

FDA AUDIT PROCESS FOR A CLINICAL TRIAL UNDER THE OVERSIGHT OF AN EXTERNAL IRB

PROCESS FOR A SCHEDULED OR UNANNOUNCED FDA AUDIT:

1. Scheduling an Audit
 - a. An FDA inspector(s) contacts the Principal Investigator (PI) or research designee by telephone or in writing to schedule an appointment, or the inspector(s) may come to a site without notice.
 - b. If there are extenuating circumstances (ie, if the PI is not available), a sub-investigator (Sub-I) may request a short delay for the audit and request rescheduling at a mutually convenient time. The FDA does not have to honor this request.
 - c. The WMed staff member who receives the initial notification of an FDA audit from the FDA notifies the WMed Human Research Protection Program (HRPP) Director or listed alternate and the primary Clinical Research Coordinator (CRC).
 - d. The WMed HRPP Director, or listed alternate, facilitates communication and oversight of the FDA visit until its completion utilizing the WMed FDA Audit Response Plan Checklist.

2. Preparing for the Audit
 - a. The WMed HRPP Director, or alternate, works with appropriate designee to assign and facilitate the notification of the following staff with pertinent details, if applicable:
 - 1) PI and/or Sub-I(s)
 - 2) Primary & Back-up CRCs
 - 3) Sponsor/CRO/Monitor
 - 4) Regulatory Document Specialist
 - 5) Investigational pharmacy or designated pharmacist
 - 6) Additional study support staff that have been involved in the study
 - 7) Medical Records
 - 8) WMed Assistant Dean for Clinical Research Operations
 - 9) Center for Clinical Research Director and employees
 - 10) WMed Department Chair, if applicable
 - 11) WMed Dean (Institutional Official)
 - 12) WMed Associate Dean for Research
 - 13) WMed Associate Dean Administration and Finance (Compliance Officer)
 - 14) Legal Services
 - 15) WMed Assistant Dean for Research Compliance
 - 16) WMed IRB and/or the Central IRB
 - 17) If the audit will involve off-site record review at Bronson, contact:
President & CEO, Vice President and Chief Compliance Officer, Chief Quality Officer, Senior VP of Legal & Legislative Affairs (Institutional Official), Director of Quality & Safety and VP of IT and Medical Records Director
 - 18) If the audit will involve off-site record review at Borgess, contact:
President & CEO, Chief Strategy Officer (Institutional Official), Borgess Legal Services, Accreditation & Regulation Consultant, IT and Medical Records

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- 19) If the audit will involve off-site record review at WMed Oakland Drive Campus, contact:
Administrative Assistant, Associate Dean for Clinical Affairs, Director of Nursing, Manager of Laboratory Services, Director of Facilities, IT Manager, and Health Information Management
 - 20) WMed IT Department (for electronic record access)
 - b. The primary CRC or designee ensures that all documentation, including informed consent forms, source documents, case report forms, and the regulatory binder(s) for the study identified as the focus of the audit are accurate, complete, and available for review by the inspector(s).
 - c. The primary CRC or designee ensures that the study drug dispensing or device accountability records are accurate, complete, and available for review. If there were any instances in which emergency breaking of the blind was required, the WMed designee makes sure that documentation is available.
 - d. The Quality Control Specialist and HRPP Education-Quality Improvement Program (E-QIP) personnel will work with the primary CRC when possible to help ensure all study documentation is in good order and available for review.
3. Inspector(s) Arrival
 - a. Upon arrival, the FDA inspector(s) shows credentials and an FDA badge. Proper identification is required prior to review of records.
 - b. The inspector(s) presents a "Notice of Inspection" (Form FDA 482).
 - c. The PI and primary CRC will be notified upon inspector(s) arrival and will be asked to make time available for the duration of the audit.
 - d. The inspector(s) may request a short interview with the PI before beginning the audit. Other staff should also attend this meeting as assigned above.
 - e. The Director of HRPP or designee provides the inspector(s) with a quiet area, free from excessive interruptions in which to work. The inspector(s) may request that a telephone be available.
 4. During the Audit
 - a. The primary CRC or designee provides orientation and access to the study records and files related only to the study to be inspected.
 - b. SOPs may be printed upon request.
 - c. As much as possible, all binders and/or documents requested by the inspector(s) will be reviewed by the Director of HRPP or designee, Quality Control Specialist, E-QIP personnel, primary CRC, and Regulatory Document Specialist, if applicable, prior to providing them to the FDA inspector(s). This review should not impede the inspection.
 - d. A designated research staff member is available at all times to bring requested materials to the inspector(s) and to make copies of requested documents. The primary and/or back-up CRC(s) should be available as needed for any questions and/or clarifications related to study and to facilitate electronic medical record access. The WMed designee makes duplicate copies of any photocopied documents provided to the inspector(s). These copies are to be maintained at WMed (separate from study-related documents) and made available for the sponsor for review while on site.
 - e. An individual is designated to take notes of the audit, including but not limited to items reviewed, questions asked, individuals interviewed, responses provided.

