

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

This guidance is intended to remain in effect until November 7, 2023, unless superseded by a revised final guidance before that date. For further information, refer to 88 FR 15417, March 13, 2023, available at <https://www.federalregister.gov/documents/2023/03/13/2023-05094/guidance-documents-related-to-coronavirus-disease-2019-covid-19>.

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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Contains Nonbinding Recommendations

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1 **Notifying FDA of a Permanent Discontinuance or Interruption in**
2 **Manufacturing Under Section 506C of the FD&C Act**
3 **Guidance for Industry¹**
4

5
6 This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on
7 this topic. It does not establish any rights for any person and is not binding on FDA or the public. You
8 can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.
9 To discuss an alternative approach, contact the FDA office responsible for this guidance as listed on the
10 title page.
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14 **I. INTRODUCTION**
15

16 The Food and Drug Administration (FDA or Agency) plays a critical role in protecting the
17 United States from threats including emerging infectious diseases, including the Coronavirus
18 Disease 2019 (COVID-19) pandemic. FDA is committed to providing timely guidance to support
19 response efforts to this pandemic.
20

21 Due to the COVID-19 pandemic, FDA has been closely monitoring the medical product supply
22 chain with the expectation that it may be impacted by the COVID-19 outbreak, potentially
23 leading to supply disruptions or shortages of drug and biological products in the United States.
24 FDA is issuing this guidance to assist applicants and manufacturers in providing FDA timely,
25 informative notifications about changes in the production of certain drugs and biological
26 products that will, in turn, help the Agency in its efforts to prevent or mitigate shortages of such
27 products.
28

29 The guidance discusses the requirement under section 506C of the Federal Food, Drug, and
30 Cosmetic Act (FD&C Act) (21 U.S.C. 356c) and FDA's implementing regulations for applicants
31 and manufacturers to notify FDA of a permanent discontinuance in the manufacture of certain
32 products or an interruption in the manufacture of certain products that is likely to lead to a
33 meaningful disruption in supply of that product in the United States.² This guidance also
34 recommends that applicants and manufacturers provide additional details and follow additional
35 procedures to ensure FDA has the specific information it needs to help prevent or mitigate
36 shortages. In addition, the guidance explains how FDA communicates information about
37 products in shortage to the public.
38

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.

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

45
46 This guidance is intended to remain in effect for the duration of the public health emergency
47 related to COVID-19 declared by HHS, including any renewals made by the Secretary in
48 accordance with section 319(a)(2) of the Public Health Service Act (42 U.S.C. 247d(a)(2)).
49 However, the recommendations and processes described in the guidance are expected to assist
50 the Agency more broadly in its efforts to prevent and mitigate shortages, including under
51 circumstances outside of the COVID-19 public health emergency, and reflect the Agency's
52 current thinking on this issue. Therefore, within 60 days following the termination of the public
53 health emergency, FDA intends to revise and replace this guidance with any appropriate changes
54 based on comments received on this guidance and the Agency's experience with implementation.

55
56 In general, FDA's guidance documents, including this guidance, do not establish legally
57 enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic
58 and should be viewed only as recommendations, unless specific regulatory or statutory
59 requirements are cited. The use of the word *should* in Agency guidances means that something is
60 suggested or recommended, but not required.

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62

63 **II. BACKGROUND**

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65 There is currently an outbreak of respiratory disease caused by a novel coronavirus. The virus
66 has been named "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2) and the
67 disease it causes has been named "Coronavirus Disease 2019" (COVID-19). On January 31,
68 2020, HHS issued a declaration of a public health emergency related to COVID-19 and
69 mobilized the Operating Divisions of HHS.³ In addition, on March 13, 2020, the President
70 declared a national emergency in response to COVID-19.⁴ As explained above, during the
71 COVID-19 outbreak, FDA has been closely monitoring the medical product supply chain with
72 the expectation that it may be impacted by the COVID-19 outbreak, potentially leading to supply
73 disruptions or shortages of drug and biological products in the United States.

