Notifying FDA of a Permanent Discontinuance or Interruption in Manufacturing Under Section 506C of the FD&C Act

Guidance for Industry

In light of the Coronavirus Disease 2019 (COVID-19) public health emergency, this guidance is being implemented without prior public comment in accordance with 21 U.S.C. 701(h)(1)(C)(i)) and 21 CFR 10.115(g)(2), but it remains subject to comment in accordance with the Agency's good guidance practices. Comments may be submitted at any time for Agency consideration. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Submit electronic comments to https://www.regulations.gov. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this document, contact (CDER) Drug Shortage Staff, 240-402-7770, or (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010.

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

March 2020
Procedural

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U.S. Department of Health and Human Services
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Notifying FDA of a Permanent Discontinuance or Interruption in Manufacturing Under Section 506C of the FD&C Act Guidance for Industry[1]

I. INTRODUCTION

The Food and Drug Administration (FDA or Agency) plays a critical role in protecting the United States from threats including emerging infectious diseases, including the Coronavirus Disease 2019 (COVID-19) pandemic. FDA is committed to providing timely guidance to support response efforts to this pandemic.

Due to the COVID-19 pandemic, FDA has been closely monitoring the medical product supply chain with the expectation that it may be impacted by the COVID-19 outbreak, potentially leading to supply disruptions or shortages of drug and biological products in the United States. FDA is issuing this guidance to assist applicants and manufacturers in providing FDA timely, informative notifications about changes in the production of certain drugs and biological products that will, in turn, help the Agency in its efforts to prevent or mitigate shortages of such products.

The guidance discusses the requirement under section 506C of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 356c) and FDA's implementing regulations for applicants and manufacturers to notify FDA of a permanent discontinuance in the manufacture of certain products or an interruption in the manufacture of certain products that is likely to lead to a meaningful disruption in supply of that product in the United States.[2] This guidance also recommends that applicants and manufacturers provide additional details and follow additional procedures to ensure FDA has the specific information it needs to help prevent or mitigate shortages. In addition, the guidance explains how FDA communicates information about products in shortage to the public.

[1] This guidance has been prepared by the Drug Shortage Staff and the Office of Regulatory Policy in the Center for Drug Evaluation and Research (CDER), in conjunction with the Office of Compliance and Biologics Quality in the Center for Biologics Evaluation and Research (CBER).

[2] This guidance addresses only the notification requirement in section 506C of the FD&C Act; it does not address the contents of other notifications, for example, those that may be required under section 506I of the FD&C Act (21 U.S.C. 356i) when drug products are discontinued.

Given the public health emergency related to COVID-19 declared by the Department of Health and Human Services (HHS), this guidance is being implemented without prior public comment because the FDA has determined that prior public participation for this guidance is not feasible or appropriate (see section 701(h)(1)(C)(i) of the FD&C Act and 21 CFR 10.115(g)(2)). This guidance document is being implemented immediately, but it remains subject to comment in accordance with the Agency's good guidance practices.

This guidance is intended to remain in effect for the duration of the public health emergency related to COVID-19 declared by HHS, including any renewals made by the Secretary in accordance with section 319(a)(2) of the Public Health Service Act (42 U.S.C. 247d(a)(2)). However, the recommendations and processes described in the guidance are expected to assist the Agency more broadly in its efforts to prevent and mitigate shortages, including under circumstances outside of the COVID-19 public health emergency, and reflect the Agency's current thinking on this issue. Therefore, within 60 days following the termination of the public health emergency, FDA intends to revise and replace this guidance with any appropriate changes based on comments received on this guidance and the Agency's experience with implementation.

In general, FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

There is currently an outbreak of respiratory disease caused by a novel coronavirus. The virus has been named "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2) and the disease it causes has been named "Coronavirus Disease 2019" (COVID-19). On January 31, 2020, HHS issued a declaration of a public health emergency related to COVID-19 and mobilized the Operating Divisions of HHS.[3] In addition, on March 13, 2020, the President declared a national emergency in response to COVID-19.[4] As explained above, during the COVID-19 outbreak, FDA has been closely monitoring the medical product supply chain with the expectation that it may be impacted by the COVID-19 outbreak, potentially leading to supply disruptions or shortages of drug and biological products in the United States.

