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Providing Regulatory Submissions for Medical Devices in Electronic Format — Submissions Under Section 745A(b) of the Federal Food, Drug, and Cosmetic Act

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Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.

Document issued on September 26, 2019.

You should submit comments and suggestions regarding this draft document within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions about this document regarding CDRH-regulated devices, contact the Office of Regulatory Programs at 301-796-5640 or esubpilot@fda.hhs.gov. For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach, and Development (OCOD) at 1-800-835-4709 or 240-402-8010.

U.S. FOOD & DRUG ADMINISTRATION

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research

Preface

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CDRH

Additional copies are available from the Internet. You may also send an e-mail request to CDRH-Guidance@fda.hhs.gov to receive a copy of the guidance. Please include the document number 19031 and complete title of the guidance in the request.

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Additional copies are available from the Center for Biologics Evaluation and Research (CBER), Office of Communication, Outreach, and Development (OCOD), 10903 New Hampshire Ave., Bldg. 71, Room 3128, Silver Spring, MD 20993-0002, or by calling 1-800-835-4709 or 240-402-8010, by email, ocod@fda.hhs.gov or from the Internet at https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances.

Table of Contents

Providing Regulatory Submissions for Medical Devices in Electronic Format — Submissions Under Section 745A(b) of the Federal Food, Drug, and Cosmetic Act

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Draft Guidance for Industry and Food and Drug Administration Staff

This draft guidance, when finalized, will represent 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

Section 745A(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), amended by section 207 of the FDA Reauthorization Act of 2017 (FDARA) (Pub. L. 115-52[1]), requires that pre-submissions and submissions for devices under section 510(k), 513(f)(2)(A), 515(c), 515(d), 515(f), 520(g), 520(m), or 564 of this Act or section 351 of the Public Health Service Act, and any supplements to such pre-submissions or submissions, including appeals of those submissions, be submitted in electronic format specified by the Food and Drug Administration (FDA or the Agency) beginning on such date as specified by FDA in final guidance. It also mandates that FDA issue draft guidance not later than October 1, 2019, providing for further standards for the submission by electronic format, a timetable for establishment of these further standards, and criteria for waivers of and exemptions from the requirements.[2] In addition, in the Medical Device User Fee Amendments of 2017 (MDUFA IV) Commitment Letter[3] from the Secretary of Health and Human Services to Congress, FDA committed to developing "electronic submission templates that will serve as guided submission preparation tools for industry to

[1] https://www.govinfo.gov/content/pkg/PLAW-115publ52/html/PLAW-115publ52.htm.
[2] See 745A(b)(3)(B).
[3] See 163 CONG. REC. S4729-S4736 (daily ed. August 2, 2017) (Food and Drug Administration User Fee Reauthorization), also available at https://www.fda.gov/media/102699/download.

improve submission consistency and enhance efficiency in the review process" and "[by] FY [fiscal year] 2020, the Agency will issue a draft guidance document on the use of the electronic submission templates." This guidance is intended to satisfy the draft guidance documents referenced in section 745A(b)(3) and the MDUFA IV Commitment Letter.

The Agency has concluded that it is not feasible to describe and implement the electronic format(s) that would apply to all the submissions covered by section 745A(b)(3) in one guidance document. Accordingly, this guidance describes how FDA interprets and plans to implement the requirements of section 745A(b)(3), while individual guidances will be developed to specify the formats for specific submissions and corresponding timetables for implementation. Specifically, this guidance discusses (1) the submission types that must be submitted electronically, (2) the timetable and process for implementing the requirements, and (3) criteria for waivers of and exemptions from the submissions in electronic format requirements.

Under the process described in this guidance, FDA will periodically issue guidances relating to the submission in electronic format guidelines for certain submission types to the Center for Devices and Radiological Health (CDRH) or the Center for Biologics Evaluation and Research (CBER). These submission types are identified in section III.A of this guidance. FDA believes that issuing this guidance related to submissions solely in an electronic format will harmonize and streamline the process for implementing the various requirements for submission in electronic format under section 745A(b) of the FD&C Act. The process described in this guidance is also intended to provide a meaningful opportunity for the public to comment on guidances that the Agency intends to issue pursuant to section 745A(b) of the FD&C Act.

In section 745A(b)(3) of the FD&C Act, Congress granted explicit statutory authorization to FDA to specify in guidance the electronic submissions requirement by providing standards, criteria for waivers and exemptions, and a timetable for such submissions. Accordingly, to the extent that this document provides such requirements under section 745A(b)(3), indicated by the use of mandatory words, such as *must* or *required*, this document is not subject to the usual restrictions in FDA's good guidance practices (GGPs) regulations, such as the requirement that guidances not establish legally enforceable responsibilities. See 21 CFR 10.115(d).

