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.

FOR FURTHER INFORMATION CONTACT: Elizabeth Giaquinto Friedman, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 4162, Silver Spring, MD 20993, 240–402–7930, *Elizabeth.Giaquinto@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

Advanced manufacturing is a general term for an innovative pharmaceutical manufacturing technology or approach that has the potential to improve the reliability and robustness of the manufacturing process and supply chain, and increase timely access to quality medicines for the American public. For the purposes of the discussion paper, all references to drugs include both human drugs and biological products (including those regulated by CBER), unless otherwise specified. Advanced manufacturing can: (1) integrate novel technological approaches, (2) use established techniques in an innovative way, or (3) apply production methods in a new domain. Advanced manufacturing can potentially be used for new or existing and large or small molecule drugs.

FDA has recognized and embraced the potential of advanced manufacturing for many years. CDER established the Emerging Technology Program in 2014 to work collaboratively with companies to support the use of advanced manufacturing. CDER has observed a rapid emergence of advanced manufacturing technologies through the Emerging Technology Program and recognizes that regulatory policies and programs may need to evolve to enable the timely adoption of these technologies. The National Academies of Sciences, Engineering, and Medicine issued a 2021 report entitled ''Innovation in Pharmaceutical Manufacturing on the Horizon: Technical Challenges, Regulatory Issues, and Recommendations'', noting potential innovations in integrated, flexible, and distributed manufacturing. These potential innovations include modular approaches to streamline drug development and production, and the deployment and use of highly portable manufacturing units. A range of drug manufacturers have recently engaged CDER through the Emerging Technology Program specifically regarding the development of portable and distributed manufacturing platforms.

CBER established the CBER Advanced Technologies Team in 2019 to promote dialogue, education, and input between CBER and prospective innovators and developers of advanced manufacturing technologies. Through these interactions, CBER has observed interest from manufacturers in the implementation of novel manufacturing approaches for CBER-regulated products. CBER also recognizes the need to consider developing a regulatory framework to facilitate the adoption of these emerging technologies. CBER expects the development of advanced manufacturing technologies associated with DM and POC manufacturing for products that it regulates.

The discussion paper (available on FDA's website at: CDER's Framework for Regulatory Advanced Manufacturing Evaluation (FRAME) Initiative | FDA) presents areas for consideration and policy development identified by CDER scientific and policy experts associated with DM and POC manufacturing that would be valuable as FDA considers developing a regulatory framework that contemplates these technologies for CDER- and CBER-regulated drug and biological products. For the purposes of the discussion paper, CDER and CBER define DM to be a decentralized manufacturing strategy consisting of a manufacturing platform of manufacturing units deployed to multiple locations; POC manufacturing is defined as a subset of DM that uses manufacturing units distributed to host sites in proximity to patient care (*e.g.,* healthcare facilities). Regulatory areas of consideration include applicable statutory provisions, regulations, and guidance related to quality assessment and inspections that could affect an applicant's ability to comply with the current regulatory framework or FDA's assessment of a marketing application.

II. Requested Information and Comments

Interested persons are invited to provide detailed comments to CDER and CBER (see **ADDRESSES**) on all aspects described in the discussion paper. The discussion paper is available on FDA's website for the FRAME initiative at: CDER's Framework for Regulatory Advanced Manufacturing Evaluation (FRAME) Initiative | FDA. To facilitate input, FDA has developed a series of questions after each technology described in the discussion paper. The questions are not meant to be exhaustive, and FDA is also interested in any other pertinent information stakeholders would like to share on this topic. This feedback will help inform the Agency's policy development regarding the technologies described in the discussion paper. FDA encourages stakeholders to provide the specific rationale and basis for their comments, including any available supporting data and information.

Dated: October 11, 2022.

Lauren K. Roth,

Associate Commissioner for Policy.

[FR Doc. 2022–22386 Filed 10–13–22; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2016–D–0973]

Comparability Protocols for Postapproval Changes to the Chemistry, Manufacturing, and Controls Information in a New Drug Application, Abbreviated New Drug Application, or Biologics License Application; 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 ''Comparability Protocols for Postapproval Changes to the Chemistry, Manufacturing, and Controls Information in an NDA, ANDA, or BLA.'' This final guidance is intended to assist original applicants and holders of approved new drug applications (NDAs), abbreviated new drug applications (ANDAs), and biologics

license applications (BLAs) on implementing a chemistry, manufacturing, and controls (CMC) postapproval change(s) through the use of a comparability protocol (CP). In many cases, submission and approval of a CP will facilitate the subsequent implementation and reporting of CMC changes, which could result in moving a drug or biological product into distribution or facilitating a proactive approach to reinforcing the supply of a product sooner than if a CP were not used. This final guidance recommends a framework to promote continuous improvement in the manufacturing of quality drug and biological products. This document finalizes a revised draft guidance that published on April 20, 2016, entitled ''Comparability Protocols for Human Drugs and Biologics: Chemistry, Manufacturing, and Controls Information.'' A related draft guidance entitled ''Comparability Protocols—Protein Drug Products and Biological Products—Chemistry, Manufacturing, and Controls Information'' that published in September 2003, was withdrawn on May 6, 2015.

DATES: The announcement of the guidance is published in the **Federal Register** on October 14, 2022.