Title X of the Food and Drug Administration Safety and Innovation Act (FDASIA), enacted on July 9, 2012,[5] amended the FD&C Act to help the Agency address the problem of drug shortages

[3] Secretary of Health and Human Services Alex M Azar, Determination that a Public Health Emergency Exists. (Jan. 31, 2020), available at https://www.phe.gov/emergency/news/healthactions/phe/Pages/2019-nCoV.aspx).

[4] Proclamation on Declaring a National Emergency Concerning the Novel Coronavirus Disease (COVID-19) Outbreak (Mar. 13, 2020), *available at* https://www.whitehouse.gov/presidential-actions/proclamation-declaring-national-emergency-concerning-novel-coronavirus-disease-covid-19-outbreak/.

[5] Public Law 112-144.

in the United States, including by amending requirements related to notifying FDA about product discontinuances and manufacturing interruptions. While some supply disruptions and shortages cannot be predicted or prevented, early communication and detailed notifications from manufacturers to the Agency play a significant role in decreasing the incidence, impact, and duration of supply disruptions and shortages.

As explained below, under section 506C of the FD&C Act (as amended by FDASIA) and FDA's implementing regulations,[6] persons covered by the notification requirement must notify FDA of a permanent discontinuance in the manufacture of covered drugs and biological products or an interruption in the manufacture of covered drugs and biological products that is likely to lead to a meaningful disruption[7] (or, in the case of blood or blood components intended for transfusion, a significant disruption[8]) in the supply of such products in the United States, and the reasons for such discontinuance or interruption.[9] The products covered by the notification requirement are prescription drugs and biological products (including blood or blood components for transfusion)[10] that are (1) life supporting, life sustaining,[11] or intended for use in the prevention

[6] Section 506C(i) of the FD&C Act required FDA to issue regulations implementing section 506C of the FD&C Act. On July 8, 2015, FDA issued the final rule, "Permanent Discontinuance or Interruption in Manufacturing of Certain Drug or Biological Products" (80 FR 38915) to implement section 506C and other drug shortage provisions of the FD&C Act, as amended by FDASIA (see §§ 310.306, 314.81(b)(3)(iii), and 600.82 (21 CFR 310.306, 314.81(b)(3)(iii), and 21 CFR 600.82)).

[7] *Meaningful disruption* means a change in production that is reasonably likely to lead to a reduction in the supply of a drug by a manufacturer that is more than negligible and affects the ability of the manufacturer to fill orders or meet expected demand for its product, and does not include interruptions in manufacturing due to matters such as routine maintenance or insignificant changes in manufacturing so long as the manufacturer expects to resume operations in a short period of time (see section 506C(h)(3) of the FD&C Act and §§ 314.81(b)(3)(iii)(*f*) and 600.82(f)).

[8] *Significant disruption* means a change in production that is reasonably likely to lead to a reduction in the supply of blood or blood components by a manufacturer that substantially affects the ability of the manufacturer to fill orders or meet expected demand for its product, and does not include interruptions in manufacturing due to matters such as routine maintenance or insignificant changes in manufacturing so long as the manufacturer expects to resume operations in a short period of time (see § 600.82(f)). FDA intends to consider an interruption in manufacturing that leads to a reduction of 20 percent or more of an applicant's own supply of blood or blood components over a 1-month period to "substantially affect" the ability of the applicant to fill orders or meet expected demand; accordingly, such an interruption would be considered a "significant disruption" in supply (see 80 FR 38915 at 38920-21).

[9] Section 506C(i)(3) of the FD&C Act permitted FDA to apply the section, by regulation, to biological products (as defined in section 351 of the Public Health Service Act), including plasma products derived from human plasma protein and their recombinant analogs, if FDA determined that including these products would benefit the public health. FDA's 2015 final rule extended drug shortage notification requirements to applicants of certain biological products, including recombinant therapeutic proteins, monoclonal antibody products, vaccines, allergenic products, plasma derived products and their recombinant analogs, blood or blood components for transfusion, and cellular and gene therapy products (see § 600.82 and 80 FR 38915 at 38918).

