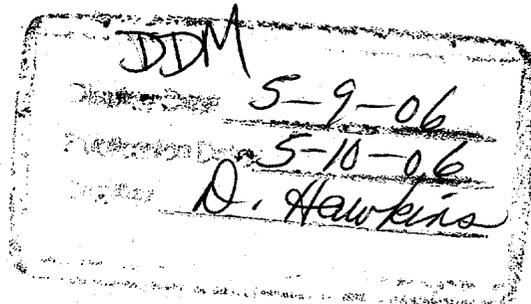


DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 2006D-0172]



Draft Guidance for Clinical Investigators, Institutional Review Boards, and Sponsors; Process for Handling Pediatric Referrals to the Food and Drug Administration: Additional Safeguards for Children in Clinical Investigations

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance entitled "Guidance for Industry; Process for Handling Pediatric Referrals to FDA: Additional Safeguards for Children in Clinical Investigations." This guidance is intended to assist clinical investigators, institutional review boards (IRBs), sponsors, and other interested parties in understanding FDA's process for handling clinical investigations that include children as subjects and that have been referred to FDA for review under FDA regulations on additional safeguards for children in clinical investigations. The draft guidance describes the procedures FDA generally intends to follow in handling clinical investigations referred for review under these regulations and in reaching final determinations in accordance with these regulations.

DATES: Submit written or electronic comments on the draft guidance by [*insert date 60 days after date of publication in the Federal Register*]. General comments on agency guidance documents are welcome at any time.

ADDRESSES: Submit written requests for single copies of the draft guidance to the Office of Policy (HF-11), Office of the Commissioner, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. Send one self-addressed adhesive label to assist that office in processing your requests. Submit telephone requests to 800-835-4709 or 301-827-1800.

Submit written comments on the draft guidance to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to <http://www.fda.gov/dockets/ecomments>. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Erik Mettler, Office of Policy (HF-11), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-3360.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance entitled "Guidance for Industry; Process for Handling Referrals to FDA Under 21 CFR 50.54: Additional Safeguards for Children in Clinical Investigations." FDA issued 21 CFR part 50, subpart D, "Additional Safeguards for Children in Clinical Investigations," (part 50, subpart D) as an interim final rule on April 24, 2001 (66 FR 20598). Under these regulations, an IRB must review clinical investigations involving children as subjects and covered by subpart D and approve only those clinical investigations that satisfy the criteria described in §§ 50.51, 50.52, or 50.53, as well as the conditions of all other applicable sections in subpart D.

Under § 50.54, if an IRB does not believe that a clinical investigation within the scope described in §§ 50.1 and 56.101 (21 CFR 56.101) and involving children as subjects meets the requirements of §§ 50.51, 50.52, or 50.53, the clinical investigation may proceed only if the following occurs: (1) The IRB finds and documents that the clinical investigation presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and (2) the Commissioner of Food and Drugs, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, determines either of the following: (1) The clinical investigation in fact satisfies the conditions of §§ 50.51, 50.52, or 50.53, as applicable, or (2) the following conditions are met: (A) The clinical investigation presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; (B) the clinical investigation will be conducted in accordance with sound ethical principles; and (C) adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in § 50.55.

The draft guidance describes the procedures FDA generally will follow in handling clinical investigations referred for review under § 50.54 and in reaching final determinations under that regulation. The draft guidance is based in part on FDA's experience to date with such referrals. The Department of Health and Human Services (HHS) has human subject protection regulations that also govern research involving children as subjects and supported or conducted by HHS. (See 45 CFR part 46, subpart D.) The draft guidance also

addresses situations in which a clinical investigation is subject to both 21 CFR 50.54 and 45 CFR 46.407.

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 agency's current thinking on the process for handling referrals to FDA under 21 CFR 50.54. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

II. The Paperwork Reduction Act of 1995

Under the Paperwork Reduction Act (44 U.S.C. 3501–3520) (the PRA), 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 below.

