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4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2019-D-0362]

A Risk-Based Approach to Monitoring of Clinical Investigations--Questions and Answers; 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 "A Risk-Based Approach to Monitoring of Clinical Investigations--Questions and Answers." This guidance provides information on risk-based approaches to monitoring investigational studies of human drug and biological products, medical devices, and combination products. The guidance contains recommendations on planning a monitoring approach, developing the content of a monitoring plan, and addressing and communicating monitoring results. This guidance expands on the guidance for industry entitled "Oversight of Clinical Investigations--A Risk-Based Approach to Monitoring" (August 2013) by providing additional information to facilitate sponsors' implementation of risk-based monitoring. This guidance finalizes the draft guidance entitled "A Risk-Based Approach to Monitoring of Clinical Investigations: Questions and Answers," issued on March 15, 2019.

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-2019-D-0362 for "A Risk-Based Approach to Monitoring of Clinical Investigations--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, 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 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; the Office of Policy, Guidance and Policy Development, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Room 5431, Silver Spring, MD 20993-0002; or the Office of Clinical Policy, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 32, Rm. 5103, Silver Spring, MD 20993. 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: Mona Shing, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 3355, Silver Spring, MD 20993-0002, 301-796-0910, mona.shing@fda.hhs.gov; Diane Maloney, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993-0002, 240-402-7911; Martin Hamilton, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 5431, Silver Spring, MD 20993-0002, 301-796-5666, CDRHClinicalEvidence@fda.hhs.gov; Sheila Brown, Office of Clinical Policy, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 32, Rm. 5109, Silver Spring, MD 20993, 301-796-6563, Sheila.Brown@fda.hhs.gov; or Hector Colon, Office of Regulatory Affairs/Office of Bioresearch Monitoring Operations, 12420 Parklawn Dr., Rockville, MD 20857, 301-796-3899, orabimoinspectionpoc@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled "A Risk-Based Approach to Monitoring of Clinical Investigations--Questions and Answers." Sponsors of clinical investigations involving human drugs, biological products, medical devices, and combination products are required to provide oversight of the conduct of their clinical investigations. Such oversight helps to ensure adequate protection of the rights, welfare, and

safety of human subjects and the integrity of the data submitted to FDA. Therefore, FDA recommends that sponsors implement a system to manage risks to human subjects and data integrity throughout all stages of the clinical investigation process.

This system to manage the quality of the investigation should help ensure data integrity while safeguarding the rights, safety, and welfare of trial participants by, for example, focusing on the design of efficient clinical trial protocols, tools for identifying and tracking potential risks, and procedures for data collection and processing. This system should include a risk-based approach to monitoring tailored to the potential risks for the specific clinical investigation. Clinical investigation monitoring is a quality control tool for determining whether investigation activities are being carried out as planned, so that, among other things, deficiencies can be identified and corrected. The types and intensity of monitoring activities should be proportionate to the risks to participants' rights, safety, and welfare and to data integrity inherent in the investigation. Effective implementation of risk-based monitoring of clinical investigations, including the prioritization of monitoring and other oversight activities directed at processes and procedures critical for human subject protection and maintaining data integrity, should help maximize the quality of a clinical investigation.

This guidance finalizes the draft guidance entitled "A Risk-Based Approach to Monitoring of Clinical Investigations: Questions and Answers," issued on March 15, 2019 (84 FR 9531). FDA considered comments received on the draft guidance as the guidance was being finalized and revised the guidance as appropriate in response to the comments. Additionally, editorial changes were made to improve clarity.

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 "A Risk-Based Approach to Monitoring of Clinical Investigations--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.

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 50 have been approved under OMB control number 0910-0130; the collections of information in 21 CFR part 312 have been approved under OMB control number 0910-0014; the collections of information in 21 CFR part 812 have been approved under OMB control number 0910-0078; the collections of information in 21 CFR part 11 have been approved under OMB control number 0910-0303; and the collections of information in FDA's guidance for industry entitled "Oversight of Clinical Investigations--A Risk-Based Approach to Monitoring" have been approved under OMB control number 0910-0733.

III. Electronic Access

Persons with access to the internet may obtain the guidance at https://www.fda.gov/regulatory-information/search-fda-guidance-documents, 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/medical-devices/device-advice-comprehensive-regulatory-assistance/guidance-documents-medical-devices-and-radiation-emitting-products, or https://www.regulations.gov.

Dated: April 7, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

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