[10] For purposes of the notification requirement, the term *product* refers to a specific strength, dosage form, and route of administration of a drug or biological product. See 80 FR 38915 at 38919 and 38928.

[11] *Life supporting or life sustaining* means a product that is essential to or that yields information that is essential to, the restoration or continuation of a bodily function important to the continuation of human life (see §§ 314.81(b)(3)(iii)(*f*) and 600.82(f)).

or treatment of a debilitating disease or condition,[12] including any such product used in emergency medical care or during surgery; and (2) not radiopharmaceutical drug products or any other products designated by FDA.[13] The persons covered by the notification requirement (collectively referred to in this guidance as "manufacturers") are as follows:

- Applicants with an approved new drug application (NDA) or approved abbreviated new drug application (ANDA) for a covered drug product[14]

- Applicants with an approved biologics license application (BLA) for a covered biological product, other than blood or blood components[15]

- Applicants with an approved BLA for blood or blood components for transfusion, if the applicant is a manufacturer of a significant percentage of the U.S. blood supply[16,17]

- Manufacturers of a covered drug product marketed without an approved NDA or ANDA[18]

Under the statute and implementing regulations, the notifications must include, at a minimum:[19]

- Name of the product, including the National Drug Code (NDC) number, or, for biological products, an alternative standard for identification and labeling if one has been recognized as acceptable by the Center Director[20]

- Name of the application holder (for approved products) or manufacturer (for unapproved drugs)

[12] *Intended for use in the prevention or treatment of a debilitating disease or condition* means a product intended for use in the prevention or treatment of a disease or condition associated with mortality or morbidity that has a substantial impact on day-to-day functioning (see §§ 314.81(b)(3)(iii)(*f*) and 600.82(f)).

[13] See section 506C(a) of the FD&C Act; §§ 310.306, 314.81(b)(3)(iii)(*a*), and 600.82(a).

[14] See § 314.81(b)(3)(iii).

[15] See § 600.82(a)(1).

[16] See § 600.82(a)(2).

[17] FDA intends to consider an applicant that holds a BLA for blood or blood components to be a manufacturer of a "significant percentage" of the U.S. blood supply if the applicant manufactures 10 percent or more of the U.S. blood supply (see 80 FR 38915 at 38917).

[18] See § 310.306, which applies § 314.81(b)(3)(iii) in its entirety to covered drug products marketed without an approved NDA or ANDA.

[19] See section 506C(a) of the FD&C Act; §§ 310.306(b), 314.81(b)(3)(iii)(*c*), and 600.82(c).

[20] See § 600.82(c)(1).

- Whether the notification relates to a permanent discontinuance of or an interruption in manufacturing the product

- Description of the reason for the permanent discontinuance or interruption in manufacturing

- Estimated duration of the interruption in manufacturing

Notifications under section 506C of the FD&C Act must be submitted to FDA at least 6 months in advance of a permanent discontinuance or an interruption in manufacturing.[21] However, if 6 months advance notice is not possible because the discontinuance or interruption in manufacturing was not reasonably anticipated, then the notification must be submitted as soon as practicable thereafter, but in no case later than 5 business days after the discontinuance or interruption in manufacturing occurs.[22]

Consistent with section 506E of the FD&C Act (21 U.S.C. 356e) and the implementing regulations,[23] FDA maintains up-to-date lists of drugs and biological products that FDA has determined to be in shortage in the United States.[24] These lists include:

- Established name of the product in shortage; brand name of the product in shortage, if applicable; the NDC number, presentation, strength(s), and package size, as available

- Name of each application holder (for approved products) or manufacturer (for unapproved drugs)

- Name of the distributor, if different from the application holder (for approved products) or manufacturer (for unapproved drugs)

- Reason for the shortage from the following categories:

  - Requirements related to complying with good manufacturing practices
  - Regulatory delay
  - Shortage of an active ingredient
  - Shortage of an inactive ingredient component
  - Discontinuation of the manufacture of the product
  - Delay in shipping
  - Demand increase
  - Other reason

[21] See section 506C(b) of the FD&C Act; §§ 310.306(b), 314.81(b)(3)(iii)(*b*)(*1*), and 600.82(b)(1).

