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

Guidance for Industry

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)

December 2014
Electronic Submissions

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I. INTRODUCTION

Section 745A(a) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), added by section 1136 of the Food and Drug Administration Safety and Innovation Act (FDASIA) (Public Law 112-144), requires that submissions under section 505(b), (i), or (j) of the FD&C Act[2] and submissions under section 351(a) or (k) of the Public Health Service Act (PHS Act)[3] be submitted in electronic format specified by the Food and Drug Administration (FDA or the Agency) beginning no earlier than 24 months after FDA issues a final guidance specifying an electronic submission format.

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(a) in one guidance document. Accordingly, this guidance describes how FDA interprets and plans to implement the requirements of section 745A(a), while individual guidances (e.g., *Providing Regulatory Submissions in Electronic Format -- Standardized Study Data*[4] and *Providing Regulatory and Submissions in Electronic Format -- Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*[5]) 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) exemptions from and criteria for waivers of the electronic submission requirements, and (3) the timetable and process for implementing the requirements.

Under the process described in this guidance, FDA will periodically issue guidances specifying the electronic format for types of submissions to new drug applications (NDAs), abbreviated new drug applications (ANDAs), biologics license applications (BLAs), and investigational new drug applications (INDs) to the Center for Drug Evaluation and Research (CDER) or the Center for Biologics Evaluation and Research (CBER). FDA believes that issuing this electronic submission guidance will harmonize and streamline the process for implementing the various required formats for electronic submissions under section 745A(a) 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(a) of the FD&C Act.

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[1] This guidance has been prepared by the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration.
[2] 21 U.S.C. 355(b), (i), or (j).
[3] 42 U.S.C. 262 (a) or (k).
[4] See http://www.fda.gov/forindustry/datastandards/studydatastandards/default.htm.
[5] See http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM333969.pdf.

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 this guidance contains only binding provisions.

II. BACKGROUND

FDASIA was enacted on July 9, 2012. Section 1136 of FDASIA amended the FD&C Act by adding section 745A, which addresses electronic submissions. Drug and biological product submissions are addressed in section 745A(a), while section 745A(b) applies to medical device submissions.[6]

Section 745A(a)(1) of the FD&C Act describes the general scope of section 745A(a) and provides that submissions under NDAs, ANDAs, BLAs, and INDs must be in electronic format specified in FDA guidance:

> Beginning no earlier than 24 months after the issuance of a final guidance issued after public notice and opportunity for comment, submissions under subsection (b), (i), or (j) of section 505 of this Act or subsection (a) or (k) of section 351 of the Public Health Service Act shall be submitted in such electronic format as specified by the Secretary in such guidance.

Section 745A(a)(2) states that the guidance issued by FDA may provide a timetable for future standards and criteria for waivers and exemptions:

> In the guidance under paragraph (1), the Secretary may (A) provide a timetable for establishment by the Secretary of further standards for electronic submission as required by such paragraph; and (B) set forth criteria for waivers of and exemptions from the requirements of this subsection.

Section 745A(a)(3) provides that the requirements described in section 745A(a) do not apply to submissions under section 561 of the FD&C Act.[7]

In Section 745A(a) of the FD&C Act, Congress granted explicit statutory authorization to FDA to specify in guidance the format for the electronic submissions required under this section. Accordingly, to the extent that this document relates to such requirements under

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[6] The electronic submission requirements of section 745A(b) fall outside the scope of this guidance and are not discussed in this guidance. We note, however, that FDA issued the final guidance entitled *eCopy Program for Medical Device Submissions* that implements the electronic copy provisions of section 745A(b) for medical device submissions to FDA. We update guidances periodically. For the most recent version of a guidance, see the FDA Drugs Guidance Web page at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm and its Biologics Web page at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/default.htm.

