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**Temporary Policy for
Compounding of Certain Drugs for
Hospitalized Patients by Pharmacy
Compounders not Registered as
Outsourcing Facilities During the
COVID-19 Public Health
Emergency (Revised)**

Guidance for Industry

**April 2020
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**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Office of Compliance**

Preface

Public Comment

This guidance is being issued to address the Coronavirus Disease 2019 (COVID-19) public health emergency. This guidance is being implemented without prior public comment because the Food and Drug Administration (FDA or Agency) has determined that prior public participation for this guidance is not feasible or appropriate (see section 701(h)(1)(C) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 371(h)(1)(C)) 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.

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 FDA-2020-D-1136 and complete title of the guidance in the request.

Additional Copies

Additional copies are available from the FDA webpage titled "COVID-19-Related Guidance Documents for Industry, FDA Staff, and Other Stakeholders," *available at* <https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/covid-19-related-guidance-documents-industry-fda-staff-and-other-stakeholders>, and the FDA webpage titled "Search for FDA Guidance Documents," *available at* <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>. You may also send an e-mail request to compounding@fda.hhs.gov to receive an additional copy of the guidance. Please include the document number FDA-2020-D-1136 and complete title of the guidance in the request.

Questions

For questions about this document, contact FDA's human drug compounding team at compounding@fda.hhs.gov.

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Temporary Policy for Compounding of Certain Drugs for Hospitalized Patients by Pharmacy Compounders not Registered as Outsourcing Facilities During the COVID-19 Public Health Emergency (Revised)

Guidance for Industry

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or Office responsible for this guidance as listed on the title page.

I. Introduction

FDA plays a critical role in protecting the United States from threats such as 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.

FDA is issuing this guidance to communicate its temporary policy for the compounding of certain human drug products for hospitalized patients by State-licensed pharmacies and Federal facilities, including hospital and health system pharmacies, that are not registered with FDA as outsourcing facilities (referred to collectively in this guidance as “pharmacies”) for the duration of the public health emergency declared by the Secretary of Health and Human Services (HHS) on January 31, 2020, or for such shorter time as FDA may announce through updated guidance.

This policy is intended to remain in effect for no longer than the duration of the public health emergency related to COVID-19 declared by HHS, including any renewals made by the HHS Secretary in accordance with section 319(a)(2) of the Public Health Service Act (PHS Act) (42 U.S.C. 247d(a)(2)). FDA is continually assessing the needs and circumstances that make issuance of this guidance appropriate. As relevant needs and circumstances evolve, FDA intends to update, modify, or withdraw policies in this guidance as appropriate.

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Given this public health emergency, and as discussed in the Notice in the *Federal Register* of March 25, 2020, titled “Process for Making Available Guidance Documents Related to Coronavirus Disease 2019,” available at <https://www.govinfo.gov/content/pkg/FR-2020-03-25/pdf/2020-06222.pdf>, this guidance is being implemented without prior public comment because FDA has determined that prior public participation for this guidance is not feasible or appropriate (see section 701(h)(1)(C) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 371(h)(1)(C)) 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.

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 guidance 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 “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.¹ In addition, on March 13, 2020, the President declared a national emergency in response to COVID-19.²

FDA has received a number of reports related to increased demand and supply interruptions involving FDA-approved drug products used in the treatment of hospitalized patients with COVID-19. Many of these drug products are needed to support COVID-19 patients who have been intubated, or for other procedures involved in the care of such patients. Some reports involve drug products that appear on the drug shortage list in effect under section 506E of the FD&C Act (21 U.S.C. 356e) (“FDA’s drug shortage list”). In addition, with respect to certain other drug products needed to support hospitalized COVID-19 patients but that do not appear on FDA’s drug shortage list, certain hospitals have concerns about accessing them due, for example, to regional disparities in COVID-19 infection rates, or other regional conditions that may evolve quickly during the public health emergency.

FDA is working with manufacturers in the global pharmaceutical supply chain to prevent and mitigate drug shortages and access problems, using all of the Agency’s authorities to restore or increase the supply of FDA-approved drug products.

If an FDA-approved drug is on FDA’s drug shortage list, it may be compounded by an outsourcing facility that has registered with FDA or by a licensed pharmacist in a State-licensed pharmacy or

¹ Secretary of Health and Human Services Alex M. Azar, Determination that a Public Health Emergency Exists. (Jan. 31, 2020, renewed April 21, 2020), available at <https://www.phe.gov/emergency/news/healthactions/phe/Pages/default.aspx>.

