested clarification about the fields on Form FDA 3911 to describe the product that is the subject of the notification. Specifically, commenters wanted clarification about the terms “generic” and “trade” names.

FDA Response to Issue Four: FDA has clarified the names of these fields on the Form FDA 3911 and the associated instructions. The field called "Generic Name" was changed to "Name of Product as it appears on the label". The field called "Trade Name (if applicable)" was changed to "Primary Ingredients" and the instructions were amended to request that the notifying person or entity list the active pharmaceutical or biological ingredients if known and if the information is not already listed in the "Name of Product as it appears on the label" field. These changes will clarify how the notifying person or entity should describe the product that is the subject of the notification.

Issue Five: Several commenters wanted clarification about the fields on Form FDA 3911 for identification of company versus the reporter.

FDA Response to Issue Five: The FDA modified the Form FDA 3911 to make it clearer that we want information about the company who is responsible for making the notification. The "reporter" is the person whom the FDA may contact for additional information about the notification. FDA considers the company with the illegitimate product in its possession or control, or a manufacturer that has made a determination that a product has a high risk of illegitimacy, to be the company that is making the notification, even if that company contracts with another person or entity to submit the notification on its behalf.

Issue Six: Commenters asked about the term "unique facility identifier" since the D-U-N-S number is a corporate identifier not a facility identifier. The commenter requested that FDA clarify that it is asking for the unique "Corporate" and not "Facility" identifier.

FDA Response to Issue Six: The FDA uses a site specific identifier called the unique facility identifier (UFI) as a useful resource in identifying and confirming certain business information for the company responsible for making the notification. FDA currently prefers the

D-U-N-S number as the UFI. Since the commenters were confused about the term “facility”, we clarified in the instructions to Form FDA 3911that the unique facility identifier for the company making the notification is the number being requested.

Issue Seven: Several commenters requested a notification reference number for identification purposes.

FDA Response to Issue Seven: FDA agrees with the commenters and has added a field for an incident number. FDA plans to assign an incident number when the initial notification is received. FDA will send the incident number in the response that confirms the receipt of the initial notification to the notifying person or entity. This incident number should be used in all future correspondence about the specific incident/event that is the subject of the initial notification, including the request for termination. The form, instructions, and process in the guidance have been amended to include the incident number. There is no additional burden to the company making the notification to include this number on any additional correspondence with FDA including the request for termination.

Issue Eight: Commenters requested the addition of an FDA contact be added to Form FDA 3911 for questions about the form.

FDA Response to Issue Eight: FDA has added a contact telephone number in addition to the e-mail address previously provided on the Drug Notification Webpage referenced in the guidance.

Issue Nine: Commenters requested a field to indicate that the company making the notification (wholesale distributor, repackager, or dispenser) has consulted with the manufacturer when determining whether a product is illegitimate.

FDA Response to Issue Nine: The DSCSA requires that repackagers, wholesale drug distributors, and dispensers coordinate with the manufacturer when determining whether a product is illegitimate. The Form FDA 3911 should be used to submit a notification after the determination that a product is illegitimate is made. A separate field was not designated for this topic, because the company making the notification may identify the manufacturer they coordinated with in the "Description of Event/Issue" Field. This option has been added to the instructions.

Issue Ten: Commenters requested a field on the Form FDA 3911 to list all trading partners that they believe may possess the illegitimate product.

FDA Response to Issue Ten: FDA did not add a specific field to Form FDA 3911 for companies to list the names of trading partners that may have illegitimate product. While not required, a company may identify all trading partners that they believe may possess the illegitimate product in the "Description of Event/Issue" Field. Under the DSCSA, trading partners are responsible for making notifications to all immediate trading partners they have reason to believe may have received such product. Each trading partner found to have illegitimate product must notify FDA.

Issue Eleven: Commenters requested a space or field to list a case or report number associated with a Medwatch report or other report submitted to FDA.

FDA Response to Issue Eleven: FDA agrees with commenters that it may be useful to know the report or case number for other required or voluntary submissions made to FDA about the same issue. This information may be included in the "For Notification: Description of Event/Issue" or "For Request for Termination of Notification: Description of why notification is

no longer necessary" fields. FDA amended the instructions on the Form FDA 3911 for notifying parties to provide this information if known.

Issue Twelve: Commenters requested a check box to indicate that testing of the drug product was completed.

