4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2023-D-3031]

Alternative Tools: Assessing Drug Manufacturing Facilities Identified in Pending Applications; Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a final guidance for industry entitled "Alternative Tools: Assessing Drug Manufacturing Facilities Identified in Pending Applications." This guidance provides information to applicants on how FDA intends to use alternative tools to assess drug manufacturing facilities identified in a marketing application (i.e., a new drug application (NDA), an abbreviated new drug application (ANDA), a biologics license application (BLA), or a supplement to any of these types of applications). As part of the negotiations relating to the reauthorization of the Prescription Drug User Fee Act (PDUFA) and the Biosimilar User Fee Act (BsUFA), as described in "PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2023 Through 2027" (PDUFA VII commitment letter) and "Biosimilar Biological Product Reauthorization Performance Goals and Procedures for Fiscal Years 2023 Through 2027" (BsUFA III commitment letter), FDA agreed to issue guidance on the use of alternative tools to assess manufacturing facilities named in pending applications and to incorporate best practices from the use of such tools during the Coronavirus Disease 2019 (COVID-19) pandemic. This guidance finalizes the draft guidance of the same title issued on September 22, 2023.

DATES: The announcement of the guidance is published in the *Federal Register* on [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

ADDRESSES: You may submit either electronic or written comments on Agency guidances at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: https://www.regulations.gov. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to https://www.regulations.gov will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on https://www.regulations.gov.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2023-D-3031 for "Alternative Tools: Assessing Drug Manufacturing Facilities Identified in Pending Applications." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at https://www.regulations.gov or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on https://www.regulations.gov. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to https://www.regulations.gov and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of the guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: Jessica Dunn, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 4214, Silver Spring, MD 20993-0002, 240-402-8985; or Phillip Kurs, Center for Biologics Evaluation and Research, Food and Drug Administration, 240-402-0467.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled "Alternative Tools: Assessing Drug Manufacturing Facilities Identified in Pending Applications." This guidance provides information to applicants on how FDA intends to use alternative tools to assess drug manufacturing facilities identified in an NDA, an ANDA, a BLA, or a supplement to any of these types of applications. As part of the negotiations relating to the reauthorization of BsUFA and PDUFA, FDA agreed to issue guidance on the use of alternative tools to assess manufacturing facilities named in pending applications and to incorporate best practices from the use of such tools during the COVID-19 pandemic. This guidance, within the context of approval and licensure decisions by FDA, describes the use of alternative tools to assess manufacturing facilities identified in an NDA, an ANDA, or a BLA to establish that these facilities meet the applicable requirements, including under section 501(a)(2)(B) of the FD&C Act (21 U.S.C. 351(a)(2)(B)) and either section 505 of the FD&C Act (21 U.S.C. 355) or section 351 of the Public Health Service Act (42 U.S.C. 262). FDA considered the applicability of Executive Order 14192, per OMB guidance in M-25-20, and finds this action to be deregulatory in nature.

During the pandemic, FDA expanded its use of alternative tools to evaluate drug manufacturing facilities to support regulatory decision making when facility inspections were not feasible. The following alternative tools were used during the COVID-19 public health emergency:

- Requesting records and other information, pursuant to section 704(a)(4) of the FD&C Act (21 U.S.C. 374(a)(4)), directly from facilities and other entities subject to inspection
- Performing remote interactive evaluations (e.g., remote live streaming video of operations, teleconferences, screen sharing)
- Requesting existing inspection reports and other information from trusted foreign regulatory partners through mutual recognition agreements and other agreements

FDA has strategically used these tools within the context of decisions related to preapproval inspections (PAIs) or prelicense inspections (PLIs) to maximize facility assessment efficiency as part of appropriate, risk-based assessments. Given the success of these innovative approaches, FDA intends to continue risk-based use of these alternative tools and to apply certain virtual technological capabilities within a specific inspectional context defined within this guidance. When used in advance or in lieu of PAIs and PLIs or to support PAIs and PLIs, the appropriate use of these approaches will help FDA maintain operational flexibility to support timely facility evaluations and application decisions.

This guidance finalizes the draft guidance entitled "Alternative Tools: Assessing Drug Manufacturing Facilities Identified in Pending Applications" issued on September 22, 2023 (88 FR 65396). FDA considered comments received on the draft guidance as the guidance was finalized. Based on the comments received, FDA updated the guidance with additional clarification on: (1) the recommended timeframe for facilities to respond to section 704(a)(4) of the FD&C Act records requests; (2) the timeframes for when facilities may expect to receive requests from FDA to use a remote subject matter expert (SME) during an inspection; (3) Agency efforts to coordinate logistical approaches and technologies with facilities regarding

FDA's use of alternative tools; and (4) the effect of a facility declining to allow FDA to use a remote SME or when a facility is unable to support the virtual interaction with a remote SME.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the current thinking of FDA on "Alternative Tools: Assessing Drug Manufacturing Facilities Identified in Pending Applications." 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.

II. Paperwork Reduction Act of 1995

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. The previously approved collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521). The collections of information in 21 CFR parts 210 and 211 relating to current good manufacturing practice requirements and electronic records and signatures have been approved under OMB control numbers 0910-0139 and 0910-0303, respectively. The collections of information in 21 CFR part 314 relating to the submission of NDAs and ANDAs have been approved under OMB control number 0910-0001. The collections of information in 21 CFR part 601 relating to the submission of BLAs have been approved under OMB control number 0910-0338.

III. Electronic Access

Persons with access to the internet may obtain the guidance at https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs, https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances, https://www.fda.gov/regulatory-information/search-fda-guidance-documents, or https://www.regulations.gov.

Grace R. Graham

Deputy Commissioner for Policy, Legislation, and International Affairs.

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