[22] See section 506C(b) of the FD&C Act; §§ 310.306(b), 314.81(b)(3)(iii)(*b*)(*2*), and 600.82(b)(2).

[23] See section 506E of the FD&C Act; §§ 310.306(c), 314.81(b)(3)(iii)(*d*)(*1*), and 600.82(d)(1).

[24] See https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm for shortages tracked by CDER; see https://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/Shortages/ucm351921.htm for shortages tracked by CBER.

- Estimated duration of the supply disruption or shortage, anticipated date of availability, and resolution dates

- Any additional information related to the shortage that the manufacturer chooses to share as described below in section IV

III. NOTIFYING FDA OF A PERMANENT DISCONTINUANCE OR AN INTERRUPTION IN MANUFACTURING

A. Why It Is Important To Notify FDA

A critical component of preventing or mitigating drug shortages is for manufacturers to notify FDA as soon as possible of a permanent discontinuance or an interruption in manufacturing that is likely to lead to a meaningful disruption in supply. As well as being timely, it is important that notifications include specific information about the situation that will allow the Agency to evaluate the situation and determine an appropriate course of action.[25] Early, informative notifications are the best tool FDA has to help prevent a shortage from occurring and to mitigate the impact of an unavoidable shortage. When FDA does not receive timely, informative notifications, the Agency's ability to respond appropriately is limited.

Notifications regarding discontinuances or potential manufacturing issues that are sent to FDA to meet other reporting requirements, for example, under section 506I of the FD&C Act (reports of marketing status) or 21 CFR 314.81(b)(1) (field alert reports), are not a substitute for the notifications required under section 506C. It is important that notifications pursuant to section 506C be submitted to the appropriate staff in CDER and CBER (as described in section III.E) to ensure timely review and action by the Agency.

B. Who Should Notify FDA

The notification requirement set forth in section 506C of the FD&C Act and implementing regulations applies to the manufacturers of certain drugs and biological products, as discussed in section II.[26] In general, the notification requirement applies to each individual manufacturer regardless of market share, number of other manufacturers marketing products that are

[25] See CDER's Manual of Policies and Procedures (MAPP) 4190.1, Rev. 3, on *Drug Shortage Management* for information about CDER's policies and procedures for evaluating and managing drug shortage situations, available at: https://www.fda.gov/media/72447/download. See CBER's Standard Operating Procedures and Policies 8506: Management of Shortages of CBER-Regulated Products, Version #3, for information about CBER's policies and procedures for evaluating and managing shortage situations, available at: https://www.fda.gov/media/83301/download

[26] The notification requirement applies regardless of any determination with respect to whether the product is medically necessary (see generally CDER's MAPP 4190.1 Rev. 3).

therapeutically equivalent, or the amount of product that may be in distribution.[27] If a manufacturer is not certain whether products it manufactures are subject to the notification requirement, we recommend that the manufacturer contact the Agency as described in section III.E below.

In the case of products that are marketed under approved applications, the *applicant* is solely responsible for reporting to FDA a permanent discontinuance or an interruption in manufacturing, whether the product is manufactured *by* the applicant itself or *for* the applicant under contract with one or more different entities.[28] Accordingly, the applicant should establish a process with any relevant contract manufacturer, active pharmaceutical ingredient supplier, or other entity that ensures that the applicant can provide a complete and accurate notification to FDA within the required time frame.

C. When To Notify FDA

Manufacturers must inform FDA at least 6 months in advance of (1) a permanent discontinuance in manufacturing of a product or (2) an interruption in manufacturing of a product that is likely to lead to a meaningful disruption in supply of the product in the United States.[29] If 6 months' advance notice is not possible because the discontinuance or interruption was not reasonably anticipated, the notification must be submitted as soon as practicable thereafter, but in no case later than 5 business days after the discontinuance or interruption in manufacturing occurs.[30] After the initial notification of an interruption in manufacturing, FDA recommends that manufacturers provide updates every 2 weeks on the situation, including the expected timeline for recovery, even if the status remains unchanged. These updates are important to ensure that FDA remains informed and can act on the most current information. We recommend that such updates be submitted until the shortage has been resolved (see section IV for a description of when FDA considers a shortage to be resolved.).

