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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

Guidance for Industry

April 2020

**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 the 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 web page 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 web page 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 a 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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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

The Food and Drug Administration (FDA or Agency) 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.

Due to the COVID-19 pandemic, FDA has received a number of queries from compounders related to the impact of supply interruptions of face masks, gowns, gloves, and other garb, which we refer to collectively in this document as *personal protective equipment (PPE)*.¹

¹ For the purposes of this guidance, the term *PPE* includes face masks, gloves, gowns, shoe covers, hair/head covers, and other garb worn during the compounding of drug products that are intended to be sterile, to help protect the product from contamination. Although the focus of this guidance is protection of the product, we use “PPE” as a matter of consistency with nomenclature in USP General Chapter <797>. This guidance does not address PPE use during compounding of hazardous drugs (e.g., drugs that are carcinogenic).

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FDA is issuing this guidance to communicate its temporary policy related to PPE use during human drug compounding^{2,3} at State-licensed pharmacies or Federal facilities that are not registered with FDA as outsourcing facilities (referred to collectively in this guidance as *compounders*).⁴ This policy is intended to remain in effect only for the duration of the public health emergency related to COVID-19 declared by the U.S. Department of Health and Human Services (HHS), including any renewals made by the HHS Secretary in accordance with section 319(A)(2) of the Public Health Service Act (42 U.S.C. 247d(a)(2)).

Given this public health emergency, and as discussed in the Notice in the *Federal Register* of March 25, 2020 (58 FR 16949), 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.⁵ In addition, on March 13, 2020, the President declared a national emergency in

² This policy is distinct from FDA’s policy regarding the use of PPE by health care professionals that engage in patient care during the COVID-19 public health emergency, where the primary consideration is protection of the health care professional.

³ This guidance was prepared by multiple offices in the Center for Drug Evaluation and Research, in consultation with the Center for Devices and Radiological Health, the Center for Veterinary Medicine, and the Office of Regulatory Affairs. This guidance and other guidances are available on the FDA web page titled “COVID-19-Related Guidance Documents for Industry, FDA Staff, and Other Stakeholders” (<https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/covid-19-related-guidance-documents-industry-fda-staff-and-other-stakeholders>).

⁴ This guidance applies only to compounders regulated under section 503A of the FD&C Act (21 U.S.C. 353a) and does not apply to outsourcing facilities, which are subject to current good manufacturing practice requirements and under which different PPE considerations may apply. FDA may issue further guidance for outsourcing facilities if warranted.

⁵ 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>.

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response to COVID-19.⁶

The COVID-19 pandemic has led to significant effects on health care systems and has resulted in an increased demand from health care professionals for personal protective equipment (PPE). FDA understands that the need for PPE may outpace the supply available to health care professionals during the pandemic, and that this demand has also affected the supply available to compounders.

Personnel who compound human drugs that are intended or required to be sterile use PPE to reduce the risk of microbes and other particles present on human skin, hair, and clothing contaminating a drug product they are preparing. PPE used in sterile compounding is carefully manufactured, maintained, and used to serve this purpose. If contaminants enter a purportedly sterile drug product during compounding, they could be introduced into the patient's bloodstream, eye, or spinal cord and have the potential to cause serious infection and death.

Under the FD&C Act, a drug is adulterated if it has been 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 (section 501(a)(2)(A) of the FD&C Act (21 U.S.C. 351(a)(2)(A)) (insanitary conditions provision). Drug compounders are not exempt from this provision, which remains in effect as an important protection for patient health and drug quality. Examples of insanitary conditions related to improper use of PPE applicable to the production of sterile drugs, include but are not limited to, the following:

- Performing aseptic manipulations with exposed skin or hair in International Organization for Standardization Class 5 (ISO 5) areas
- Engaging in aseptic processing wearing critical gown components (e.g., gloves) that are non-sterile
- Putting on gowning apparel in a way that may cause the gowning apparel to become contaminated
- Engaging in aseptic processing after leaving the cleanroom and reentering from a non-classified area without first replacing gowning apparel (e.g., mask, goggles, foot covers, gloves)
- Failing to disinfect or change gloves frequently enough given the nature of the operations to prevent contamination

⁶ 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/>.

III. Discussion

FDA understands that due to the COVID-19 pandemic, some compounders are currently experiencing difficulties obtaining PPE and that these supply challenges may be especially acute for hospital and health-system pharmacies.

In areas where PPE shortages become severe, such shortages have the potential to significantly impact the quality, purity, and even the availability of drugs that are compounded for patients, including those in critical need.

Preserving PPE Supply and Obtaining Alternative Equivalent or Better PPE

If the PPE a compounder relies on is in limited supply, we recommend the compounder modify its practices as follows:

- Preserve the supply of available PPE by:
 - Limiting the number of personnel conducting sterile compounding activities.
 - Reducing sterile compounding activities, considering the risks and need for the compounded product intended to be sterile.
- If obtainable, use other PPE that confer equivalent or better protection for the compounded product intended to be sterile.⁷

FDA Enforcement Policy

Further, as a temporary measure during the public health emergency posed by COVID-19, or until FDA otherwise withdraws or revises this guidance, and while PPE shortages impact compounding operations, FDA does not intend to take enforcement action regarding compliance with the insanitary conditions provision when drugs intended or expected to be sterile are compounded without standard PPE⁸ provided the following circumstances are present:

⁷ For information on FDA-regulated PPE, please see FDA's guidance entitled *Enforcement Policy for Face Masks and Respirators During the Coronavirus Disease (COVID-19) Public Health Emergency (Revised)* (April 2020) and FDA's guidance entitled *Enforcement Policy for Gowns, Other Apparel, and Gloves During the Coronavirus Disease (COVID-19) Public Health Emergency* (March 2020). We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>. Note that this guidance does not address PPE use during compounding of hazardous drugs.

