4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2022-D-0142]

Research Involving Children as Subjects and Not Otherwise Approvable by an Institutional Review Board: Process for Referrals to Food and Drug Administration and Office for Human Research Protections, Guidance for Institutional Review Boards, Investigators, and Sponsors; Draft Guidance for Industry; Availability; Agency Information Collection Activities; Proposed Collection; Comment Request

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled "Research Involving Children as Subjects and Not Otherwise Approvable by an IRB: Process for Referrals to FDA and OHRP." This guidance is intended to assist institutional review boards (IRBs), institutions, investigators, and sponsors in understanding the processes used for review of research involving children as subjects that is not otherwise approvable by an IRB and has been referred to FDA, the Office for Human Research Protections (OHRP), or both, for review. When final, this guidance will replace the final guidance issued by FDA in December 2006 entitled, "Guidance for Clinical Investigators, Institutional Review Boards and Sponsors: Process for Handing Referrals to FDA Under 21 CFR 50.54: Additional Safeguards for Children in Clinical Investigations" and the guidance issued by the OHRP entitled "Children as Research Subjects and the HHS '407' Process," issued on May 26, 2005. This draft guidance is not final nor is it in effect at this time.

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure that the Agency and OHRP consider your comment on this draft guidance before they begin

work on the final version of the guidance. Submit electronic or written comments on the proposed collection of information in the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF THE PUBLICATION OF THE *FEDERAL REGISTER*].

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-2022-D-0142 for "Research Involving Children as Subjects and Not Otherwise Approvable by an IRB: Process for Referrals to FDA and OHRP, Guidance for Institutional Review Boards, Investigators, and Sponsors." 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 Office of Pediatric Therapeutics, Office of the Commissioner, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 32, Rm. 5126, Silver Spring, MD 20993-0002; or Office for Human Research Protections, Division of Policy and Assurances, 1101 Wootton Pkwy., Suite 200, Rockville, MD 20852. Send one self-addressed adhesive label to assist that office in processing your request or include a Fax number to which the draft guidance may be sent. See the SUPPLEMENTARY INFORMATION section for information on electronic access to the draft guidance.

FOR FURTHER INFORMATION CONTACT:

With regard to the draft guidance: Donna Snyder, Office of Pediatric Therapeutics, Office of the Commissioner, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 32, Rm. 5121, Silver Spring, MD 20993-0002, 301-796-1397, optpediatricethics@fda.hhs.gov; or Natalie Klein, Office for Human Research Protections, 1101, Wootton Pkwy., Suite 200, Rockville, MD 20852, 240-453-6900 or toll free within the United States, 866-447-4777, Natalie.Klein@hhs.gov.

With regard to the proposed collection of information: Domini Bean, Office of Operations, Food and Drug Administration, Three White Flint North, 10A-12M, 11601 Landsdown St., North Bethesda, MD 20852, 301-796-5733, PRAStaff@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

FDA and the OHRP are announcing the availability of a draft guidance for IRBs, institutions, investigators, and sponsors entitled "Research Involving Children as Subjects and Not Otherwise Approvable by an IRB: Process for Referrals to FDA and OHRP, Guidance for Institutional Review Boards, Investigators, and Sponsors." This guidance is intended to assist IRBs, institutions, investigators, and sponsors in understanding the processes for review of research involving children as subjects that is not otherwise approvable by an IRB and has been referred to FDA under § 50.54 (21 CFR 50.54), OHRP under 45 CFR 46.407, or both, for review.

The Department of Health and Human Services (HHS) issued 45 CFR part 46, subpart D, "Additional Protections for Children Involved as Subjects in Research" as a final rule on March 8, 1983 (48 FR 9814). FDA issued part 50, subpart D (21 CFR part 50, subpart D), "Additional Safeguards for Children in Clinical Investigations of Food and Drug Administration-Regulated Products," as a final rule on February 26, 2013 (78 FR 12937). These regulations, hereinafter referred to collectively as subpart D, are similar, with some minor differences. (For a full discussion of the differences between FDA and HHS human subject protection regulations, see 78 FR 12937-12947.)