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- f. The inspection contains two parts:
 - 1) Part one determines the facts surrounding the study. Issues may include:
 - a) Responsibilities of site personnel
 - b) Delegation of authority
 - c) Location of study-related activities
 - d) Data collection methods and procedures
 - e) Test article accountability
 - f) Communication between sponsor and PI
 - g) Where and in what condition study documents are archived
 - 2) Part two involves an audit of the data:
 - a) The FDA inspector(s) compares the information submitted to the sponsor with the source documentation maintained at the study site.
 - b) The inspector(s) reviews any/all patient data.
 - c) The inspector(s) interviews the PI and any other WMed personnel involved in conducting the study.
 - g. The primary CRC or designee keeps the sponsor informed of the progress of the audit.
5. Follow-up After the Audit
- a. The Director of HRPP or designee, the PI, the primary CRC and any other required staff members participate in the exit interview with the FDA inspector(s).
 - b. The Director of HRPP asks when a report will be provided.
 - c. The Director of HRPP, in conjunction with the primary CRC or designee responds to the audit report no later than 15 business days following receipt of the report.
 - d. The Director of HRPP in conjunction with the primary CRC or designee develops and maintains a separate binder with all documentation from the audit, including:
 - 1) Record of communication with the sponsor
 - 2) Copy of records provided to the FDA
 - 3) FDA Form 483 (if applicable) or regulatory report document
 - 4) Response to FDA Form 483 (if applicable)
 - 5) Establishment inspection Report (EIR)
 - e. The Director of HRPP provides a copy of the report and correspondence to the primary CRC or designee.
 - f. If applicable, the Director of HRPP, in consultation with the Assistant Dean for Clinical Research Operations and Assistant Dean for Research Compliance, evaluates the audit report to identify areas for improvement and facilitates the development of a CAPA to improve quality.

REFERENCES:

- 1. 21 CFR 312.60 – General responsibilities of investigators
- 2. 21 CFR 312.62 – Investigator recordkeeping and record retention
- 3. 21 CFR 312.64 – Investigator reports
- 4. 21 CFR 312.66 – Assurance of IRB review
- 5. 21 CFR 312.50 – Protection of Human Subject's
- 6. 21 CFR 312.56 – Institutional Review Boards
- 7. 21 CFR Part 812 – Investigational Device Exemptions

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8. ICH GCP Part 4.9 – Records and Reports
9. ICH GCP Part 5.15 – Record Access
10. Information Sheet Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors: Clinical Investigator Administrative Actions – Disqualification, May 2010 (updated March 2014)
11. Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors: FDA Inspections of Clinical Investigators, June 2010

CCR02 Roles and Responsibilities of Clinical Team Members

CCR03 Investigator Responsibilities

CCR12 Trial Master File

GEN01 Code of Professional Conduct

GEN04 Conflicts of Interest and Commitment

HRP01 Human Research Protection Program

WMed Human Research Protection Program (HRPP) and Institutional Review Board (IRB) Handbook

ATTACHMENTS:

None