With respect to the following collection of information, FDA invites comment 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 on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

The draft guidance is intended to assist clinical investigators, IRBs, sponsors, and other interested parties in understanding the FDA's process for handling clinical investigations that include children as subjects and that have been referred to FDA for review under 21 CFR part 50, subpart D.

Title: Draft Guidance for Industry; Process for Handling Referrals to FDA Under 21 CFR 50.54: Additional Safeguards for Children in Clinical Investigations.

Burden Estimate: The information that must be submitted to FDA by sponsors for approval of clinical investigations involving children is contained in the investigational new drug application (IND) and investigational device exemption (IDE) regulations (21 CFR parts 312 and 812 (parts 312 and 812), respectively) and is approved under OMB control number 0910-0014 (expires March 31, 2009) for INDs and under OMB control number 0910-0078 (expires August 31, 2006) for IDEs. In addition to the collections of information already required under parts 312 and 812, the draft guidance requests that an IRB submitting a clinical investigation for consideration under § 50.54 include with that submission/referral the documentation of its finding under § 50.54(a) that the clinical investigation presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children.

Under § 50.54(a), IRBs must find and document that the clinical investigation presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children. The requirement to “document” the finding is a recordkeeping requirement. IRB recordkeeping requirements are set forth in FDA regulations on IRBs (part 56) at § 56.115, and are approved under OMB control number 0910-0130 until November 30, 2007. Thus, only the submission to FDA of the IRB’s finding would not already be required under § 50.54(a). FDA estimates that each submission would take no more than 15 minutes because, as required by the regulation, the IRB will already have prepared and documented the finding, and the IRB would only have to send the documentation of that finding to FDA.

The draft guidance also contains a second collection of information. The introductory paragraph to § 50.54 states that if an IRB does not believe that a clinical investigation within the scope described in §§ 50.1 and 56.101 and involving children as subjects meets the requirements of §§ 50.51, 50.52, or 50.53, the clinical investigation may proceed only if certain conditions set forth in § 50.54 are met. The draft guidance requests that the IRB include, when submitting its finding under § 50.54 that the clinical investigation presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children, an explanation why the IRB does not believe that the clinical investigation meets the requirements of §§ 50.51, 50.52, or 50.53. FDA believes that in most cases this explanation will already be part of the IRB meeting minutes. Because the IRB may need to summarize these minutes in order to send them to FDA, FDA estimates that each explanation would take approximately 1 hour to prepare.

According to a 1998 Office of the Inspector General (OIG) report, there are 3,000 to 5,000 IRBs in the United States, and most are associated with hospitals and academic centers (see Department of Health and Human Services, Office of the Inspector General, *Institutional Review Boards: A Time for Reform*, page 3, June 8, 1998). However, based on FDA's experience to date with IRB referrals under § 50.54, only a very small percentage of IRBs (approximately 5 per year) are expected to refer a clinical investigation to FDA under 21 CFR part 50, subpart D.

The information collection resulting from the draft guidance that is not already approved by OMB is summarized as follows:

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN¹

	Number of Respondents	Number of Responses per Respondent	Total Annual Responses	Hours per Response	Total Hours
Submission of finding required under § 50.54(a)	5	1	5	15 min.	1 hour, 15 minutes
Explanation why investigation does not meet §§ 50.51, 50.52, or 50.53	5	1	5	1	.5
Total					6 hours, 15 minutes

¹There are no capital costs or operating and maintenance costs associated with this collection.

III. Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding this document. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

IV. Electronic Access

Persons with access to the Internet may obtain the document at either <http://www.fda.gov/cder/guidance/index.htm> or <http://www.fda.gov/ohrms/dockets/default.htm>.

Dated: 5/2/06
May 2, 2006.



Jeffrey Shuren,
Assistant Commissioner for Policy.

[FR Doc. ⁰⁶03-~~03~~????? Filed ??-??-⁰⁶03; 8:45 am]

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