FDA's part 50, subpart D regulations apply to clinical investigations regulated by FDA as described in 21 CFR 50.1(a). HHS regulations apply to all research involving human subjects conducted or supported by HHS in accordance with 45 CFR 46.101(a). FDA-regulated clinical investigations conducted or supported by HHS are subject to both sets of regulations. As a result, many sponsors, investigators, and IRBs need to be familiar and comply with both FDA's and HHS's regulations.

The draft guidance describes an overview of the review process as it relates to FDA referral and review (§ 50.54), OHRP referral and review (45 CFR 46.407), joint FDA and OHRP review, multisite research, and FDA and OHRP review of similar research. 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 research involving children as subjects not otherwise approvable by an IRB and the process for referrals to FDA and OHRP. 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

Under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521), Federal Agencies must obtain approval from the Office of Management and Budget (OMB) for each collection of information they conduct or sponsor. "Collection of information" is defined in 44 U.S.C. 3502(3) and 5 CFR 1320.3(c) and includes Agency requests or requirements that members of the public submit reports, keep records, or provide information to a third party. Section 3506(c)(2)(A) of the PRA (44 U.S.C. 3506(c)(2)(A)) requires Federal Agencies to provide a 60-day notice in the *Federal Register* concerning each proposed collection of information before submitting the collection to OMB for approval. To comply with this requirement, FDA is publishing notice of the proposed collection of information set forth in this document.

With respect to the following collection of information, FDA invites comments on these topics: (1) whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Protection of Human Subjects and Institutional Review Boards

OMB Control Number 0910-0130--Revision

This information collection supports FDA regulations governing requirements for informed consent and IRBs that are intended to protect the rights and safety of human subjects involved in FDA-regulated clinical investigations (parts 50 and 56 (21 CFR parts 50 and 56)). A "clinical investigation" is any experiment that involves a test article and one or more human subjects and is subject to requirements for prior submission to FDA under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(i) or 360j(g)), or is not subject to requirements for prior submission to FDA under these sections of the FD&C Act, but the results of which are intended to be submitted later to, or held for inspection by, FDA as part of an application for a research or marketing permit (§ 50.3).

Under § 50.54, FDA will accept IRB referrals of clinical investigations involving children as subjects that are not otherwise approvable by an IRB under part 50 subpart D. The collections of information in parts 50 and 56 are currently approved under OMB control number 0910-0130; however, the submission of records to FDA as part of an IRB referral under § 50.54, as recommended in the draft guidance document, is not called for in the regulations themselves. We are therefore revising the information collection to include submissions of records to the Agency that may occur under § 50.54. Based on a review of Agency data regarding the frequency of IRB referrals under § 50.54, we expect that fewer than one such submission would be made annually. The records that the draft guidance recommends be sent to FDA as part of an IRB's referral are records that are kept by IRBs in the ordinary course of their business, and where necessary, information collections related to the creation and retention of these documents are already approved under OMB control number 0910-0130. We assume that no more than 1 hour would be needed to complete the task of transmitting this existing information to FDA in accordance with the draft guidance recommendations. We invite comment on our estimate and assumptions.

This draft guidance also refers to previously approved collections of information by HHS' OHRP under OMB control numbers 0990-0481 and 0990-0260. Specifically, on February

14, 2022, OMB approved the collection of information identified with the OMB control number 0990-0481 without change. The approved collection of information consists of a requirement that IRB records be submitted when an IRB or its institution request an HHS consultation process for proposed research involving, respectively: (1) pregnant women, human fetuses or neonates; (2) prisoners; or (3) children, as subjects that are not otherwise approvable by an IRB.

This draft guidance also refers to previously approved FDA collections of information. 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.

III. Electronic Access

Persons with access to the internet may obtain an electronic version of the draft guidance at either https://www.fda.gov/regulatory-information/search-fda-guidance-documents or https://www.regulations.gov.

Dated: March 27, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

[FR Doc. 2023-06649 Filed: 3/30/2023 8:45 am; Publication Date: 3/31/2023]