² Proclamation 9994 of March 13, 2020, 85 FR 15337 (Mar. 18, 2020), available at <https://www.whitehouse.gov/presidential-actions/proclamation-declaring-national-emergency-concerning-novel-coronavirus-disease-covid-19-outbreak/>.

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Federal facility that is not registered as an outsourcing facility.³ However, compounded drug products are not FDA-approved, which means they have not undergone FDA premarket review for safety, effectiveness, and quality.

FDA has issued a temporary policy regarding the compounding of certain drugs for hospitalized patients by outsourcing facilities during the COVID-19 public health emergency, when, among other things, hospitals are unable to obtain FDA-approved versions of these drugs.⁴ As noted in FDA's guidance announcing this policy, outsourcing facilities are required to register with FDA, are inspected by FDA according to a risk-based schedule, and are subject to current good manufacturing practice (CGMP) requirements, among other conditions and requirements.

In contrast, drug products compounded by State-licensed pharmacies and Federal facilities that do not register with FDA as outsourcing facilities are regulated under different conditions, as set forth in section 503A of the FD&C Act. Drug products compounded under section 503A of the FD&C Act are not subject to CGMP requirements, and compounding pharmacies regulated under this section generally do not register with FDA. FDA may only become aware of the drug products compounded by such pharmacies if the Agency receives a report of an adverse event or product quality complaint.

One of the conditions in section 503A of the FD&C Act is that each drug product must be compounded for an identified individual patient based on the receipt of a valid prescription order, or a notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified patient.⁵ The prescription requirement is a critical mechanism to distinguish compounding under section 503A of the FD&C Act from conventional manufacturing, or compounding by outsourcing facilities, and helps ensure that drug products that pharmacies compound under section 503A of the FD&C Act are provided to a patient only based on individual patient need.

Another condition in section 503A of the FD&C Act is that a licensed pharmacist or licensed physician does not compound regularly or in inordinate amounts any drug products that are essentially copies of commercially available drug products.⁶ Although compounded drugs can

³ With respect to pharmacies regulated under section 503A of the FD&C Act, which are the subject of this guidance, the statute provides that a drug product compounded by a licensed pharmacist in a State-licensed pharmacy or a Federal facility can qualify for exemptions from requirements under three other sections of the FD&C Act: adequate directions for use (section 502(f)(1) (21 U.S.C. 352(f)(1))), new drug approval requirements (section 505 (21 U.S.C. 355)), and CGMP requirements (section 501(a)(2)(B) (21 U.S.C. 351(a)(2)(B))) if all of the conditions in section 503A of the FD&C Act (21 U.S.C. 353a) are met. The conditions in section 503A of the FD&C Act that apply to compounding a drug product that is essentially a copy of a commercially available drug do not apply to compounding a drug on FDA's drug shortage list because FDA does not consider products on FDA's drug shortage list to be commercially available. See section 503A(b)(1)(D) of the FD&C Act, and FDA's guidance for industry: *Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act* (January 2018), available at <https://www.fda.gov/media/98973/download>. We update guidances periodically. For the most recent version of the guidance, check the FDA guidance web page at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>.

⁴ Guidance for industry; *Temporary Policy for Compounding of Certain Drugs for Hospitalized Patients by Outsourcing Facilities During the COVID-19 Public Health Emergency* (April 2020), <https://www.fda.gov/media/137031/download>.

⁵ See section 503A(a) of the FD&C Act. See also FDA's guidance for industry *Prescription Requirement Under Section 503A of the Federal Food, Drug, and Cosmetic Act* (December 2016) available at <https://www.fda.gov/files/drugs/published/Prescription-Requirement-Under-Section-503A-of-the-Federal-Food--Drug--and-Cosmetic-Act-Guidance-for-Industry.pdf>.

⁶ Section 503A(b)(1)(D) of the FD&C Act.

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serve an important need, they can also pose a higher risk to patients than FDA-approved drugs. This limitation on the compounding of drugs that are essentially copies of commercially available drug products helps to ensure that drugs compounded under section 503A of the FD&C Act, which are subject to a lower regulatory standard than FDA-approved drugs, are only distributed to health care facilities or dispensed to patients to fulfill the needs of patients whose medical needs cannot be met by an FDA-approved drug.

