4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2020-D-0276]

Compliance Policy for the Quantity of Bioavailability and Bioequivalence Samples Retained Under 21 CFR 320.38(c); Guidance for Industry; Availability

AGENCY: Food and Drug Administration, Health and Human Services (HHS).

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a final guidance for industry entitled "Compliance Policy for the Quantity of Bioavailability and Bioequivalence Samples Retained Under 21 CFR 320.38(c)." This guidance describes FDA's policy concerning the conditions under which the Agency generally does not intend to take regulatory action against an applicant or a contract research organization (CRO) that retains less than the quantity of reserve samples (that is, samples of the test article and reference standard that were used in bioavailability (BA) or bioequivalence (BE) testing) required in our regulations. FDA developed this guidance in light of technological advances in FDA's ability to test retention samples and in response to communications from applicants and CROs requesting to retain a lower quantity of these reserve samples.

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-2020-D-0276 for "Compliance Policy for the Quantity of Bioavailability and Bioequivalence Samples Retained Under 21 CFR 320.38(c)." 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.

- 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.

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 Office of Communications, 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 two self-addressed adhesive labels to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: Melissa Mannion, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993, 301-796-2747, Melissa.Mannion@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled "Compliance Policy for the Quantity of Bioavailability and Bioequivalence Samples Retained Under 21 CFR 320.38(c)." The Agency is issuing this guidance consistent with good guidance practices (GGP) regulations (21 CFR 10.115) and is implementing this guidance without prior public comment because FDA has determined that prior public participation is not feasible or appropriate as public comment would not affect the specifications of FDA's testing of retention samples

(§10.115(g)(2)). FDA has made this determination under §10.115(g)(2) because, with technological advances, the reduced quantity of reserve samples is now sufficient for FDA testing; this reduced quantity will provide a less burdensome approach for applicants and CROs but remains consistent with the Agency's mission to ensure public health. Although this guidance document is immediately in effect, it remains subject to comment in accordance with FDA's GGP regulation and FDA will consider all comments received and revise the guidance document as appropriate (§10.115(g)(3)).

On November 8, 1990, we issued an interim rule that amended, in relevant part, part 320 (21 CFR 320) by adding a requirement to retain reserve samples of drug products (that is, samples of the drug products that were used to conduct BA or BE studies) for a specified period and, when specifically requested, to release the reserve samples to us. The interim rule was intended to help ensure BE between generic drugs and their reference listed drugs and to help us investigate possible fraud in BA and BE testing. After consideration of public comments, we published a final rule in the *Federal Register* on April 28, 1993 (58 FR 25918).

In the final rule, 21 CFR 320.38 and 320.63 require a new drug application or abbreviated new drug application applicant (or its CRO) to retain reserve samples of the test article and reference standard that were used in conducting any in vivo BA and in vivo or in vitro BE study that supports the approval of an application or supplemental application. Specifically, § 320.38(c) requires these applicants (or their CROs) to retain a quantity of the test article and reference standard that were used in BA or BE testing that is at least five times the amount of product required for release testing.

Section 320.38(c) requires that reserve samples of the test article and reference standard used in a BA or BE study are of a sufficient quantity to perform five times all of the release tests

required in the application or supplemental application. Since the final rule was issued in 1993, technological advances in our ability to test these products have led to test methods that are less destructive and more sensitive, allowing us to detect the identity and composition of the test article and reference standard with smaller volumes of samples. Consistent with these developments, FDA has received communications from applicants and CROs requesting to retain a lower quantity of the reserve samples.

In light of these technological advances, this guidance discusses the conditions under which we do not generally intend to take regulatory action against an applicant or CRO that retains an appropriate reduced quantity of reserve samples of the test article and reference standard that were used in its BA or BE testing.

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 "Compliance Policy for the Quantity of Bioavailability and Bioequivalence Samples Retained Under 21 CFR 320.38(c)." 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

This guidance refers to previously approved collections of information found in FDA regulations. These 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 21 CFR parts 312 and 314 have been approved under OMB control numbers 0910-0014 and 0910-0001, respectively. The collections of information in part 320 for "Investigational New Drug Safety Reporting Requirements for Human Drug and Biological

Products and Safety Reporting Requirements for Bioavailability and Bioequivalence Studies in Humans" have been approved under OMB control number 0910-0672. The recordkeeping requirement for CGMP sample retention in 21 CFR 211.170 has been approved under OMB control number 0910-0139.

III. Electronic Access

Persons with access to the internet may obtain the guidance at either https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs or https://www.regulations.gov. Use the FDA website listed in the previous sentence to find the most current version of the guidance.

Dated: August 10, 2020.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

[FR Doc. 2020-17798 Filed: 8/18/2020 8:45 am; Publication Date: 8/19/2020]