FDA Response to Issue Twelve: FDA did not add a check box to indicate if testing was completed. However, the company making the notification or request for termination should provide this type of information in the fields, "For Notification, Description of Event/Issue" or "For Request for Termination of Notification: Description of why notification is no longer necessary."

Issue Thirteen: Commenters asked for clarification about the purpose of the "drug use" and "drug description" fields.

FDA Response to Issue Thirteen: The DSCSA applies to prescription drugs for human use. Including these fields helps FDA confirm that the DSCSA requirement applies to the product(s) subject to the notification. The fields also provide flexibility for future use of this form in other contexts. FDA included an "other" option under the "drug use" field to choose if a drug has multiple approvals for use. An instruction to explain "other" when selected by a notifying person or entity was added. We have also included more choices under the "drug description" field to help FDA distinguish between products regulated by the Center for Drug Evaluation and Research and the Center for Biologics Evaluation and Research.

High Risk of Illegitimacy-related Issues:

Issue Fourteen: Several manufacturers requested clarification and specific information about how to document that a notification is for a product with "a high risk of illegitimacy."

FDA Response to Issue Fourteen: In the draft guidance, FDA did not distinguish between illegitimate product notifications and high risk of illegitimacy notifications because the timing and process for these submissions is the same. However, because we received several comments, FDA has revised the guidance to specify the process for notifications for products with a "high risk of illegitimacy" that are required by the DSCSA to be submitted by manufacturers. The guidance provides direction for manufacturers on how to submit notifications for the high risk of illegitimacy. It also clarifies what a manufacturer should do if a product with high risk of illegitimacy is found to be an illegitimate product. FDA also amended the instructions for Form FDA 3911 to indicate that manufacturers document a notification for product with a "high risk of Illegitimacy" in the "For Notification, Description of Event/Issue" field. FDA clarified the instructions for several other fields on the Form FDA 3911 to indicate that they apply to both notifications for illegitimate products and for products with a high risk of illegitimacy.

Timing-related Issues:

Issue Fifteen: Commenters asked for clarification regarding the requirement to submit a notification within 24 hours of making the determination that a product is illegitimate or has a high risk of illegitimacy.

FDA Response to Issue Fifteen: The DSCSA specifies that notifications are to be submitted no later than 24 hours after making the determination that a product in the possession or control of the trading partner is illegitimate. This same timeframe also applies to manufacturers notifying FDA and other trading partners when they determine that a product has a high risk of illegitimacy. This timeframe will help prevent or limit illegitimate product or

product with a high risk of illegitimacy from entering or being further distributed in the U. S. supply chain.

Issue Sixteen: Several commenters indicated that a 10-day timeframe for FDA to provide a consultation in response to a request for termination is too long and could result in drug shortages. Commenters stated that the process for requesting expedited consultation was unclear.

FDA Response to Issue Sixteen: FDA will review and consult with notifying parties regarding requests for termination as soon as possible. The timing of FDA's review and consultation will depend on the number of requests and the circumstances surrounding the requests for termination that are received. Since notifications under the DSCSA are submitted to FDA when it has been determined by trading partners that a product is illegitimate or by manufacturers that a product has a high risk of illegitimacy, in many cases, these products would be counterfeit, intentionally adulterated, diverted, stolen, or otherwise unfit for further distribution and would likely not be further distributed. As FDA indicated in the draft guidance, FDA will consider requests for expedited review when included with a request for termination. We have clarified the process for requesting expedited review by adding an instruction to Form FDA 3911 directing the company that is requesting termination to also request and justify the need for expedited review when explaining why the notification is no longer necessary.

Duplication of submission-related Issues

Issue Seventeen: Comments were received requesting an explanation of why the development of Form FDA 3911 was necessary instead of using the standard field alert report (FAR) for notifications under the DSCSA.

FDA Response to Issue Seventeen: The FAR is a required postmarketing report made by an application holder (new drug or generic drug) when there is a quality problem associated with a drug as outlined in 21 C.F.R. § 314.81(b)(1). FDA developed Form FDA 3911 because the FAR form was inadequate for making notifications required under the DSCSA for a product that is illegitimate or has a high risk of illegitimacy for a reason not necessarily related to product quality (e.g., diverted, stolen, etc.). In addition, only applicant holders are required to submit the FAR to FDA. Illegitimate product notifications are required to be sent to FDA by manufacturers, repackagers, distributors, and dispensers. Notifications of products with a high risk of illegitimacy are also required to be submitted by manufacturers. It is not known how frequently the same incident will generate submission of a FAR and Form FDA 3911 notifications. FDA is collecting information on the FDA Form 3911 that will enable us to quantify duplication of submissions.

