4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 211

[Docket No. FDA-2024-D-5374]

Considerations for Complying with 21 CFR 211.110; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Availability of draft guidance.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled "Considerations for Complying With 21 CFR 211.110." This guidance, when finalized, will describe considerations for complying with the requirements for ensuring batch uniformity and drug product integrity. In addition, this guidance discusses related quality considerations for drug products that are manufactured using advanced manufacturing. FDA is committed to supporting and enabling pharmaceutical innovation and modernization as part of the Agency's mission to protect and promote the public health. FDA encourages industry representatives and manufactures who are interested in using innovative control strategies to contact the Agency.

DATES: Submit either electronic or written comments on the draft guidance by **[INSERT DATE 90 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]** to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.

ADDRESSES: You may submit comments on any guidance 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-2024-D-5374 for "Considerations for Complying With 21 CFR 211.110." 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 this draft 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; the Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research,

Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002; or Policy and Regulations Staff, HFV-6, Center for Veterinary Medicine, Food and Drug Administration, 7500 Standish Place, Rockville, MD 20855. Send one self-addressed adhesive label to assist that office in processing your requests. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Brittany Avaritt, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 75, Rm. 6649, Silver Spring, MD 20993-0002, 240-402-5982; James Myers, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bld. 71, Rm. 7301, Silver Spring, MD 20993-002, 240-402-7911; or Kevin Rice, Center for Veterinary Medicine, Food and Drug Administration, 7500 Standish Place, Rockville, MD 20855, 240-402-0680.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled "Considerations for Complying with 21 CFR 211.110." This guidance, when finalized, will describe considerations for complying with the requirements in § 211.110 (21 CFR 211.110) to ensure batch uniformity and drug product integrity. In addition, this guidance discusses related quality considerations for drug products that are manufactured using advanced manufacturing. It also discusses how manufacturers can incorporate process models into commercial manufacturing control strategies. This guidance applies to the manufacture of human drug products, including biological products, and animal drug products. This guidance does not apply to the manufacture of active ingredients.

To ensure batch uniformity and drug product integrity, the current good manufacturing practice (CGMP) regulations[1] require, among other things, that manufacturing processes are

[1] See 21 CFR parts 210 and 211. Positron emission tomography drug products are subject to CGMP regulations at 21 CFR part 212 and are not covered by this guidance.

designed and controlled to ensure that in-process materials consistently and reliably meet predetermined quality requirements.[2] This guidance explains the requirements for drug product manufacturing in § 211.110. This guidance also describes considerations for the use of advanced manufacturing (e.g., 3D printing, continuous manufacturing) and the use of process models as a part of commercial manufacturing control strategies. FDA supports the adoption of advanced manufacturing as a foundation for improving the overall quality and availability of drug products for patients.

All manufacturers, regardless of whether they are using advanced manufacturing, should apply a scientific- and risk-based approach to controlling processes and ensuring drug product quality. This approach should be based on robust product and process understanding. Advanced manufacturing (such as continuous manufacturing) generally lends itself to more extensive understanding and control of the manufacturing process; thus, it is generally suitable for implementing process models as part of the control strategy. FDA is aware of industry's interest in using in-process control strategies that rely solely on process models to satisfy the requirements of § 211.110. However, control strategies that rely solely on current process models would be insufficient to satisfy the requirements of § 211.110.

FDA is committed to supporting and enabling pharmaceutical innovation and modernization as part of the Agency's mission to protect and promote the public health. This guidance provides information on how process models can be paired with in-process material testing or process monitoring to meet current regulatory requirements. As the science supporting innovative in-process control tools and methods continues to develop, FDA anticipates that these scientific advancements can be leveraged to pursue in-process control strategies that increasingly rely on process models. FDA encourages industry representatives and manufacturers to discuss their proposed innovative control strategies with the Agency to help inform future policy development.

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[2] See § 211.110.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on "Considerations for Complying With 21 CFR 211.110." 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[3].

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 (44 U.S.C. 3501-3521). The collections of information in parts 210 and 211 relating to CGMP have been approved under OMB control number 0910-0139.

III. Electronic Access

Persons with access to the internet may obtain an electronic version of the draft 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, https://www.fda.gov/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/default.htm, https://www.fda.gov/regulatory-information/search-fda-guidance-documents, or https://www.regulations.gov.

Dated: December 23, 2024.

P. Ritu Nalubola,

Associate Commissioner for Policy.

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[3] The Office of the Federal Register has published this document under the category "Rules and Regulations" pursuant to its interpretation of 1 CFR 5.9(b). We note that the categorization as such for purposes of publication in the Federal Register does not affect the content or intent of the document. See 1 CFR 5.1(c).