This document provides guidance on FDA's interpretation of the statutory requirement for submission in electronic format; however, this document also contains guidance on additional submission types for which submission in electronic format is anticipated to be recommended. Therefore, to the extent that this guidance describes recommendations that are not "standards," "timetable," or "criteria for waivers" and "exemptions" under section 745A(b)(3), this document does not create or confer any rights for or on any person and does not operate to bind FDA or the public, but does represent the Agency's current thinking on this topic. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff listed on the title page of this guidance.

To comply with the GGP regulations and make sure that regulated entities and the public understand that guidance documents are nonbinding, FDA guidances ordinarily contain standard

language explaining that guidances should be viewed only as recommendations unless specific regulatory or statutory requirements are cited. FDA is not including this standard language in this guidance because it is not an accurate description of all of the effects of this guidance. This guidance contains both binding and nonbinding provisions. Insofar as this guidance provides "standards," "timetable," or "criteria for waivers" and "exemptions" pursuant to section 745A(b) of the FD&C Act, it will have binding effect.

II. Background

Food and Drug Administration Safety and Innovation Act (FDASIA) was enacted on July 9, 2012, amending the FD&C Act by adding section 745A, which addresses submissions in electronic format. Medical device submissions are addressed in section 745A(b), while section 745A(a) applies to drug and biological product submissions.[4] Section 745A(b) of the FD&C Act was amended by FDARA adding section 745A(b)(3).

Section 745A(b)(3)(A) of the FD&C Act authorizes FDA to specify in guidance that submissions (described in section III.A below) are required to be submitted solely in electronic format.

Section 745A(b)(3)(B) of the FD&C Act states that FDA shall issue draft guidance providing for additional standards for submission in electronic format, a timetable for these future standards, and criteria for waivers and exemptions:

> (i) any further standards for submission by electronic forma required under subparagraph (A);
> (ii) a timetable for the establishment by the Secretary of such further standards; and
> (iii) criteria for waivers of and exemptions from the requirements of this subsection.

Section 745A(b)(3)(C) of the FD&C Act provides that FDA will issue final guidance no later than 1 year following the close of the public comment period for the draft guidance.

III. Submissions Under section 745A(b) of the FD&C Act

As discussed in section II above of this guidance, the requirements of section 745A(b) of the FD&C Act apply to all submissions listed in section A below. In this section, we discuss our interpretation of section 745A(b); specifically, its scope, the timetable and process for implementing the requirements under section 745A(b), and waivers of and exemptions from the submissions in electronic format requirements.

[4] The electronic format for submissions requirements of section 745A(a) fall outside the scope of this guidance and are not discussed in this guidance.

A. Which submissions must be submitted solely in electronic format?

In accordance with section 745A(b)(3) of the FD&C Act, submission solely in electronic format is required for the following submission types:

- Premarket notification submissions (510(k)s) under section 510(k);
- Evaluation of automatic class III designation request (De Novos) under section 513(f)(2);
- Premarket approval applications (PMAs), including Transitional PMAs under section 515(c), 515(d);
    - This includes all PMA submission types, including, but not limited to, original PMAs, panel-track supplements, 180-day supplements, manufacturing site change supplements, 30-day notices, 135-day supplements, and post-approval study supplements and reports, as well as amendments involving changes in the correspondent or ownership and requests for extensions.
- Modular PMAs under 515(c)(4);
- Product development protocols (PDPs) under section 515(f);
- Investigational device exemption (IDE) applications under section 520(g);
    - This includes all IDE application types including Original IDEs, IDE reports, IDE supplements and amendments to each of those [see Exemptions below].[5]
- Humanitarian device exemption (HDE) applications under section 520(m);
    - This includes all HDE application types, including, but not limited to, original HDEs, 180-day supplements, manufacturing site change supplements, 30-Day Notices, 135-Day Supplements, and post-approval study supplements and reports, as well as amendments involving changes in the correspondent or ownership and requests for extensions.
- Emergency Use Authorizations (EUAs)[6] under section 564;
- Certain investigational new drug applications (INDs) under section 351 of the Public Health Service (PHS) Act;
    - Applicable only to those INDs required prior to the submission of a BLA for devices that are regulated by CBER as biological products. Such INDs are generally those intended for use in screening donated blood for transfusion transmissible diseases.
- Certain biologics license applications (BLAs) under section 351 of the PHS Act;
    - Applicable only to those devices that are regulated by CBER as biological products whether or not they also require submission of an IND prior to submission of a BLA. Such devices are generally those intended for use in screening donated blood for transfusion transmissible diseases and compatibility testing. This includes Original Applications, Efficacy Supplements, Prior

[5] For a description of IDE application types, please see section 9 of FDA Guidance, "FDA Decisions for Investigational Device Exemption Clinical Investigations," at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-decisions-investigational-device-exemption-clinical-investigations.

