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Supplements for Approved Premarket Approval (PMA) or Humanitarian Device Exemption (HDE) Submissions During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency

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Guidance for Industry and Food and Drug Administration Staff

May 2020

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health (CDRH)
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 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) 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-1138 and complete title of the guidance in the comment.

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 CDRH-Guidance@fda.hhs.gov to receive an additional copy of the guidance. Please include the document number 20028 and complete title of the guidance in the request.

Additional copies are available from the Center for Biologics Evaluation and Research (CBER), Office of Communication, Outreach, and Development (OCOD), 10903 New Hampshire Ave., WO71, Room 3128, Silver Spring, MD 20903, or by calling 1-800-835-4709 or 240-402-8010, by e-mail, ocod@fda.hhs.gov, or from the Internet at https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances.

Questions

For questions about this document regarding CDRH-regulated devices, contact the Office of Regulatory Policy/Division of Submission Support at 301-796-5640 or CDRHPremarketProgramOperations@fda.hhs.gov.

For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach, and Development (OCOD) by email at ocod@fda.hhs.gov or at 800-835-4709 or 240-402-8010.

Supplements for Approved Premarket Approval (PMA) or Humanitarian Device Exemption (HDE) Submissions During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency

Guidance for Industry and Food and Drug Administration Staff

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 provide a policy to help address current manufacturing limitations or supply chain issues due to disruptions caused by the COVID-19 public health emergency.

This policy is intended to remain in effect only for the duration of the public health emergency related to COVID-19 declared by the Secretary of HHS on January 31, 2020, effective January 27, 2020, 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)).

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) 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, effective January 27, 2020, 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]

COVID-19 has demonstrated the capability to spread rapidly, leading to significant impacts on health care systems and causing societal disruption. The potential public health threat posed by COVID-19 is high, both globally and to the United States including reduced availability of components and materials used in device manufacturing, as well as temporary closure of manufacturing facilities. Due to these and other COVID-19 related developments, numerous manufacturers may need to make immediate changes such as adjusting manufacturing processes to allow for social distancing, adapting their manufacturing or design due to supply chain disruption, or to moving device production to a region that is less impacted by COVID-19. To help foster the continued availability of medical devices during the COVID-19 public health emergency, FDA does not intend to object to limited modifications to the design and manufacturing of devices approved through either a PMA or HDE without prior submission of a PMA or HDE supplement or 30-day notice for the duration of the public health emergency.

As discussed below, this policy applies to limited modifications affecting the safety or effectiveness of a device approved through the PMA program that would trigger the requirement that a manufacturer submit a PMA supplement or 30-day notice to FDA per section 515(d)(5)(A) of the FD&C Act and 21 CFR 814.39.[3]

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[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 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/.

[3] FDA's interpretation of this section of the FD&C Act is discussed in the guidance documents "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process," *available at* https://www.fda.gov/regulatory-information/search-fda-guidance-documents/modifications-devices-subject-premarket-approval-pma-pma-supplement-decision-making-process, and "30-Day Notices, 135-Day Premarket Approval (PMA) Supplements and 75-Day Humanitarian Device Exemption (HDE) Supplements for Manufacturing Method or Process Changes," *available at* https://www.fda.gov/regulatory-information/search-fda-guidance-documents/humanitarian-device-exemption-hde-program.

This policy also applies to limited modifications affecting the safety or probable benefit of a device approved through the HDE program which would trigger the requirement that a manufacturer submit an HDE supplement or 30-day notice to FDA per 21 CFR 814.108.[4]

Examples of types of such modifications may include, but are not limited to:

- Design and manufacturing changes to address component unavailability due to supply chain disruptions
- Manufacturing changes to allow the establishment to maintain operations and accommodate social distancing practices
- Changes in manufacturing facility or establishment
- Changes to packaging procedures

We believe this policy may help address current manufacturing limitations or supply chain issues due to COVID-19 disruptions, such as adding production lines or manufacturing at alternative sites which may have different manufacturing equipment to increase manufacturing capacity and supply and/or reduce supply chain interruptions and manufacturing bottlenecks. The policy set forth in this guidance does not apply to design or manufacturing changes made for reasons other than addressing manufacturing limitations or supply chain issues resulting from the COVID-19 public health emergency or to any proposed changes described in a regulatory submission already received by FDA.