Issue Eighteen: Commenters requested clarification about whether every trading partner should submit a separate notification to the FDA about the same illegitimate product.

FDA Response to Issue Eighteen: The DSCSA requires that certain trading partners (manufacturers, repackagers, wholesale distributors, and dispensers) with illegitimate product in their possession or control submit a notification. Trading partners should submit notifications as required.

Issue Nineteen: Commenters requested clarification about whether they are required to submit a notification to the FDA if they are notified of a suspect or illegitimate product by the FDA and determine that they have it in their possession or control.

FDA Response to Issue Nineteen: The DSCSA requires trading partners to submit an illegitimate product notification to the FDA, if a trading partner receives a notification from the

FDA about a suspect or illegitimate product and finds, after the appropriate investigation as required by DSCSA, that they have illegitimate product in their possession or control.

Notifying trading partners-related Issues:

Issue Twenty: Several comments asked for clarification about the process for notifying trading partners of an illegitimate product. Commenters stated that FDA should clarify that existing systems and processes can be used to make notifications to trading partners as well as informing them of terminations of such notifications.

FDA Response to Issue Twenty: In the guidance, FDA specified that existing processes and systems can be used to inform trading partners that a notification has been terminated. FDA agrees with the comments received and has added to the guidance that trading partners can use existing systems and processes to provide notification to trading partners that they believe may have possession or control of the illegitimate product or a product with high risk of illegitimacy.

Issue Twenty-One: A commenter requested that FDA develop a system that would allow for notification of FDA and other trading partners at the same time.

FDA Response to Issue Twenty-One: Manufacturers, repackagers, wholesale distributors, and dispensers with illegitimate product or manufacturers that determine that a product has a high risk of illegitimacy are responsible for notifying their trading partners in addition to the FDA. FDA developed a process for trading partners to use to notify FDA using Form FDA 3911. As clarified in the guidance and Issue Twenty above, the notifying person or entity can use its existing systems and processes to provide the necessary notification to trading partners. Form FDA 3911 can also be used to notify other trading partners in addition to FDA.

Issue Twenty-Two: A commenter asked for clarification if dispensers' immediate trading partners include other pharmacies in the same group of chain pharmacies as well as the wholesale distributor or manufacturer from whom the dispenser purchased drug.

FDA Response to Issue Twenty-Two: The intent of the notification provisions in the DSCSA is to prevent illegitimate product entering or being further distributed into the supply chain to protect public health. FDA expects that a dispenser that has illegitimate product in its possession or control would let the other pharmacies that are part of the same group of chain pharmacies know about such illegitimate product if the dispenser has reason to believe that the other pharmacies might have possession or control of the same product.

Termination Process-related Issues:

Issue Twenty-Three: One commenter stated that FDA should publish guidance on criteria to terminate a notification so that the FDA does not have to play "gatekeeper" for the termination of a notification.

FDA Response to Issue Twenty-Three: The DSCSA requires that a notification be terminated in consultation with the FDA. FDA believes that this guidance addresses the process by which trading partners should use Form FDA 3911 to make requests for termination, and the form will serve as a request to consult with FDA.

Issue Twenty-Four: Comments were received asking for clarification about which entities could request to terminate a notification. Several commenters thought that FDA should be able to self-initiate a termination. Other commenters suggested that the request for termination could be made by any involved trading partner and not limited to the trading partner making the initial notification.

FDA Response to Issue Twenty-Four: FDA believes that the trading partner making the initial notification should be responsible for making the request for termination because they know if the illegitimate product in their possession or control has been satisfactorily dispositioned and if the notification is no longer necessary. The process in the guidance has been amended to clarify this point.

Paper-Work Reduction Act (PRA) Analysis Related Issues.

Issue Twenty-Five: One commenter stated that the estimates in the PRA analysis did not take into account the time it takes to investigate and make the determination that a product is illegitimate. It only included the time to fill out the form and notify trading partners.

FDA Response to Issue Twenty-Five: While the commenter's assessment is correct; the PRA analysis in this guidance was calculated for the process for making and terminating notifications to the FDA and notifying immediate trading partners who are believed to have the drug. This guidance assumes that the determination has already been made that the drug is illegitimate or has a high risk of illegitimacy. The FDA intends to publish additional guidance that will address the investigation of suspect product to determine that a product is illegitimate. The PRA analysis for those activities will be covered at that time.