III. Discussion

Many hospitals are currently experiencing difficulties accessing FDA-approved drug products used for patients with COVID-19. In addition, due to the large number of persons infected with COVID-19 and subsequent hospitalizations, it is possible that other FDA-approved drug products may become unavailable in the future.

As noted above, FDA generally tries to address potential and actual drug shortages by working through the global pharmaceutical supply chain, rather than relying on compounded drugs, and focuses on restoring supplies of FDA-approved drugs. However, in light of unprecedented disruptions to, and demands on, the global pharmaceutical supply chain as a result of the COVID-19 pandemic, and in order to respond to evolving regional conditions, additional flexibility is temporarily needed to help ensure that treatment options are available when hospitals are unable to obtain FDA-approved drugs used for hospitalized patients with COVID-19.

When a hospital is unable to access FDA-approved drug products and is considering the use of compounded drugs for hospitalized patients, outsourcing facilities may be able to offer a supply of compounded drugs that are subject to more robust quality standards than are drugs produced by State-licensed pharmacies or Federal facilities that are not required to comply with CGMP requirements. However, FDA understands that during the COVID-19 public health emergency, even with the regulatory flexibility provided in the guidance for industry *Temporary Policy for Compounding of Certain Drugs for Hospitalized Patients by Outsourcing Facilities During the COVID-19 Public Health Emergency* (April 2020), the drugs compounded by outsourcing facilities also may not be sufficient, in some circumstances, to meet urgent needs.

Therefore, as a temporary measure during the public health emergency related to COVID-19, or for such shorter time as FDA may announce by updating or withdrawing this guidance based on evolving needs and circumstances, FDA does not intend to take action against a pharmacy for compounding a drug that is essentially a copy of a commercially available drug,⁷ or for providing a drug to a hospital without obtaining a patient-specific prescription,⁸ if all of the following circumstances are present⁹ and the other conditions of section 503A of the FD&C Act are met.¹⁰

⁷ *Id.*

⁸ Section 503A(a) of the FD&C Act.

⁹ FDA recognizes that a pharmacy may be able to prepare a drug that meets the condition in section 503A(b)(1)(D) of the FD&C Act, e.g., if the drug is on FDA's drug shortages list, or may provide a drug to a hospital after receiving a valid, patient-specific prescription. This guidance provides temporary regulatory flexibility with respect to the conditions in sections 503A(a) and (b)(1)(D) if a compounded drug violates either or both of these conditions, under the circumstances described herein.

¹⁰ In addition, pharmacy compounders are subject to section 501(a)(2)(A) of the FD&C Act (21 U.S.C. 351(a)(2)(A)), which provides that a drug may not be prepared, packed, or held under insanitary conditions whereby it may have been contaminated with filth, or whereby it may have been rendered injurious to health.

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FDA may withdraw or revise this guidance, at any time and without advance notice, based on the Agency's consideration of patient needs, actual and potential benefits and risks to patients, and any other factors the Agency believes are appropriate.

- a. The compounded drug product appears on the list of drugs used for hospitalized patients with COVID-19 maintained on FDA's website at <https://www.fda.gov/media/138279/download>¹¹ and contains only one active ingredient.
- b. The compounded drug is provided directly to a hospital that informs the pharmacy that:
 - i. The hospital is treating patients with COVID-19; and
 - ii. The hospital has made reasonable attempts to obtain, and has not been able to obtain:
 1. Adequate supplies of an FDA-approved drug product containing the same active ingredient for the same route of administration, and
 2. Adequate supplies of a product made by an outsourcing facility containing the same active ingredient for the same route of administration.
- c. The compounded drug product is labeled with a default beyond-use-date (BUD) in accordance with the table in Appendix A,¹² except that the pharmacy uses a shorter BUD:
 - i. If literature or other scientific information, including relevant commercially available product labeling for a similar drug (e.g., components, dosage form, route of administration, primary container-closure type), indicates that the drug product may not be physicochemically stable for the duration of the default BUD period listed in Appendix A, in which case the pharmacy uses such shorter BUD that is supported by the literature or other scientific information, or
 - ii. If the pharmacy has been unable to obtain a sufficient supply of the personal protective equipment (PPE) that it typically relies on to assure compliance with the insanitary condition provision in the FD&C Act¹³ (or PPE that is equivalent or better), in which case the pharmacy applies BUDs of 24 hours for products stored at room temperature and 3 days for products stored refrigerated.¹⁴

¹¹ We recommend checking this list periodically for updates.