[7] Section 561 of the FD&C Act (21 U.S.C. 360bbb) relates to expanded access to investigational products for the diagnosis, monitoring, or treatment of serious or immediately life-threatening diseases or conditions.

section 745A(a), indicated by the use of the words *must* or *required*, this document is not subject to the usual restrictions in FDA's good guidance practice (GGP) regulations, such as the requirement that guidances not establish legally enforceable responsibilities. See 21 CFR 10.115(d).

III. SUBMISSIONS UNDER SECTION 745A(a) OF THE FD&C ACT

As discussed in section II of this guidance, the requirements of section 745A(a) of the FD&C Act apply to all submissions to NDAs, ANDAs, BLAs, and INDs. Below we discuss our interpretation of section 745A(a), specifically its scope, waivers of and exemptions from the electronic submission requirements, and the timetable and process for implementing the requirements under section 745A(a).

A. Which submissions must be submitted electronically?

Section 745A(a) of the FD&C Act applies to submissions under section 505(b), (i), or (j) of the FD&C Act and under section 351(a) or (k) of the PHS Act. These include the following submission types:

- Certain investigational new drug applications (INDs)[8]
- New drug applications (NDAs)
- Abbreviated new drug applications (ANDAs)
- Certain biologics license applications (BLAs)[9]

Section 745A(a) also applies to all subsequent submissions, including amendments, supplements, and reports, to the submission types identified above. Twenty-four months or more after FDA issues a final guidance covering any of these submission types, applicants or sponsors must electronically submit any amendments, supplements, and reports to those submission types, even if the original submission was submitted to FDA prior to implementation of the electronic submission requirements.

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.

[8] This guidance is not applicable to those devices that are regulated by CBER as biological products under section 351 of the PHS Act and that 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. These submissions are subject to the requirements under section 745A(b). See the final guidance entitled *eCopy Program for Medical Device Submissions*, note 6.

[9] This guidance is not applicable to those devices that are regulated by CBER as biological products under section 351 of the PHS Act, including those that do not require submission of an IND prior to the submission of the BLA. These submissions are subject to the requirements under section 745A(b). Such devices generally include those reagents used in determining donor/recipient compatibility in transfusion medicine. See the final guidance entitled *eCopy Program for Medical Device Submissions*, note 6.

Under section 745A(a)(3) of the FD&C Act, the electronic submission requirements do not apply to submissions described in section 561 of the FD&C Act. FDA will continue to accept submissions under section 561 in alternative formats.

B. Which submissions are exempted from the electronic submission requirements?

Section 745A(a)(2)(B) authorizes FDA to establish exemptions from the electronic submission requirements. As a general matter, the following submission types will be exempt from the electronic submission requirements under section 745A(a):

1. Noncommercial INDs, such as those that are described in Section 505(i)(1) of the FD&C Act.[10]

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

C. Will FDA issue waivers of the electronic submission 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.

D. How will FDA implement specific electronic submission requirements?

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

1. Individual draft guidances will be developed to specify the electronic formats, subject matter, and scope of applicability for submissions under section 745A(a). The draft guidances will be posted on FDA's Drugs Guidance Web page and its Biologics Guidance Web page[11] and will be announced in the list of new, revised, and withdrawn guidances.

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

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[10] For purposes of this guidance, the term "noncommercial products" refers to products that are not intended to be distributed commercially and includes investigator-sponsored INDs and expanded access INDs (e.g., emergency use INDs and treatment INDs).

[11] FDA's Drugs Guidance Web page is available at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm, and its Biologics Guidance Web page is available at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/default.htm. See *Providing Regulatory Submissions in Electronic Format – Standardized Study Data* as an example of an individual guidance under 745A(a).

3. Once the Agency has completed its review of the draft guidance, including 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 submission guidance. The notice will provide a date on which the new electronic submission formats specified in the guidance will be required for the submission types identified in the guidance document. FDA will post the final guidance on its Drugs Guidance Web page and its Biologics Guidance Web page and will announce the guidance in the list of new, revised, and withdrawn guidances.