Issue Twenty-Six: One commenter stated that, based on their experience, FDA estimates for notifications are high.

FDA Response to Comment Twenty-Six: FDA reexamined the estimate of notifications in response to this comment. FDA originally estimated that a total of approximately 5,000 notifications per year would be made by all manufacturers, repackagers, wholesale distributors, and dispensers based on FDA's experience with Field Alert Reports (FARs) (Form FDA 3331) required to be submitted by holders of approved drug applications for certain drug quality issues

(21 CFR 314.81(b)(1)), and with reports of the falsification of drug sample records, diversion, loss, and known theft of prescription drug samples as currently required under the Prescription Drug Marketing Act (PDMA). We determined that the 5,000 FARs and 5,000 sample reporting under PDMA received each year included initial, follow-up, and final reports. While FDA does not know the exact number of notifications that will be submitted, we lowered the estimate to 1,000 notifications in response to the comment and our reexamination of the data and adjusted the PRA analysis accordingly.

Issue Twenty-Seven: Commenters stated that the FDA estimated number of trading partners that would likely have the illegitimate product and have to be notified was high.

FDA Response to Comment Twenty-Seven: FDA recognizes that not every trading partner will possess illegitimate product. However, until serialization is required and implemented, the initial notifying person or entity may not be able to identify which specific immediate trading partners may possess or control illegitimate product. FDA assumed that the initial notifying person or entity would have to notify all trading partners and we have chosen not to amend the number of trading partners that are notified at this time.

Issue Twenty-Eight: A major stakeholder association stated that they did not believe, based on past experience, that wholesale distributors would be making as many notifications as FDA estimated both to FDA and to trading partners.

FDA Response to Issue Twenty-Eight: In the original estimates, FDA assumed that most notifications will be made by three trading partners, manufacturers, repackagers, and wholesale distributors. FDA reexamined the proportion of notification expected from each of the regulated groups. The commenter had speculated that they believed that manufacturers would be making most notifications. In addition, manufacturers are required to submit notifications of high risk of

illegitimacy. In response to the comment and the fact that only manufacturers submit notifications of high risk of illegitimacy, FDA is changing the proportion of notifications that will be made by manufacturers and repackagers from 50 percent to 80 percent (800), from 45 percent to16 percent by wholesale distributors (160), and 5 percent to 4 percent by pharmacies (40). FDA had also originally assumed that wholesale distributors would have to notify an average of 2,350 trading partners for each notification. We agree with the commenters that this was an overestimation and have lowered the number of trading partners to be notified by wholesale distributors to 1,175 (50 percent) for each notification.

9. Explanation of Any Payment or Gift to Respondents

There is no payment or gift to respondents associated with this guidance.

10. Assurance of Confidentiality Provided to Respondents

The submitted information will be handled according to Agency regulations, the Freedom of Information Act, and other applicable disclosure law. Confidentiality of the information submitted under these requirements is protected under 21 CFR Part 20. The unauthorized use or disclosure of trade secrets is specifically prohibited under Section 310(j) of the FD&C Act. FDA will not disclose any information that is considered to be a trade secret and prohibited under section 310(j) of the FD&C Act if such information is included in the notification to FDA.

The forms submitted to FDA are handled by FDA employees. The information from all forms received will be electronically extracted into an internal database. The electronic files and forms will be maintained according to FDA document retention schedules and destroyed when no longer needed for administrative, legal, or audit purposes.

11. Justification for Sensitive Questions

There are no sensitive questions associated with this guidance.

12. Estimates of Annualized Burden Hours and Costs

12a. Annualized Hour Burden Estimate

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

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

FDA originally estimated that a total of approximately 5,000 notifications per year would be made by all manufacturers, repackagers, wholesale distributors, and dispensers. This estimate included the notifications by trading partners that have determined that illegitimate product is in their possession or control, as well as notifications by manufacturers that have determined a product poses a high risk of illegitimacy. As discussed in the June 11, 2014, Federal Register

notice, this estimate was based on FDA's experience with Field Alert Reports (FARs) (Form FDA 3331) required to be submitted by holders of approved drug applications for certain drug quality issues (21 CFR §314.81(b)(1)), and with reports of the falsification of drug sample records, diversion, loss, and known theft of prescription drug samples as currently required under the Prescription Drug Marketing Act (PDMA). FDA received a comment in response to the Federal Register notice stating that the estimate of 5,000 notifications was too high based on experience. In response to the comment, FDA reexamined the estimate of 5,000 notifications. We determined that the 5,000 FARs and 5,000 sample reports under PDMA received each year included initial, follow-up, and final reports. While FDA does not know the exact number of notifications that will be submitted, we lowered the estimate to 1,000 notifications in response to the comment and our reexamination of the data, and adjusted the PRA accordingly.