¹² When preparing these products, it is important that pharmacies consider storage and handling conditions per USP standards and approved labeling for the comparable FDA-approved product. In addition, as a general matter, pharmacies should be aware of communications related to certain syringes and rubber stoppers associated with loss of potency in certain products: <https://www.fda.gov/drugs/drug-safety-and-availability/fda-notifies-health-care-professionals-becton-dickinson-replaced-problematic-rubber-stoppers-its>.

¹³ Section 501(a)(2)(A) of the FD&C Act.

¹⁴ In this case, the pharmacy should prepare drugs as described in this guidance document and FDA's *Temporary Policy Regarding Non-Standard PPE Practices for Sterile Compounding by Pharmacy Compounders not Registered as Outsourcing Facilities During the COVID-19 Public Health Emergency* (April 2020) (Non-Standard PPE guidance). FDA intends to apply the enforcement discretion policy in its Non-Standard PPE guidance if the compounded drug product is prepared as described in this guidance and the Non-Standard PPE guidance, even if the drug product fails to comply with the prescription requirement in section 503A(a) or the essentially a copy condition in section 503A(a)(2)(D).

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- d. If the pharmacy and the hospital are not owned and controlled by the same entity, the pharmacy (1) marks the order with a notation indicating that the drug is provided to the hospital to treat patients during the COVID-19 public health emergency; and (2) requests that the hospital provide, to the extent allowed by applicable laws, the records that identify the patients to whom the drugs were administered and document such request within one month of sending the compounded drug to the hospital.
- e. Before providing the drug product to the hospital, a State-licensed pharmacy notifies the following State authorities, and the State authorities inform the pharmacy that they do not object to the pharmacy providing the drug product to the hospital without first obtaining a patient-specific prescription:
 - i. The State authority that regulates pharmacy compounding in the State where the pharmacy is located, and,
 - ii. If different, the State authority that regulates pharmacy compounding in the State where the hospital is located.¹⁵
- f. The pharmacy reports adverse events associated with the products produced under this enforcement policy as soon as possible but no later than 15 days after receipt of such information to FDA's [MedWatch Adverse Event Reporting](#) program,¹⁶ and includes, at minimum, compounder name and contact information, patient information (if available), product information (ingredients, strength, dosage form, lot number, and beyond-use date), and description of the adverse event.

FDA recommends that hospitals that obtain non-patient-specific supplies of drugs on the list of drugs used for hospitalized patients with COVID-19 maintained on FDA's website at <https://www.fda.gov/media/138279/download> from pharmacies maintain records of both the entity supplying the hospitals with such products and the patients that receive such products. FDA also encourages hospitals to provide to the pharmacies, to the extent allowed by applicable laws, records that identify the patients to whom the drugs were administered. Such records may be important to allow follow-up if quality issues or adverse events are reported associated with drugs the pharmacy has provided.

¹⁵ FDA recommends that State-licensed pharmacies consult with State authorities regarding local requirements.

¹⁶ The pharmacy should complete and submit Form FDA 3500 for Healthcare Professionals online at <https://www.accessdata.fda.gov/scripts/medwatch/index.cfm>, or should download and complete the form at <https://www.fda.gov/media/76299/download> and then submit it via fax at 1-800-FDA-0178.

Appendix A: Beyond Use Dates

| Processing Conditions | Storage Conditions | |
|--|--|-----------------------------|
| | Controlled Room Temperature (20° to 25°C) | Refrigerator (2° to 8°C) |
| <ul style="list-style-type: none">• Finished drug product is aseptically processed; and• A sterility test has not been completed before release | 4 days | 6 days |
| <ul style="list-style-type: none">• Finished drug product is terminally sterilized;• A verified sterilization cycle that uses biological indicators is employed; and• A sterility test has not been completed before release | 10 days | 12 days |
| <ul style="list-style-type: none">• Finished drug product is aseptically processed or terminally sterilized and has a completed, passing sterility test before release¹⁷ | 20 days | 22 days |

¹⁷ The default beyond use dates in this row include the time necessary to complete a sterility test, which may include rapid sterility test methods as well as sterility testing described under US Pharmacopeia (USP) General Chapter <71>.