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Policy for Certain REMS Requirements During the COVID- 19 Public Health Emergency

Guidance for Industry and Health Care Professionals

March 2020

**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)**

Preface

Public Comment

This guidance is being issued to address the Coronavirus Disease 2019 (COVID-19) public health emergency. This 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 Federal Food, Drug, and Cosmetic Act (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.

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-1106 and complete title of the guidance in the request.

Additional Copies

Additional copies are available from the FDA webpage titled "Coronavirus Disease 2019 (COVID-19)," available at <https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/coronavirus-disease-2019-covid-19> and from 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 druginfo@fda.hhs.gov to receive a copy of the guidance. Please include the document number FDA-2020-D-1106 and complete title of the guidance in the request.

Questions

For questions about this document, contact Claudia Manzo, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 1102, Silver Spring, MD 20993-0002, 301-796-0182, or Office of Communications, Outreach and Development, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993-0002, 240-402-8010 or 1-800-835-4709.

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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 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 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.

FDA is issuing this guidance to communicate its temporary policy for certain risk evaluation and mitigation strategies (REMS) requirements for the duration of the public health emergency (PHE) declared by the Secretary of Health and Human Services (HHS)¹ on January 31, 2020.²

¹ A PHE declaration lasts until the Secretary declares that the PHE no longer exists or upon the expiration of the 90-day period beginning on the date the Secretary declared a PHE exists, whichever occurs first. The Secretary may extend the PHE declaration for subsequent 90-day periods for as long as the PHE continues to exist, and may terminate the declaration whenever he determines that the PHE has ceased to exist.
<https://www.phe.gov/Preparedness/legal/Pages/phe-qa.aspx#faq7>

² The HHS Public Health Emergency Declaration is available at
<https://www.phe.gov/emergency/news/healthactions/phe/Pages/2019-nCoV.aspx>.

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Given this PHE, 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 Federal Food, Drug, and Cosmetic Act (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.

In general, FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidance describes 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 that was first detected in Wuhan City, Hubei Province, China, and that has now been detected in many locations internationally, including cases in the United States. 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, the Department of Health and Human Services (HHS) issued a declaration of a PHE related to COVID-19 and mobilized the Operating Divisions of HHS.³ In addition, on March 13, 2020, the President of the United States declared a National Emergency in response to COVID-19.⁴

Due to the COVID-19 pandemic, the Agency has received a number of queries concerning REMS that include laboratory monitoring requirements and the impact of these requirements on patient access to certain REMS drugs when patients self-isolate or are subject to quarantine.

³ Secretary of Health and Human Services Alex M. Azar II, 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/>.

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Section 505-1 of the FD&C Act (21 U.S.C. 355-1) authorizes FDA to require REMS for certain drugs⁵ if FDA determines that a REMS is necessary to ensure that the benefits of the drug outweigh its risks.^{6, 7, 8}

A REMS may include a Medication Guide, a patient package insert, a communication plan, and/or certain packaging and safe disposal technologies for drugs that pose a serious risk of abuse or overdose.⁹ FDA also may require certain *elements to assure safe use* (ETASU) as part of the REMS for a drug.¹⁰

ETASU may be required if the drug has been shown to be effective, but it is associated with a specific serious risk and can be approved only if, or would be withdrawn unless, such elements are required as part of a strategy to mitigate a specific serious risk(s) listed in the labeling of the drug. ETASU may be required for approved drug products that were initially approved without ETASU when other elements are not sufficient to mitigate a serious risk.

Specifically, ETASU may include one or any combination of the following requirements¹¹:

- Health care providers who prescribe the drug have particular training or experience, or are specially certified;
- Pharmacies, practitioners, or health care settings that dispense the drug are specially certified;
- The drug be dispensed to patients only in certain health care settings, such as hospitals;
- The drug be dispensed to patients with evidence or other documentation of safe use conditions, such as laboratory test results;
- Each patient using the drug be subject to monitoring; or
- Each patient using the drug be enrolled in a registry.

If a REMS includes certain ETASU, the REMS may also include an implementation system to enable the applicant to monitor, evaluate, and improve the implementation of the elements (e.g.,

⁵ Section 505-1 of the FD&C Act applies to applications for prescription drugs submitted or approved under subsections 505(b) (i.e., new drug applications) or (j) (i.e., abbreviated new drug applications) of the FD&C Act and to applications submitted or approved under section 351 (i.e., biologics license applications) of the Public Health Service Act (42 U.S.C. 262). For the purposes of this document, unless otherwise specified, the term *drug* refers to human prescription drugs, including those that are licensed as biological products (biologics).

⁶ Public Law 110-85, September 27, 2007, available at <https://www.gpo.gov/fdsys/pkg/PLAW-110publ85/html/PLAW-110publ85.htm>, accessed November 19, 2018.

⁷ Public Law 112-144, July 9, 2012, available at <http://www.gpo.gov/fdsys/pkg/PLAW-112publ144/pdf/PLAW-112publ144.pdf>, accessed November 19, 2018.

⁸ See Section 505-1(a) of the FD&C Act.

⁹ Section 505-1(e)(2)-(4) of the FD&C Act.

¹⁰ See Section 505-1(f)(1) of the FD&C Act.

¹¹ See Section 505-1(f)(3) of the FD&C Act.

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development of a REMS-specific website or call center to facilitate enrollment; establishment of electronic databases of certified health care settings).¹²

III. Discussion

For a limited number of drugs that are subject to a REMS with ETASU, the REMS requires laboratory testing (e.g., liver enzyme testing) or imaging studies (e.g., magnetic resonance imaging) under sections 505-1(f)(3)(d) or (e) of the FD&C Act (21 U.S.C. 355-1 (f)(3)(d) or (e)).

FDA recognizes that during the COVID-19 PHE, completion of REMS-required laboratory testing or imaging studies may be difficult because patients may need to avoid public places and patients suspected of having COVID-19 may be self-isolating and/or subject to quarantine. Under these circumstances, undergoing laboratory testing or imaging studies in order to obtain a drug subject to a REMS can put patients and others at risk for transmission of the coronavirus.

For drugs subject to these REMS with laboratory testing or imaging requirements, health care providers prescribing and/or dispensing these drugs should consider whether there are compelling reasons not to complete these tests or studies during the PHE, and use their best medical judgment in weighing the benefits and risks of continuing treatment in the absence of laboratory testing and imaging studies. Health care providers should also communicate with their patients regarding these judgments, including the risks associated with it.

Although all REMS requirements remain in effect, FDA does not intend to take enforcement action against sponsors or others for accommodations made regarding laboratory testing or imaging study requirements imposed under sections 505-1(f)(3)(d) or (e) of the FD&C Act (21 U.S.C. 355-1 (f)(3)(d) or (e)) during the PHE declared by the Secretary of HHS on January 31, 2020, provided that such accommodations were made based on the judgment of a health care professional.¹³ Manufacturers should document and summarize in their next REMS Assessment Report steps that were taken to accommodate patient access to these REMS drugs during this COVID-19 PHE.

¹² See Section 505-1(f)(4) of the FD&C Act.

¹³ This guidance is limited to our enforcement policy with respect to laboratory testing and imaging study requirements and does not address other REMS requirements, such as those for in-person administration.