FDA is combining the estimates for manufacturers and repackagers because FDA's establishment and drug product listing database indicates that many companies perform activities of both manufacturers and repackagers. While the DSCSA specifically defines dispensers, for estimation purposes, FDA is using estimates for pharmacies in general terms based on those that must comply with the new requirements under section 582(d) of the FD&C Act.

Because, collectively, manufacturers, repackagers, and wholesale distributors are responsible for prescription drugs from the point of manufacturing through distribution in the drug supply chain, in the June 11, 2014, Federal Register notice, FDA assumed that most notifications of illegitimate products would be made by these three trading partners. FDA received a comment from a major stakeholder group stating that they believed that the number of notifications estimated for wholesale distributors was too high based on their past experience. The commenter speculated that most notifications would be made by manufacturers. In addition,

manufacturers are the only stakeholder group required to submit notifications of high risk of illegitimacy. FDA originally estimated that approximately 50 percent of the notifications will be made by manufacturers and repackagers, 45 percent by wholesaler distributors, and 5 percent by pharmacies. In response to the comment and the fact that only manufacturers submit notifications of high risk of illegitimacy, FDA is changing the proportion that will be made by manufacturers and repackagers to 80 percent (800), 16 percent by wholesale distributors (160), and 4 percent by pharmacies (40).

FDA estimates that the number of annual notifications will vary from 0-2 for manufacturers/repackagers, as well as from pharmacies, with the vast majority of companies making no notifications. While the FDA's establishment and drug product listing database currently contains registrations for approximately 6,500 manufacturers and repackagers, we estimate that approximately 800 manufacturers/repackagers will notify FDA of illegitimate product an average of one time per year. While FDA estimates approximately 69,000 pharmacy sites in the United States, based on data from the National Association of Chain Drug Stores, the National Community Pharmacists Association, and the American Hospital Association, we estimate that approximately 40 pharmacies will notify FDA of illegitimate product an average of one time per year. Because, according to Healthcare Distribution Management Association approximately 30 wholesale distributors are responsible for over 90 percent of drug distributions, based on sales, and because FDA is estimating that over 2,200 small wholesale distributors might be responsible for the remaining 10 percent of drug sales, we estimate that distributors will be responsible for making about an average of 0-1notification per year to account for the an estimated 160 notifications FDA will receive regarding illegitimate product.

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

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

Because the extent of distribution of any illegitimate product is likely to vary from one situation to another, FDA assumed a wide distribution of each illegitimate product. FDA estimates that for each notification made by a manufacturer or repackager to FDA, approximately 30 trading partners (based on the number of distributors) will also be notified. This results in approximately 24,000 notifications annually to trading partners of manufacturers/repackagers. This estimate includes the notifications by manufacturers and

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

FDA estimates that a large wholesale distributor may have up to 4,500 trading partners, but a small wholesale distributor may have 200 trading partners, for an average of approximately 2,350. FDA originally estimated that a wholesale distributor would notify all 2,350 trading partners for each of the illegitimate products identified. However, comments received from a trade association indicated that they believed this number was too high based on past experience. FDA has reduced the number of trading partners that a wholesale distributor would notify to 50 percent resulting in the notification of 1,175 trading partners for each of the 160 notifications resulting in a total of 188,000 notifications to trading partners.

FDA estimates that a pharmacy purchases prescription drugs from an average of two wholesale distributors. Therefore, a pharmacy would notify 2 trading partners for each of the 40 illegitimate products identified, resulting in approximately 80 notifications annually to pharmacy trading partners.

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

total burden hours of making notifications to trading partners is approximately 42,416 hours annually (table 2).