⁸ Specifically, FDA does not intend to take action for violations of the insanitary conditions requirement in section 501(a)(2)(A) of the FD&C Act for compounding without standard PPE under the circumstances described in this guidance document. The policy in this guidance does not apply to other conditions under which compounded drugs are prepared, packed, or held, e.g., conditions relating to the design of the compounding area and surrounding areas. In addition, the policy does not extend to products that are deemed adulterated for reasons other than the insanitary conditions provision in section 501(a)(2)(A), e.g., actual contamination that violates section 501(a)(1).

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- (1) The compounder is unable to obtain sufficient supply of PPE that it typically relies on (or PPE that is equivalent or better) to assure compliance with the insanitary conditions provision for its compounding activities (referred to as *standard PPE*). If PPE is not appropriate to assure compliance with the insanitary conditions provision (e.g., if a mask is beyond the manufacturer's shelf life or is reused) it is not considered standard PPE for purposes of this guidance.
- (2) The drugs compounded meet the conditions in section 503A of the FD&C Act (21 U.S.C. 353a) and applicable FD&C Act requirements.
- (3) The compounder:
 - a. employs the mitigation strategies as described below to reduce the risk of product contamination related to compounding when compounding is performed without standard PPE; or
 - b. employs terminal sterilization where standard PPE is not used, as long as basic garbing expectations (e.g., hairnet, clean garment, non-sterile gloves, other appropriate coverings) are followed.
- (4) The compounder:
 - a. keeps a record when compounding is performed without standard PPE;
 - b. keeps a record when there are changes in the sterilization approach (e.g., from aseptic processing to terminal sterilization); and
 - c. documents mitigation strategies in a new or updated standard operating procedure.

Records of compounding without standard PPE may be essential to allow follow-up if quality issues or adverse events are reported for the products the compounder has released.

Although FDA is establishing this temporary policy due to the current public health emergency, FDA expects that compounders will carefully consider the risk and benefit of conducting compounding activities without standard PPE by considering the potential for contamination of the product, risk to patients, and the need for the drug to support patient care. FDA expects compounders will be in close communication with prescribers and other providers to support these decisions during this time.

Mitigation Strategies to Reduce the Risk of Product Contamination Related to Compounding Without Standard PPE

Strategies related to reuse of PPE or the use of inferior PPE

- Use unused face masks, gloves, or other PPE that is beyond the manufacturer-designated shelf life, only if the PPE has been stored under appropriate conditions and has no visible holes, discoloration, or other physical defects.
- If masks that are beyond their manufacturer-designated life are unavailable:

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- Reuse masks during the same shift, taking care to handle and store them when not in use in a manner consistent with minimizing contamination. Masks should not be removed from the compounding area between periods of use and should not be shared among personnel.
- If extending the use of masks to an entire shift does not alleviate the supply issue, reuse masks on subsequent days only if masks have no visible holes, discoloration, or other physical defects. Store masks to be reused in clean, low-particle-shedding fabric mesh bags or stainless steel lattice containers that allow for airflow and can promote drying, and that are kept in a controlled or classified area.
- Use an appropriate agent to disinfect masks when reused multiple times based on mask material, scientific data, and user safety.
- If masks are unavailable and reuse as described in the three bullets immediately above does not adequately alleviate the supply issue, use clean fabric to cover the nose and mouth, but only if new coverings are used for each compounding session and the fabric is labeled as low linting.
- If sterile gloves that are beyond their manufacturer-designated shelf life are unavailable, use nonsterile gloves that have been disinfected with an appropriate agent, based on the agent's compatibility with glove material of construction, disinfectant efficacy data, and user safety and toxicity information.
- Foot covers should not be reused. If unused foot covers that have no visible holes or discoloration are unavailable, use dedicated cleanroom shoes that are regularly cleaned and disinfected.

Strategies to reduce risk of contamination in the compounding environment when compounding without standard PPE

- Increase the frequency of cleaning and disinfecting surfaces within compounding areas.
- Judiciously use sporicidal agents on surfaces within compounding areas.
- Disinfect gloves more frequently during compounding activities.
- Consider more frequent environmental monitoring (e.g., fingertip sampling after each shift, weekly surface sampling in ISO 5 areas, or more frequent passive air sampling) to assess the effectiveness of cleaning and disinfecting.

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Strategies to reduce risk of microbial proliferation in a potentially contaminated product

- Utilize the following beyond use dates: 24 hours for products stored at room temperature; 3 days for products stored refrigerated; and 45 days for frozen products.
- When available, use a sterilizing and pharmaceutical grade syringe filter during compounding to remove microbial contamination that may have been inadvertently introduced by operating under conditions where standard PPE is unavailable.⁹ This measure is only applicable when the compounded formulation is chemically and physically compatible with the syringe filter. Low-protein binding filters should be used for preparation and administration of biological products.

FDA understands that due to the exigencies of the COVID-19 public health emergency, compounders may consider alternate risk mitigation strategies when standard PPE is unavailable. Compounders should consider such alternate approaches carefully and on a case-by-case basis to evaluate whether they provide protection to the drug product that is comparable to that provided by the risk mitigation strategies described above. FDA does not intend to object to the use of approaches that provide such comparable protection, provided the other circumstances described above¹⁰ are present.

⁹ The compounder may communicate to the provider that risk mitigating strategies have been taken due to lack of standard PPE and that a sterilizing and pharmaceutical grade syringe filter may be used as part of patient administration.

¹⁰ I.e., the circumstances described in items 1, 2, and 4 in this guidance.