4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2019-D-2330]

Pathology Peer Review in Nonclinical Toxicology Studies: Questions and Answers; Draft Guidance for Industry; Availability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SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled "Pathology Peer Review in Nonclinical Toxicology Studies: Questions and Answers." This draft guidance represents FDA's current thinking on the management and conduct of pathology peer review performed during good laboratory practice (GLP)-compliant toxicology studies. When pathology peer review occurs as part of a nonclinical laboratory study conducted in compliance with GLP regulations, it should be well-documented. However, documentation practices during pathology peer review have not been clearly defined and vary among nonclinical testing facilities. This question-and-answer (Q&A) draft guidance is intended to clarify FDA's recommendations concerning the management, conduct, and documentation of pathology peer review.

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.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-2019-D-2330 for "Pathology Peer Review in Nonclinical Toxicology Studies: Questions and Answers." 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.gpo.gov/fdsys/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 the 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 or 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. 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: Tahseen Mirza, Center for Drug Evaluation and Research, Office of Study Integrity and Surveillance, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 5330, Silver Spring, MD 20993, 301-796-7645; or Stephen Ripley, Office of the Center Director, 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; or Judy Davis, Office of Device Evaluation, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 1216, Silver Spring, MD 20993, 301-796-6636; or Hilary Hoffman, Center for Veterinary Medicine, Office of New Animal Drug Evaluation, Food and Drug Administration, 7500

Standish Place, Rm. 389, Rockville, MD, 20855, 240-402-8406; or Yuquang Wang, Center for Food Safety and Nutrition, Office of the Center Director, Food and Drug Administration, 5001 Campus Drive, Rm. 4A035, College Park, MD, 20740, 240-402-1757; or Kimberly Benson, Center for Tobacco Products, Office of Science, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. G335, Silver Spring, MD 20993, 301-796-1327.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled "Pathology Peer Review in Nonclinical Toxicology Studies: Questions and Answers." This draft guidance represents FDA's current thinking on the management and conduct of pathology peer review performed during GLP-compliant toxicology studies.

The histopathological assessment of tissue samples is one of the key activities performed during GLP-compliant toxicology studies. Commonly, histopathological assessment includes an initial read of tissue slides by the study pathologist and a subsequent review (referred to as pathology peer review) by a second pathologist. Pathology peer review may be particularly useful in situations where unique or unexpected findings are noted or when the reviewing pathologist has a particular expertise with a class of compounds. When pathology peer review occurs as part of a nonclinical laboratory study conducted in compliance with 21 CFR part 58 (GLP regulations), it should be well-documented in the study records. However, documentation practices during pathology peer review have not been clearly defined and vary among nonclinical testing facilities.

The GLP regulations include general requirements for histopathology evaluation (for example, it requires that standard operating procedures be established to cover histopathology),

and pathology peer review can be valuable to the histopathology evaluation during a GLP study even though it is not specifically addressed in the GLP regulations. This Q&A draft guidance is intended to clarify FDA's recommendations concerning the management and conduct of pathology peer review when performed during GLP-compliant toxicology studies.

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 "Pathology Peer Review in Nonclinical Toxicology Studies: Questions and Answers." 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. This guidance is not subject to Executive Order 12866.

II. Paperwork Reduction Act of 1995

This draft 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. 3501-3520). The following collections of information regarding GLP-compliant toxicology studies have been approved under OMB control number 0910-0119:

- § 58.29 related to personnel who conduct nonclinical laboratory studies;
- § 58.35 for preparing quality control units;
- § 58.81 for preparing and maintaining standard operating procedures for testing facilities; pathology peer review should be planned, conducted, documented, and reported in accordance with established procedure

- § § 58.120, 58.185, and 58.190 for preparing a final report for each study, including a protocol and any changes to the protocol and for maintaining documentation, protocols, and final reports generated from nonclinical laboratory studies.

III. Electronic Access

Persons with access to the internet may obtain the draft guidance at either https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm, https://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm, or https://www.regulations.gov.

Dated: July 26, 2019.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

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