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

FDA is making Form FDA 3911 available to trading partners on its Web page to request a termination of notification. Each request for termination of notification must include information about the person or entity initiating the request for termination, the illegitimate product or product with a high risk of illegitimacy, the notification that was issued, and an explanation about what actions have taken place or what information has become available that make the notification no longer necessary. The request for a termination will be viewed as a request for consultation with FDA. FDA estimates that the same amount of time will be required to provide the information necessary to request termination as is required to make the notification. The time required to investigate and resolve an illegitimate product notification will vary, but FDA assumes that each notification will eventually be terminated at some point. FDA assumes that the number of requests for termination of a notification per year will be the same as the original number of notifications for a given year. The estimated total burden hours of making requests for termination of notifications to FDA is approximately 1,000 hours annually (table 3).

Notifications to Trading Partners That a Notification Has Been Terminated. Sections 582(b)(4)(B)(iv), (c)(4)(B)(iv), (d)(4)(B)(iv), and (e)(4)(B)(iv) of the FD&C Act require that a trading partner that, in consultation with FDA, terminates a notification made under section 582(b)(4)(B)(ii), (c)(4)(B)(ii), (d)(4)(B)(ii), or (e)(4)(B)(ii) must also promptly notify immediate trading partners that the notification has been terminated. FDA estimates that the burden for notifying trading partners of an illegitimate product and the number of trading partners notified will be the same as the estimates for notification of termination. The estimated total burden hours of notifying trading partners that the notification is terminated is approximately 42,416 hours annually (table 4).

The total burden of drug notifications for all stakeholders is 86,832 hours.

Table 1-- Estimated Annual Reporting Burden

Notifications to FDA	No. of Respondents	No of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Manufacturers and Repackagers	800	1	800	1	800
Wholesale Distributors	160	1	160	1	160
Dispensers	40	1	40	1	40
Total					1,000

Table 2 -- Estimated Annual Third-Party Disclosure Burden

Notifications to Trading Partners of an Illegitimate Product	No. of Respondents	No. of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours
Manufacturers and Repackagers	800	30	24,000	0.20 (12 minutes)	4800
Wholesale Distributors	160	1,175	188,000	0.20 (12 minutes)	37,600
Dispensers	40	2	80	0.20 (12 minutes)	16

Total	42,416

Table 3-- Estimated Annual Reporting Burden

Consultation with FDA and termination of notification	No. of Respondents	No of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Manufacturers and Repackagers	800	1	800	1	800
Wholesale Distributors	160	1	160	1	160
Dispensers	40	1	40	1	40
Total					1,000

Table 4 -- Estimated Annual Third-Party Disclosure Burden[1]

Notifications to Trading Partners of Termination	No. of Respondents	No. of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours
Manufacturers and Repackagers	800	30	2,4000	0.20 (12 minutes)	4800
Wholesale Distributors	160	1,175	188,000	0.20 (12 minutes)	37,600
Dispensers	40	2	80	0.20 (12 minutes)	16
Total					42,416

[1]There are no capital costs or operating and maintenance costs associated with this collection of information.

12b. Annualized Cost Burden Estimate

The industry burden estimate calculated above would result in labor costs. FDA Economics Staff estimates that these types of notifications would likely be by a general operations manager for manufacturers, repackagers, and wholesale distributors and a pharmacist for a dispenser. The adjusted mean hourly wage including benefits and overhead is $139.56 for manufacturers and repackagers, as reported by the U.S. Department of Labor, Bureau of Labor Statistics, 2013

Employment Occupational Statistics for Management Occupations in Pharmaceutical and Medicine Manufacturing (North American Industry Notification, NAICS, code 325400). The mean hourly wage including benefits and overhead for wholesale distributors is $136.88 according to the U.S. Department of Labor, Bureau of Labor Statistics, 2013 Employment Occupational Statistics for Management Occupations in Drug and Druggists Sundries Merchant Wholesalers (North American Industry Notification, NAICS, 424200). The mean hourly wage including benefits and overhead for a pharmacist is $113.32 as reported by the U.S. Department of Labor, Bureau of Labor Statistics, 2013 Employment Occupational Statistics for Management Occupations for Pharmacies and Drug Stores (North American Industry Notification, NAICS, code 446110). Using these wage rates, the total labor costs for the activities listed above for each group are in Table 5 below. The total labor cost for this information collection equals approximately $**11,912,942**.

