

Information Sheet Guidance For IRBs, Clinical Investigators, and Sponsors

FDA Institutional Review Board Inspections

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**U.S. Department of Health and Human Services
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Information Sheet Guidance For IRBs, Clinical Investigators, and Sponsors¹ FDA Institutional Review Board Inspections

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

This guidance is intended to provide information about FDA inspections of Institutional Review Boards (IRBs) conducted under FDA's Bioresearch Monitoring (BIMO) Program. This document supersedes another document, "FDA Institutional Review Board Inspections," issued in September 1998, by the former Office of Health Affairs, FDA. This document has been revised to provide updated information and is being issued in accordance with the Agency's regulations on Good Guidance Practices (21 CFR 10.115)².

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

¹ This guidance document was developed by the Good Clinical Practice Program in the Office of the Commissioner (OC) in coordination with the Center for Biologics Evaluation and Research (CBER), the Center for Devices and Radiological Health (CDRH), the Center for Drug Evaluation and Research (CDER), and the Office of Regulatory Affairs (ORA).

² 65 FR 56477, September 19, 2000.

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FDA regulations generally require IRB review and approval of research involving FDA regulated products (e.g., investigational drugs, biological products, and medical devices) (21 CFR Part 56).

FDA developed its BIMO Program to ensure the protection of the rights, welfare, and safety of human subjects and the quality and integrity of data submitted to the Agency. Among other things, the FDA BIMO Program involves site visits to IRBs, clinical investigators, sponsors, monitors, contract research organizations, nonclinical (animal) laboratories, and bioequivalence analytical laboratories. This document addresses site visits to IRBs that review clinical investigations that are regulated by FDA under 21 USC 355(i) and 21 USC 360(j) and clinical investigations that support applications for research or marketing permits for products regulated by FDA.

III. WHEN ARE IRB INSPECTIONS CONDUCTED?

FDA conducts IRB inspections to determine if IRBs are operating in compliance with current FDA regulations and statutory requirements and if the IRBs are following their own written procedures. The FDA regulations pertinent to IRBs include 21 CFR Part 50 (Protection of Human Subjects), Part 56 (Institutional Review Boards), Part 312 (Investigational New Drug Application), and Part 812 (Investigational Device Exemptions).

FDA inspections of IRBs generally fall into one of two categories:

- Surveillance inspections – periodic, scheduled inspections to review the overall operations and procedures of the IRB.
- Directed inspections – unscheduled inspections focused on the IRB's review of a specific clinical trial or trials. Directed inspections generally result from a complaint, clinical investigator misconduct, or safety issues pertaining to a trial or site.

IV. HOW ARE IRB INSPECTIONS CONDUCTED?

FDA personnel from one of FDA's District Offices contact a responsible individual at the institution, usually the IRB chairperson to schedule the site visit. FDA personnel issue a notice of inspection (Form FDA 482) and present their credentials to the most responsible individual before the inspection begins. They interview appropriate people and obtain information about the IRB's policies and procedures. Usually, the IRB's performance is evaluated by tracking one or more studies that are subject to IRB review under FDA regulations. Also, the IRB's procedures and membership rosters are examined to determine whether they conform to current FDA regulations (21 CFR Part 56, subparts A-D). During the inspection, FDA personnel typically review and copy:

- Records of IRB membership
- IRB procedures and guidelines
- Minutes of IRB meetings for the past year

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- Documents related to the studies given by the clinical investigator to the IRB
- Documents related to the studies sent by the IRB to the clinical investigator
- Any other materials about these studies

V. WHAT HAPPENS AFTER AN INSPECTION?

At the end of an inspection, FDA personnel conduct an *exit interview* with responsible institutional and IRB representatives. At this interview, FDA personnel who conducted the inspection review and discuss the findings from the inspection and, if deficiencies are found, issue a written Form FDA 483 (Inspectional Observations; 483) to the most responsible IRB representative. The 483 describes any inspectional observations that, in the opinion of the FDA personnel conducting the inspection, represent deviations from applicable statutes and regulations. The IRB may respond to the 483 observations verbally during the exit interview and/or respond in writing after the inspection. If the IRB/responsible institution chooses to respond in writing to the deficiencies listed on the 483, the response should be directed to the FDA District Office listed in the upper left corner of the 483. A list of FDA District Offices is also posted on FDA's website (<http://www.fda.gov/ora>).

Following the inspection, the FDA personnel who conducted the IRB inspection prepare a written Establishment Inspection Report (EIR). The EIR, 483 (if issued), copies of any materials collected during the inspection, and any IRB response are forwarded to the appropriate FDA Center for further evaluation. After this review, one of the following types of letters is typically sent from the Center to the IRB chairperson or other responsible institutional official:

1. A *letter* that generally states that FDA observed no significant deviations from the regulations. Note that a letter is not always sent when FDA observes no significant deviations.
2. An *informational or untitled letter* that identifies deviations from statutes and regulations for which voluntary corrective action is sufficient. Occasionally, such letters request a response from the IRB.
3. A *Warning Letter* that identifies serious deviations from applicable statutes and regulations. A Warning Letter generally requests prompt correction by the IRB and a formal written response to the Agency.

Letters may also be issued in accordance with 21 CFR 56.120. In such cases, the Agency will require that the IRB or parent institution respond to the letter within a time period specified by FDA and describe the corrective actions that will be taken by the IRB or the parent institution, or both, to achieve compliance. Based on the response from the IRB or institution to these letters, FDA may schedule a reinspection to confirm the adequacy of corrective actions. In addition to issuing these letters, FDA can take other administrative actions against IRBs, or their institutions,

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for noncompliance with applicable statutes and regulations (21 CFR Part 56, subpart E). Until the IRB or parent institution takes appropriate corrective action, FDA may (for studies subject to FDA's IRB regulations):

- Withhold approval of new studies that are conducted at the institution or reviewed by the IRB
- Direct that no new subjects be added to ongoing studies
- Terminate ongoing studies when doing so would not endanger the subjects
- Notify relevant State and Federal regulatory agencies and other parties with direct interest in the Agency's action of the deficiencies in the operation of the IRB in instances when the apparent noncompliance creates a significant threat to the rights and welfare of human subjects

The FDA Commissioner can also begin proceedings to disqualify an IRB or the institution if the IRB has refused or repeatedly failed to comply with FDA's IRB regulations (21 CFR Part 56) and the noncompliance adversely affects the rights or welfare of the human subjects in a clinical investigation.

VI. WHO CAN PROVIDE MORE INFORMATION?

If, during an inspection, an IRB official has any questions the FDA personnel conducting the inspection has not answered, either the District Office Director or the contact person at the Center that assigned the inspection can be contacted. The FDA personnel conducting the inspection should be able to provide the name and telephone number of the District Office Director and the Center contact person.

In addition, the FDA Compliance Program Guidance Manual for Institutional Review Board Inspections (Program 7348.809), used by FDA to conduct these inspections, is available on the Internet at <http://www.fda.gov/ora/cpgm/default.htm#bimo> .