74

75 Title X of the Food and Drug Administration Safety and Innovation Act (FDASIA), enacted on
76 July 9, 2012,⁵ amended the FD&C Act to help the Agency address the problem of drug shortages
77 in the United States, including by amending requirements related to notifying FDA about product

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.

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78 discontinuances and manufacturing interruptions. While some supply disruptions and shortages
79 cannot be predicted or prevented, early communication and detailed notifications from
80 manufacturers to the Agency play a significant role in decreasing the incidence, impact, and
81 duration of supply disruptions and shortages.

82
83 As explained below, under section 506C of the FD&C Act (as amended by FDASIA) and FDA’s
84 implementing regulations,⁶ persons covered by the notification requirement must notify FDA of
85 a permanent discontinuance in the manufacture of covered drugs and biological products or an
86 interruption in the manufacture of covered drugs and biological products that is likely to lead to a
87 meaningful disruption⁷ (or, in the case of blood or blood components intended for transfusion, a
88 significant disruption⁸) in the supply of such products in the United States, and the reasons for
89 such discontinuance or interruption.⁹ The products covered by the notification requirement are
90 prescription drugs and biological products (including blood or blood components for
91 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)).

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

- 96
- 97 • Applicants with an approved new drug application (NDA) or approved abbreviated
98 new drug application (ANDA) for a covered drug product¹⁴
- 99
- 100 • Applicants with an approved biologics license application (BLA) for a covered
101 biological product, other than blood or blood components¹⁵
- 102
- 103 • Applicants with an approved BLA for blood or blood components for transfusion, if
104 the applicant is a manufacturer of a significant percentage of the U.S. blood
105 supply^{16,17}
- 106
- 107 • Manufacturers of a covered drug product marketed without an approved NDA or
108 ANDA¹⁸
- 109

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

- 111
- 112 • Name of the product, including the National Drug Code (NDC) number, or, for
113 biological products, an alternative standard for identification and labeling if one has
114 been recognized as acceptable by the Center Director²⁰
- 115
- 116 • Name of the application holder (for approved products) or manufacturer (for
117 unapproved drugs)
- 118
- 119 • Whether the notification relates to a permanent discontinuance of or an interruption in
120 manufacturing the product

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).

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- 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.

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- 158 • Estimated duration of the supply disruption or shortage, anticipated date of
159 availability, and resolution dates
- 160
- 161 • Any additional information related to the shortage that the manufacturer chooses to
162 share as described below in section IV
- 163
- 164

165 **III. NOTIFYING FDA OF A PERMANENT DISCONTINUANCE OR AN** 166 **INTERRUPTION IN MANUFACTURING**

167 **A. Why It Is Important To Notify FDA**

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

179 Notifications regarding discontinuances or potential manufacturing issues that are sent to FDA to
180 meet other reporting requirements, for example, under section 506I of the FD&C Act (reports of
181 marketing status) or 21 CFR 314.81(b)(1) (field alert reports), are not a substitute for the
182 notifications required under section 506C. It is important that notifications pursuant to section
183 506C be submitted to the appropriate staff in CDER and CBER (as described in section III.E) to
184 ensure timely review and action by the Agency.

185 **B. Who Should Notify FDA**

189 The notification requirement set forth in section 506C of the FD&C Act and implementing
190 regulations applies to the manufacturers of certain drugs and biological products, as discussed in
191 section II.²⁶ In general, the notification requirement applies to each individual manufacturer
192 regardless of market share, number of other manufacturers marketing products that are
193 therapeutically equivalent, or the amount of product that may be in distribution.²⁷ If a

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).

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).

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194 manufacturer is not certain whether products it manufactures are subject to the notification
195 requirement, we recommend that the manufacturer contact the Agency as described in section
196 III.E below.

197
198 In the case of products that are marketed under approved applications, the *applicant* is solely
199 responsible for reporting to FDA a permanent discontinuance or an interruption in
200 manufacturing, whether the product is manufactured *by* the applicant itself or *for* the applicant
201 under contract with one or more different entities.²⁸ Accordingly, the applicant should establish a
202 process with any relevant contract manufacturer, active pharmaceutical ingredient supplier, or
203 other entity that ensures that the applicant can provide a complete and accurate notification to
204 FDA within the required time frame.