Table 5—Annualized Cost Burden Estimate

Trading Partner	**Activity**	**Total Burden Hour**	**Hourly Wage Rate**	**Total Respondent Cost**
Manufacturer/Repackager	Notify FDA	800	$139.56	$111,648
Manufacturer/Repackager	Notify Trading Partners	4800	$139.56	$669,888
Manufacturer/Repackager	Request Termination	800	$139.56	$111,648
Manufacturer/Repackager	Terminate with Trading Partners	4800	$139.56	$669,888
Total Manufacturer/Repackager				**$1,563,072**
Wholesale Distributor	Notify FDA	160	$136.88	$21,901
Wholesale Distributor	Notify Trading	37,600	$136.88	$5,146,688

	Partners			
Wholesale Distributor	Request Termination	160	$136.88	$21,901
Wholesale Distributor	Terminate Trading Partners	37,600	$136.88	$5,146,688
Total Wholesale Distributor				**$10,337,178**
Pharmacist	Notify FDA	40	$113.32	$4,533
Pharmacist	Notify Trading Partners	16	$113.32	$1,813
Pharmacist	Request Termination	40	$113.32	$4,533
Pharmacist	Terminate Trading Partners	16	$113.32	$1,813
Total Pharmacist				**$12,692**
Total Stakeholder costs				**$11,912,942**

13. Estimates of Other Total Annual Cost Burden to Respondents and/or Recordkeepers/Capital Costs

There are no capital, start-up, operating or maintenance costs associated with this information collection. Under the guidance, manufacturers/repackagers, wholesale distributors, and pharmacies may notify their trading partners using existing systems and processes used for similar types of communications, which may include but is not limited to posting of notifications on a company website, sending an email, telephoning, mailing or faxing a letter or notification.

14. Annualized Cost to the Federal Government

The FDA developed the Form FDA 3911 using staff and contractor resources. Existing data management systems are being modified to accept the information in the notifications. The data management system will send a receipt and case number back to the notifying party, facilitate the linking of initial notifications with follow-up information and the request for termination, track assignments to FDA staff, and monitor responses to "FDA consults" for requests for termination.

FDA project management staff and contractor resources have been used to develop the Form FDA 3911 and to modify the current data management systems. These costs are one time set-up costs as indicated in Table 6 below.

Beginning January 1, 2015, manufacturers, repackagers, wholesale distributors, and dispensers (pharmacies) are to submit notification to FDA when an illegitimate product has been identified in the possession or control of the trading partner or, for manufacturers, a product with a high risk of illegitimacy has been identified. FDA staff will review notifications to see if further information or action is needed. After the trading partner believes that the notification is no longer needed, the trading partner will send a request for termination to FDA which is a request to consult with FDA. FDA staff will review the information in the request and determine if the notification can be terminated and respond to the consultation request in writing. FDA estimates receiving 1,000 notifications per year. There will be a lag in the requests for terminations but eventually we believe there will be about 1,000 per year. A contractor will be used to maintain the database. The Annualized Government cost estimates for the years following year 1 are $547,764 as indicated in Table 7.

Table 6 – Government Costs for Year 1

Type of Activity	Est. No. Hours	Hourly Rate	Total Cost
FDA Program Management for form and database development	600	$132.00	$79,200
FDA Project Management	800	$132.00	$105,600
Contract Costs for database and form development			$341,324

Total Costs for Year 1			**$526,124**

Note: The hourly rate is determined by dividing the Agency's fully-loaded cost of $275,000 per FTE by the number of hours per FTE per year (2,080) to arrive at $132 per hour.

Table 7 – Annualized Government Costs Year 2 -

Type of Activity	Est. No. Hours	Hourly Rate	Total Cost
Review of notifications	500	$137	$68,500
Review requests for terminations	1,000	$137	$137,000
Draft, clear and send responses for terminations	2,000	$137	$274,000
Contract costs for operation and maintenance of database			$68,264
Totals	3,500		$547,764

Notes:

1. The hourly rate is determined by dividing the Agency's fully-loaded cost of $285,000 per FTE (for years after 2015) by the number of hours per FTE per year (2,080) to arrive at $137 per hour.

2. The annual FTE impact is (3,500 / 2,080 hours per year) = 1.7FTE.

15. Explanation for Program Changes or Adjustments

This is a new data collection.

16. Plans for Tabulation and Publication and Project Time Schedule

There are no plans for tabulation and publication and project time scheduling.

17. Reason(s) Display of OMB Expiration Date is Inappropriate

The OMB expiration data will be displayed where required.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.