FDA interprets a permanent discontinuance to be a decision by the manufacturer to cease manufacturing and distributing a product indefinitely for business or other reasons. All such discontinuances are required to be reported within the time frame described above.[31] Upon receiving such notifications, FDA assesses the potential public health impact of the reported discontinuance and, if needed, may request further discussion with the reporting manufacturer. Manufacturers should not delay notifying FDA until after production has ceased; FDA expects to be notified well before any decline in supply occurs.

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[27] But see section II (explaining that the requirement for blood or blood components intended for transfusion only applies to applicants that manufacture a *significant percentage* of the U.S. blood supply) (emphasis added).

[28] See §§ 314.81(b)(3)(iii)(*a*) and 600.82(a)(1).

[29] See section 506C(b) of the FD&C Act; §§ 310.306(b), 314.81(b)(3)(iii)(*b*)(*1*), and 600.82(b)(1).

[30] See section 506C(b) of the FD&C Act; §§ 310.306(b), 314.81(b)(3)(iii)(*b*)(*2*), and 600.82(b)(2).

[31] See section 506C(a) of the FD&C Act; §§ 310.306(b), 314.81(b)(3)(iii)(*a*), and 600.82(a).

In the case of interruptions in manufacturing, when assessing whether a meaningful disruption in supply is likely to occur, the relevant analysis is whether a change in production is likely to lead to a reduction in the supply of a product *by the manufacturer* that is more than negligible and would affect *the manufacturer's* ability to fill orders or meet expected demand for its product.[32] In other words, the assessment is to be based solely on the reporting manufacturer's capacity and supply. The manufacturer should not consider other manufacturers' or competitors' capacities or assumed capacities, or what it understands about market demand for the product.[33] FDA expects that manufacturers will notify the Agency before a meaningful disruption in their own supply occurs. For example, FDA should not first learn of a supply disruption resulting from an interruption in manufacturing from a purchaser whose order could not be filled by the manufacturer.

If a manufacturer is unsure of whether to notify FDA of an interruption in manufacturing because the firm does not know whether a meaningful disruption in its supply is likely to occur, FDA urges the manufacturer to submit a notification. This would allow FDA to monitor the overall market and take timely steps, as necessary, to help prevent or mitigate any resulting shortage. In addition, if a manufacturer is considering taking an action that may lead to a meaningful disruption in the supply of a product (e.g., holding production to investigate a quality issue or transfer of ownership), FDA requests that the manufacturer notify FDA immediately through the process explained in section III. E.

As described above, the notification requirement in the FD&C Act and the implementing regulations is triggered by a permanent discontinuance or an interruption in manufacturing of certain products, as discussed in section II; however, there are other circumstances as well where FDA requests that manufacturers submit a notification to the Agency. FDA requests that manufacturers notify the Agency when they are unable to meet demand for products covered by the notification requirement,[34] even in the absence of an interruption in manufacturing, for example, when there is a sudden, unexpected spike in demand. Though manufacturers are not required to report this type of situation to FDA, reporting under these circumstances provides an important signal to the Agency about a potential shortage and allows FDA to take appropriate steps to address the potential shortage.

D. What Information To Include in Notifications

As explained above, notifications under section 506C of the FD&C Act are required to include certain information. This information, described in section II, is the minimum that manufacturers must provide. However, to ensure that FDA is better-equipped to help prevent or mitigate a drug

[32] See 80 FR 38915 at 38920. Manufacturers are not required to report interruptions in manufacturing due to matters such as routine maintenance or insignificant changes in manufacturing, so long as the manufacturer expects to resume operations in a short period of time (see section 506C(h)(3)(B) of the FD&C Act).