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–2016–D–0973 for ''Comparability Protocols for Postapproval Changes to the Chemistry, Manufacturing, and Controls Information in an NDA, ANDA, or BLA.'' 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://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 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 or the Center for Biologics Evaluation and Research, Office of Communication, Outreach, and Development, 10903 New Hampshire Ave., WO71, Room 3128, Silver Spring, MD 20903. 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: Stephen Moore, Center for Drug Evaluation and Research, Food and Drug Administration, Bldg. 51, Rm. 4159, 10903 New Hampshire Ave., Silver Spring, MD, 20993–0002, 301–796–7579 or Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993, 240–402–7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled ''Comparability Protocols for Postapproval Changes to the Chemistry, Manufacturing, and Controls Information in an NDA, ANDA, or BLA.'' The final guidance is intended to assist original applicants and holders of approved applications for human drugs and biological products on implementing a CMC postapproval change(s) through the use of a CP. In this guidance, a comparability protocol is synonymous with a postapproval change management protocol in the International Council for Harmonisation (ICH) Q12 guidance ''Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management'' (May 2021). The final guidance is not applicable to blood and blood components; biological products that also meet the definition of a device in section 201(h) of the Federal Food,

Drug, and Cosmetic Act; or human cells, tissues, or cellular or tissue-based products regulated solely under section 361 of the Public Health Service Act (42 U.S.C. 264) and 21 CFR part 1271.

On April 20, 2016, (81 FR 23303), FDA announced the availability of a revised draft guidance entitled ''Comparability Protocols for Human Drugs and Biologics: Chemistry, Manufacturing, and Controls Information.'' This was a revised draft of a draft guidance published in February 2003. We revised the February 2003 draft guidance in 2016 for the following reasons:

- To include current pharmaceutical quality concepts.
- To provide more flexibility regarding filing procedures for a notification of modifications to an approved CP in less burdensome reporting categories than a prior approval supplement.
- To add an appendix to address commonly asked questions.

The Center for Veterinary Medicine, which was included in the February 2003 draft guidance, published recommendations for animal drugs in a separate guidance.

We received a number of comments on the revised draft guidance, which the Agency considered carefully as it prepared this final guidance. Additional information has been included in the final guidance on proposing an appropriate reporting category for implementation of changes under a CP once approved. Additional examples have been included for notification of modifications to an approved CP in less burdensome reporting categories than a prior approval supplement. Information has been included in the appendix on cross-referencing of a master file, including a Drug Master File, in a CP and submitting a CP to a master file. Also, the recommendations in the guidance for industry ICH Q12 have been carefully considered when revising this guidance to maximize consistency. We also have made clarifications and editorial changes to the final guidance document.

This final guidance provides recommendations to original applicants and holders of approved applications for human drugs and certain biological products on implementing CMC postapproval change(s) through the use of a CP. In many cases, submission and approval of a CP will facilitate the subsequent implementation and reporting of CMC changes, which could result in moving a drug or biological product into distribution or facilitating a proactive approach to reinforcing the supply of a product sooner than if a CP were not used.

The final guidance recommends a framework to promote continuous improvement in the manufacturing of quality drug and biological products by encouraging applicants to employ the following:

- Effective use of knowledge and understanding of the product and manufacturing process;
- Risk management activities over the life cycle of a product; and
- An effective pharmaceutical quality system

This final guidance incorporates the modern regulatory concepts stated in the guidance for industry entitled ''PAT—A Framework for Innovative Pharmaceutical Development, Manufacturing, and Quality Assurance,'' the Pharmaceutical Quality for the 21st Century—A Risk Based Approach, the Critical Path Initiative, and the quality by design principles described in the guidance for industry entitled ''Q8(R2) Pharmaceutical Development.''

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 ''Comparability Protocols for Postapproval Changes to the Chemistry, Manufacturing, and Controls Information in an NDA, ANDA, or BLA.'' It does not establish any rights for any person and, with the exception of section V, 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.

As noted, insofar as section V of this guidance sets forth that certain modifications to an approved CP must be submitted in a changes being effected supplement or annual report rather than a prior approval supplement, it has binding effect, as indicated by the use of the words *must, shall,* or *required.* Such binding effect derives from section 506A of the FD&C Act, as implemented in 21 CFR 314.70 and 601.12.

II. Paperwork Reduction Act of 1995

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501–3521) is not required for this guidance. The previously approved collections of information are subject to review by OMB under the PRA. The collections of information in 21 CFR part 314 have been approved under OMB control number 0910–0001. The collections of information in 21 CFR part 601 have been approved under OMB control number 0910–0338. The collections of information in 21 CFR parts 210 and 211 relating to current good manufacturing practices have been approved under OMB control number 0910–0139. The collections of information relating to section 351(k) of the PHS Act have been approved under OMB control number 0910–0718.

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/regulatory-information/search-fda-guidance-documents,* or *https://www.regulations.gov.*

Dated: October 7, 2022.

Lauren K. Roth,

Associate Commissioner for Policy.

[FR Doc. 2022–22334 Filed 10–13–22; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2022–N–2335]

Prescription Drug User Fee Act VII; Independent Assessment of Communication Through Product Quality Information Requests During Application Review; Statement of Work; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; establishment of a public docket; request for comments.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing an opportunity for public comment on the Statement of Work to assess communication between FDA and sponsors through product quality information requests during application review and to identify best practices and areas of improvement. The independent assessment is part of FDA performance commitments under the recent reauthorization of the Prescription Drug User Fee Act (PDUFA). The independent assessment of FDA and sponsors in communicating through product quality information requests is described in detail in the document entitled ''PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2023 Through 2027.'' As part of FDA performance commitments described in this document, the assessment will be conducted by an