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

E. When will electronic submissions be required?

Under section 745A(a)(1) of the FD&C Act, electronic submissions are required no earlier than 24 months after a final guidance is issued. Therefore, no earlier than 24 months after the final version of an individual guidance specifying a new format for submissions under 745A(a) is published on FDA's Web site, the Agency will begin requiring that the submissions to NDAs, ANDAs, BLAs, or INDs identified in that guidance be submitted in the specified electronic format. The required format(s) for the specific submissions and corresponding timetable(s) for implementation will be specified in the individual guidances. Once an individual guidance is finalized 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 to NDAs, ANDAs, BLAs, or INDs.

F. When will revisions and updates to existing formats take effect?

FDA does not interpret section 745A(a) to impose a 24-month period before revisions and updates to an existing required electronic format can be implemented. Therefore, subsequent revisions and updates to existing required format(s) may be implemented on a shorter timetable (e.g., 12 or 18 months after publication of the *Federal Register* notice announcing the availability of the revised format) depending, among other things, on whether the revision or update represents a significant change to the existing format. For purposes of guidances issued pursuant to section 745A(a), FDA considers version updates and maintenance enhancements to be revisions to a specified format. Under most circumstances, FDA considers a "version update" to be a number increment (e.g., version 3.0 to 4.0) or a decimal increment (e.g., version 3.1 to 3.2) to an existing format. On the other hand, minor changes to a required format, such as corrections of typographical errors, may be implemented immediately or shortly after announcement of availability of the corrected format.

The examples below illustrate how the Agency intends to interpret section 745A(a) with respect to the timing of the implementation of new formats, as well as revisions or updates to existing formats.

Example 1: New Format (with 24-Month Implementation Period)

FDA issues a draft guidance specifying new format(s) for electronic submission of data contained in NDAs, ANDAs, BLAs, and INDs and publishes a *Federal Register* notice announcing availability of the draft guidance. Following the comment period, FDA finalizes the guidance and publishes another *Federal Register* notice announcing availability of the final guidance. The final guidance also provides that the specified format(s) will be required 24 months after the date of its publication. After the 24-month implementation period has passed, the guidance will have binding effect and the electronic formats specified in the guidance must be used for the submission types identified in the guidance document.

Example 2: New Format (with Longer Implementation Period)

FDA issues a draft guidance specifying new format(s) for electronic submission of data contained in NDAs, ANDAs, BLAs, and INDs and publishes a *Federal Register* notice announcing availability of the draft guidance. Following the comment period, FDA finalizes the guidance and publishes another *Federal Register* notice announcing availability of the final guidance. The final guidance also provides that the specified format(s) will be required 36 months after the date of its publication. After the 36-month implementation period has passed, the guidance will have binding effect and the electronic formats specified in the guidance must be used for the submission types identified in the guidance document.

Example 3: Update to Required Format

FDA has finalized a guidance specifying new format(s) for electronic submission of data contained in NDAs, ANDAs, BLAs, and INDs, and the implementation timetable specified in that guidance has passed. The guidance has binding effect, and the electronic formats specified in that guidance must be used for the submission types identified in the guidance document. At a later date, FDA revises the guidance to reflect a version update to one or more of the electronic formats specified in the final guidance. FDA also publishes a *Federal Register* notice announcing the availability of the revised guidance and a timetable for when submissions will be required to be made in the updated format. This timetable may be for a period of time less than 24 months.

Example 4: Correction to Required Format

FDA has finalized an individual guidance specifying new format(s) for electronic submission of data contained in NDAs, ANDAs, BLAs, and INDs, and the implementation timetable specified in the guidance has passed. The guidance has binding effect, and the electronic formats specified in the guidance must be used for the submission types identified in the guidance document. At a later date, FDA revises the guidance to make a correction to one or more of the formats specified in the final guidance. FDA also publishes a *Federal Register* notice to announce the availability of the revised guidance as well as a timetable for when submissions will be required to be made in the corrected format. This timetable may be for a period of time less than 24 months.