[33] See 80 FR 38915 at 38920 (explaining that manufacturers are not required or expected to predict the market-wide impact of an interruption in their own manufacturing). But see section II (explaining that the regulatory requirement for blood or blood components intended for transfusion only applies to applicants that manufacture a *significant percentage* of the U.S. blood supply) (emphasis added).

[34] See section II for a description of products covered by the notification requirement.

shortage, FDA recommends that manufacturers provide additional details about the situation and has included below questions for manufacturers to consider as they evaluate the situation and prepare to notify FDA. This list is not intended to be exhaustive; it provides questions to consider that may yield information that would help FDA determine appropriate steps to help prevent or mitigate a shortage. The more information manufacturers are able to provide on these topics, the better FDA is able to assist in preventing or mitigating a shortage.

It is important to note that manufacturers need not have answers to each question before submitting a notification; notifications can be updated at any time to include additional information. Therefore, we recommend that manufacturers not delay notifying the Agency until answers are available, but instead recommend that they provide initial notification as soon as is practicable and additional information as it becomes available.

We recommend considering the following questions when providing notification to FDA:

- Is this notification for an unavoidable supply disruption or a supply disruption that may be preventable?

- What is the underlying reason or root cause leading to this notification? (A detailed and thorough explanation beyond "manufacturing delay" or a recitation of the broad categories of reasons listed above in section II is especially important and allows FDA to identify and use the most appropriate and effective mitigation tools.)

- What is the estimated date of onset of the interruption in manufacturing or supply disruption for this product? If a supply disruption has occurred, what is the estimated duration?[35]

- If the notification is for a permanent discontinuance, what is the anticipated time frame for all existing product (on hand and in distribution channels) to be exhausted?

- What is your estimated market share for the product? Is your entire market share affected by this issue? What is the estimated volume of your historic monthly sales, usage, or demand, as applicable, for this product?

- Is this product manufactured on multiple lines or in multiple facilities?

- How much current inventory of product is at your facility or warehouse?

- When will the last batch of finished product be released into distribution? Based on the current demand, how long do you expect the supply to last in the market without additional releases?

[35] Notifications of interruptions in manufacturing must include the estimated duration of the interruption in manufacturing. See §§ 310.306(b), 314.81(b)(3)(iii)(*c*)(*5*), and 600.82(c)(5).

- Do you have an emergency or reserve supply of this product? Is allocation[36] of supply on hand or your reserve supply an option?

- Have you provided, or will you provide, public information for your stakeholders and patients regarding this actual or potential shortage (e.g., Dear Healthcare Provider (DHCP) Letters, supply or shortage information posted on your website)?

- Do you have a proposal for FDA to review to expedite availability of your product? What do you think FDA can do to help prevent or mitigate a supply disruption?

This information is intended to help FDA assess the situation and take appropriate action. As described further in section IV below, information that is submitted to FDA will not be disclosed except in accordance with applicable disclosure law, which includes restrictions on the release of confidential commercial information and trade secrets.[37] If FDA determines that a product is in shortage, the Agency intends to work with manufacturers to confirm the accuracy and appropriateness of information regarding the shortage before posting publicly on FDA's website.

E. How To Notify FDA

Notifications under section 506C of the FD&C Act must be submitted to FDA electronically in a format that FDA can process, review, and archive.[38] For products regulated by the Center for Drug Evaluation and Research (CDER), manufacturers should submit initial notifications either via email at drugshortages@fda.hhs.gov or through the CDER Direct NextGen Portal at https://edm.fda.gov/wps/portal/. Initial notifications regarding products regulated by the Center for Biologics Evaluation and Research (CBER) should be submitted to FDA electronically via email at cbershortage@fda.hhs.gov. All additional updates should be submitted by email to the applicable Center (CDER or CBER), not through the NextGen Portal.

Manufacturers should submit a separate notification for each permanent discontinuance or interruption in manufacturing. A single initial notification may include a list of all affected products.[39] Manufacturers should not provide notification about a newly affected product (e.g., a new strength) in an update, even if the issue is related to a previously reported interruption in manufacturing. Rather, a separate initial notification should be submitted to ensure the newly affected product is tracked appropriately. In addition, as explained in section III.A, notifications submitted to FDA to satisfy other reporting requirements (e.g., under section 506I of the FD&C Act) are not a substitute for the notifications required under section 506C.