III. Discussion

In developing this policy, FDA's intent is to help foster the continued availability of medical devices during the COVID-19 public health emergency while being flexible regarding limited modifications made to devices that are subject to review by FDA through either a PMA/HDE supplement or 30-day notice.

Therefore, for the duration of the public health emergency, FDA does not intend to object to limited modifications to the manufacturing of devices approved through the PMA program or the HDE program, without prior submission of the required PMA or HDE supplement or 30-day notice,[4] where the modification does not create an undue risk in light of the public health emergency, and is necessary to address current manufacturing limitations or supply chain issues due to COVID-19-related disruptions. This policy also applies to limited modifications to address current manufacturing limitations or supply chain issues due to COVID-19 that also result in changes to the performance or design specifications, circuits, components, ingredients, or physical layout of the device which would trigger the requirement to submit a 180-day or real-time PMA supplement[5] or a 75-day HDE supplement.

Examples of circumstances where FDA currently believes a modification would generally not create

[4] For additional information regarding HDE supplements, refer to the guidance document "Humanitarian Device Exemption Program," *available at* https://www.fda.gov/regulatory-information/search-fda-guidance-documents/humanitarian-device-exemption-hde-program.

[5] For more information, see the guidance "Real-Time Premarket Approval Application (PMA) Supplements," a*vailable at* https://www.fda.gov/regulatory-information/search-fda-guidance-documents/real-time-premarket-approval-application-pma-supplements.

such an undue risk in light of the public health emergency, and that may be needed to address current manufacturing limitations or supply chain issues due to COVID-19-related disruptions, include but are not limited to the following:

Changes that generally would require a PMA or HDE supplement[6]:

- Component changes due to supply interruption of the component as a result of COVID-19 and any necessary software or firmware modifications to accommodate such component changes that do not affect the performance of the device
- Device material changes due to changes in manufacturing methods that do not affect the performance of the device

Changes that generally would require a PMA or HDE 30-day notice[7]:

- Supplier changes to maintain continuity in manufacturing where specifications are unchanged
- Equipment changes to allow for processes to perform in equivalent manner to previously approved processes within the same facility
- Changes to accommodate social distancing, such as modification of manufacturing processes to promote social distancing practices among employees/operators
- Automation of existing processes that are fully verified
- Automation of certain processes, such as packaging and labeling processes to accommodate social distancing
- Addition of manufacturing lines to increase capacity in existing facilities approved as part of an original PMA or HDE application or a supplement

Changes that generally would require a PMA or HDE site-change supplement[8]:

- Change in manufacturing facility or establishment to an alternative site with established good manufacturing practices (i.e., compliance with 21 CFR Part 820) or during the public health emergency, to an alternative site that is ISO 13485 certified.

Examples of circumstances where FDA currently believes a modification would create such an undue risk include but are not limited to the following:

- Changes to the intended use of the device, including new indications for use of the device
- Changes to the labeling of the device, that are outside of the scope of recommendations described in other policies for specific devices during the public health emergency[9]
- Changes to the sterility assurance level (SAL) or sterilization method
- Changes to reduce or eliminate quality control testing
- Automation of a manufacturing process that is not fully verified
- A change that affects the performance of the device, but is not caused by component unavailability

Manufacturing and design changes must be performed in accordance with 21 CFR Part 820.

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[6] See 21 CFR 814.39(a).
[7] See 21 CFR 814.39(e), (f).
[8] See 21 CFR 814.39(c). See also the guidance "Manufacturing Site Change Supplements: Content and Submission," guidance document *available at* https://www.fda.gov/regulatory-information/search-fda-guidance-documents/manufacturing-site-change-supplements-content-and-submission.
[9] For more information, see the webpage "COVID-19-Related Guidance Documents for Industry, FDA Staff, and Other Stakeholders," *available at* https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-related-guidance-documents-industry-fda-staff-and-other-stakeholders.

Manufacturers must document any changes to the device in their device master record and change control records and make this information available to FDA, if requested, consistent with 21 CFR 820.30 and 820.180. Component changes must be documented in accordance with 21 CFR Part 820. Such records may include (depending on the specific change):

- Applicable standards to which the component conforms
- Software/firmware verification and validation
- Functional testing
- Mechanical testing (e.g., drop, vibration)
- Temperature testing (e.g., minimum storage, maximum storage, transport)

In the next period report that is due after the modification, and in accordance with the PMA or HDE approval order for the device, FDA recommends that the PMA or HDE holder identify and describe any such modification.