[6] For more information on Emergency use authorizations, refer to the FDA guidance, "Emergency Use Authorization of Medical Products," at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities.

Approval Supplements (PAS), Changes Being Effected in 30 Days (CBE-30), Changes Being Effected (CBE), Labeling Supplements, and Annual Reports; and

- Pre-submissions
  - While section 745A(b) does not require the submission of Q-submission types other than pre-submissions to be made in an electronic format, FDA recommends that all Q-submissions be submitted in electronic format to facilitate efficient review. Please refer to the Q-submission Guidance[7] for additional information.

Electronic format for all subsequent submissions to an original submission, including amendments (amendments include add-to-files and appeals), supplements, and reports (reports include annual/periodic and post-approval reports) to the submission types identified above, as well as amendments to supplements and reports, are also required. Please note, section 745A(b) of the FD&C Act does not apply to Medical Device Reports submitted under 21 CFR Part 803.

Whether it is a single-page submission (e.g., a change in correspondent) or a multi-volume submission, the submissions in electronic format requirements apply. A submission that is not in the electronic format(s) described in the relevant guidance document will not be filed or received, unless it has been exempted from the electronic submission requirements or the electronic submission requirements have been waived with respect to that submission.

B. Will FDA issue waivers from the submission solely in electronic format requirements?

The statute allows FDA to set forth criteria for waivers of the electronic submission requirements. The criteria for any waivers, if available, will be discussed in the individual guidances for specific submissions.

C. Which submissions are exempted from the electronic format requirements?

Section 745A(b)(3)(B) authorizes FDA to establish criteria for exemptions from the submission solely in electronic format requirements. As a general matter, the following types of IDE submissions will be exempt from the requirements under section 745A(b)(3):

- compassionate use requests
- adverse event reports (all types, e.g., serious, malfunctions, etc.)

Although submission in electronic format will not be required for these submission types, as per this exemption, FDA encourages submission in electronic format of these submissions, as submission templates become available, to facilitate the review process.

Additional exemptions, if applicable, will be discussed in the individual guidances for specific submissions.

[7] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/requests-feedback-and-meetings-medical-device-submissions-q-submission-program.

Although submission in electronic format is not required under section 745A(b) of the FD&C Act, FDA may also identify and recommend formats for electronic submission for the following:

- Master Access Files (MAFs);
- 513(g) Requests for Information (513(g)s); and
- Clinical Laboratory Improvement Amendments of 1988 (CLIA) categorization requests (CLIA Record; CR) and CLIA Waiver Applications (CW).[8]

Submission in electronic format for these submission types would be on a voluntary basis, as submission templates become available.

D. How will FDA implement specific submissions solely in electronic format requirements

FDA intends to use the following process to specify the electronic formats for submissions under section 745A(b):

1. Individual draft guidance documents will be developed to specify the electronic formats, subject matter, and scope of applicability for submissions under section 745A(b). The draft guidance documents will be posted on CDRH's Web site.

2. The Agency will publish a notice in the *Federal Register* announcing the availability on the FDA Web site of a new or revised submission in electronic format guidance. The notice will identify a comment period for the draft guidance.

3. Once the Agency has completed its review of the draft guidance, including consideration of comments submitted (if any), the Agency will publish a notice in the *Federal Register* announcing the availability on the FDA Web site of the final electronic format guidance. The notice and/or guidance will provide a date on which the new submissions in electronic format will be required for the submission types identified in the guidance document. FDA will post the final guidance on its Devices Guidance Web page.

4. Subsequent revisions or updates to specified formats will be announced on the FDA Web site and published in the *Federal Register*. The notice and/or guidance will provide a date on which the revised or updated electronic format for submissions specified in the guidance will be required.

[8] For additional information about CR and CW submissions, please see FDA's guidance "Administrative Procedures for CLIA Categorization," at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/administrative-procedures-clia-categorization.

E. When will submissions solely in electronic format be required?

As described above, individual guidance documents will be developed to specify the electronic format for each submission type under 745A(b) or identified in this guidance. The required format(s) for the specific submissions and corresponding timetable(s) for implementation will be specified in these individual guidances. Once an individual guidance is finalized and published on FDA's Web site, and the timetable for implementation described in that guidance has passed, the guidance will be considered to have binding effect and the electronic format(s) specified in that guidance must be used for submissions identified in section III.A above.