[36] *Allocation* generally refers to limiting the quantity distributed to customers to extend the life of the existing supply.

[37] See section 506C(d) of the FD&C Act.

[38] See §§ 310.306(b), 314.81(b)(3)(iii)(*b*), and 600.82(b); see also 80 FR 38915 at 38922.

[39] See note 10

F. Failure To Notify FDA

If a manufacturer fails to provide notification of a permanent discontinuance or an interruption in manufacturing as required by section 506C(a) of the FD&C Act and in accordance with the timelines set forth in section 506C(b) and the implementing regulations,[40] FDA will issue a letter to that manufacturer stating that the notification requirement was not met (a "noncompliance letter").[41] Note that if FDA determines that an applicant experienced a reportable interruption in manufacturing that it could not reasonably anticipate 6 months in advance, but the applicant failed to notify FDA "as soon as practicable," FDA will issue a noncompliance letter.[42] The manufacturer must respond to FDA's letter within 30 calendar days, providing the reason for noncompliance and the required information on the discontinuance or interruption.[43] Within 45 calendar days of sending the noncompliance letter to the manufacturer, FDA will post that letter and any response received on FDA's website,[44] with appropriate redactions to protect trade secrets or confidential commercial information.[45] However, FDA will not post the noncompliance letter and response if the Agency determines that the noncompliance letter was issued in error or, after review of the manufacturer's response, that the manufacturer had a reasonable basis for not notifying FDA as required.[46]

IV. HOW FDA COMMUNICATES INFORMATION ABOUT DRUGS AND BIOLOGICAL PRODUCTS IN SHORTAGE

FDA maintains public, up-to-date lists of drugs and biological products that the Agency has determined to be in shortage.[47] These lists include, among other information, the established name of the product in shortage, the reason for the shortage, and the estimated duration of the shortage based on information provided by the manufacturer. The reason for the shortage identified on the list is determined by FDA using the notification submitted and any supplementary information gathered, such as from manufacturing facility reviews conducted by FDA. Posted information may also include information that a manufacturer intends to provide or has provided to its stakeholders and patients regarding an actual or potential shortage (e.g., DHCP Letters, informed consent forms, or patient letters). The Agency does not include confidential commercial information or trade secrets.[48]

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[40] Section 506C(b) of the FD&C Act; §§ 310.306(b), 314.81(b)(3)(iii)(*b*)(*1*) and (*2*), and 600.82(b)(1) and (2).

[41] See section 506C(f)(1) of the FD&C Act.

[42] Id.

[43] See section 506C(f)(2) of the FD&C Act.

[44] Links to noncompliance letters can be found at http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm403902.htm.

[45] See section 506C(d), (f)(3) of the FD&C Act.

[46] See section 506C(f)(3) of the FD&C Act.

[47] See note 24.

[48] See section 506E(c)(2) of the FD&C Act.

FDA updates its lists regularly and strives to communicate in *real-time* so that patients and healthcare providers have the most current information on product shortages in the United States. A product is added to the CDER- or CBER-maintained list only after the Agency determines that it is in shortage; products are not added to the list(s) immediately upon receipt of a notification regarding a discontinuance or interruption in manufacturing. In cases where a shortage does not occur or is prevented through FDA or stakeholder intervention, the product will not be posted on the list. FDA generally considers a shortage to be resolved and removes the product from the "current shortage" section of the list based on an evaluation of the entire market, assessing whether all backorders have been filled and supply is meeting or exceeding demand. In making this evaluation, FDA may consider, among other factors, affected market share, ability of alternate manufacturers to cover the demand, and confirmed market stabilization.

In general, FDA works with manufacturers to confirm the accuracy and appropriateness of information before posting publicly on its website(s). FDA will continue to post information on its website(s) consistent with section 506E of the FD&C Act and the implementing regulations (see section II of this guidance), regardless of any additional information manufacturers provide to the Agency based on the recommendations in this guidance.