C. When To Notify FDA

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

220
221 FDA interprets a permanent discontinuance to be a decision by the manufacturer to cease
222 manufacturing and distributing a product indefinitely for business or other reasons. All such
223 discontinuances are required to be reported within the time frame described above.³¹ Upon
224 receiving such notifications, FDA assesses the potential public health impact of the reported
225 discontinuance and, if needed, may request further discussion with the reporting manufacturer.
226 Manufacturers should not delay notifying FDA until after production has ceased; FDA expects to
227 be notified well before any decline in supply occurs.

228
229 In the case of interruptions in manufacturing, when assessing whether a meaningful disruption in
230 supply is likely to occur, the relevant analysis is whether a change in production is likely to lead
231 to a reduction in the supply of a product *by the manufacturer* that is more than negligible and

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).

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232 would affect *the manufacturer's* ability to fill orders or meet expected demand for its product.³²
233 In other words, the assessment is to be based solely on the reporting manufacturer's capacity and
234 supply. The manufacturer should not consider other manufacturers' or competitors' capacities or
235 assumed capacities, or what it understands about market demand for the product.³³ FDA expects
236 that manufacturers will notify the Agency before a meaningful disruption in their own supply
237 occurs. For example, FDA should not first learn of a supply disruption resulting from an
238 interruption in manufacturing from a purchaser whose order could not be filled by the
239 manufacturer.

240
241 If a manufacturer is unsure of whether to notify FDA of an interruption in manufacturing
242 because the firm does not know whether a meaningful disruption in its supply is likely to occur,
243 FDA urges the manufacturer to submit a notification. This would allow FDA to monitor the
244 overall market and take timely steps, as necessary, to help prevent or mitigate any resulting
245 shortage. In addition, if a manufacturer is considering taking an action that may lead to a
246 meaningful disruption in the supply of a product (e.g., holding production to investigate a quality
247 issue or transfer of ownership), FDA requests that the manufacturer notify FDA immediately
248 through the process explained in section III. E.

249
250 As described above, the notification requirement in the FD&C Act and the implementing
251 regulations is triggered by a permanent discontinuance or an interruption in manufacturing of
252 certain products, as discussed in section II; however, there are other circumstances as well where
253 FDA requests that manufacturers submit a notification to the Agency. FDA requests that
254 manufacturers notify the Agency when they are unable to meet demand for products covered by
255 the notification requirement,³⁴ even in the absence of an interruption in manufacturing, for
256 example, when there is a sudden, unexpected spike in demand. Though manufacturers are not
257 required to report this type of situation to FDA, reporting under these circumstances provides an
258 important signal to the Agency about a potential shortage and allows FDA to take appropriate
259 steps to address the potential shortage.

D. What Information To Include in Notifications

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262
263 As explained above, notifications under section 506C of the FD&C Act are required to include
264 certain information. This information, described in section II, is the minimum that manufacturers
265 must provide. However, to ensure that FDA is better-equipped to help prevent or mitigate a drug
266 shortage, FDA recommends that manufacturers provide additional details about the situation and
267 has included below questions for manufacturers to consider as they evaluate the situation and
268 prepare to notify FDA. This list is not intended to be exhaustive; it provides questions to

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.

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269 consider that may yield information that would help FDA determine appropriate steps to help
270 prevent or mitigate a shortage. The more information manufacturers are able to provide on these
271 topics, the better FDA is able to assist in preventing or mitigating a shortage.

272
273 It is important to note that manufacturers need not have answers to each question before
274 submitting a notification; notifications can be updated at any time to include additional
275 information. Therefore, we recommend that manufacturers not delay notifying the Agency until
276 answers are available, but instead recommend that they provide initial notification as soon as is
277 practicable and additional information as it becomes available.

278
279 We recommend considering the following questions when providing notification to FDA:
280

- 281 • Is this notification for an unavoidable supply disruption or a supply disruption that
282 may be preventable?
- 283
284 • What is the underlying reason or root cause leading to this notification? (A detailed
285 and thorough explanation beyond “manufacturing delay” or a recitation of the broad
286 categories of reasons listed above in section II is especially important and allows
287 FDA to identify and use the most appropriate and effective mitigation tools.)
- 288
289 • What is the estimated date of onset of the interruption in manufacturing or supply
290 disruption for this product? If a supply disruption has occurred, what is the estimated
291 duration?³⁵
- 292
293 • If the notification is for a permanent discontinuance, what is the anticipated time
294 frame for all existing product (on hand and in distribution channels) to be exhausted?
- 295
296 • What is your estimated market share for the product? Is your entire market share
297 affected by this issue? What is the estimated volume of your historic monthly sales,
298 usage, or demand, as applicable, for this product?
- 299
300 • Is this product manufactured on multiple lines or in multiple facilities?
- 301
302 • How much current inventory of product is at your facility or warehouse?
- 303
304 • When will the last batch of finished product be released into distribution? Based on
305 the current demand, how long do you expect the supply to last in the market without
306 additional releases?
- 307
308 • Do you have an emergency or reserve supply of this product? Is allocation³⁶ of supply
309 on hand or your reserve supply an option?

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).

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

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- 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?

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

E. How To Notify FDA

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326

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

335

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

F. Failure To Notify FDA

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347 If a manufacturer fails to provide notification of a permanent discontinuance or an interruption in
348 manufacturing as required by section 506C(a) of the FD&C Act and in accordance with the
349 timelines set forth in section 506C(b) and the implementing regulations,⁴⁰ FDA will issue a letter

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

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).

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350 to that manufacturer stating that the notification requirement was not met (a “noncompliance
351 letter”).⁴¹ Note that if FDA determines that an applicant experienced a reportable interruption in
352 manufacturing that it could not reasonably anticipate 6 months in advance, but the applicant
353 failed to notify FDA “as soon as practicable,” FDA will issue a noncompliance letter.⁴²
354 The manufacturer must respond to FDA’s letter within 30 calendar days, providing the reason for
355 noncompliance and the required information on the discontinuance or interruption.⁴³ Within 45
356 calendar days of sending the noncompliance letter to the manufacturer, FDA will post that letter
357 and any response received on FDA’s website,⁴⁴ with appropriate redactions to protect trade
358 secrets or confidential commercial information.⁴⁵ However, FDA will not post the
359 noncompliance letter and response if the Agency determines that the noncompliance letter was
360 issued in error or, after review of the manufacturer’s response, that the manufacturer had a
361 reasonable basis for not notifying FDA as required.⁴⁶

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364 **IV. HOW FDA COMMUNICATES INFORMATION ABOUT DRUGS AND** 365 **BIOLOGICAL PRODUCTS IN SHORTAGE**

366

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

377

378 FDA updates its lists regularly and strives to communicate in *real-time* so that patients and
379 healthcare providers have the most current information on product shortages in the United States.
380 A product is added to the CDER- or CBER-maintained list only after the Agency determines that
381 it is in shortage; products are not added to the list(s) immediately upon receipt of a notification
382 regarding a discontinuance or interruption in manufacturing. In cases where a shortage does not
383 occur or is prevented through FDA or stakeholder intervention, the product will not be posted on

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.

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384 the list. FDA generally considers a shortage to be resolved and removes the product from the
385 “current shortage” section of the list based on an evaluation of the entire market, assessing
386 whether all backorders have been filled and supply is meeting or exceeding demand. In making
387 this evaluation, FDA may consider, among other factors, affected market share, ability of
388 alternate manufacturers to cover the demand, and confirmed market stabilization.

389
390 In general, FDA works with manufacturers to confirm the accuracy and appropriateness of
391 information before posting publicly on its website(s). FDA will continue to post information on
392 its website(s) consistent with section 506E of the FD&C Act and the implementing regulations
393 (see section II of this guidance), regardless of any additional information manufacturers provide
394 to the Agency based on the recommendations in this guidance.