

	Standard Operating Procedures
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Procedure Category:	General Study Procedures and Activities
Procedure CLN-06-01:	FDA Audit Preparation

Procedure Overview

This procedure describes preparation activities for an FDA audit.

Responsible Individuals

Qualified MICHHR personnel (including, but not limited to, Study Coordinator and Research Assistant); Investigator; Director, MICHHR

Procedure

FDA audits of investigative sites are divided into two categories: study-oriented and investigator-oriented. Study-oriented site audits are routine audits that are typically performed at least once for each NDA. Sites with high study enrollment are typically chosen for this type of audit. Investigator-oriented audits, formerly known as “for-cause” audits, are performed in response to complaints about a particular investigator, publicity about a clinical research study, or as follow-up to a study-oriented inspection. In each case, the auditor assesses adherence to FDA guidelines and applicable regulations, examines the validity of the study, and investigates whether the rights and safety of the study subjects have been protected. Typically, FDA auditors hold degrees in biology or chemistry, and are highly trained in FDA regulations and in the detection of fraud.

In preparation for the audit, all study documents should be made available for inspection. These include all signed informed consent forms, patient charts, study progress notes, CRFs, investigational material accountability records and regulatory documents. In order to minimize the consequences of any deficiencies that the auditor may find, it is advisable to conduct an internal review of the study prior to the auditor’s arrival. This allows for the identification of deficiencies prior to the FDA audit and may allow for the elimination of some or all of the deficiencies. In the case that deficiencies cannot be resolved, identifying problem areas prior to the audit and discussing them with the auditor at his or her arrival could possibly result in a more favorable outcome.

As problems with informed consent comprise the greatest portion of observations made in FDA audits, special emphasis should be placed here in preparation for the audit. In addition to reviewing the content of the informed consent form, the internal

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auditor verifies that the informed consent process was properly executed for all study subjects. Forms are reviewed to verify that the subject, the witness (if applicable) and the investigator have signed the form. Also, signature dates are checked to ensure that no study procedures were performed prior to the consent date. If an informed consent form is found to be lacking a study subject's, investigator's or witness's signature, the signature should be obtained prior to the FDA audit along with a note explaining the circumstances of the late signature. Under no circumstances should any signature be backdated.

Patient chart and study progress notes are reviewed against CRFs to verify that all data has been completely and accurately recorded. As the FDA places special emphasis on the reporting of adverse events and concomitant medications, these items should be emphasized in the internal audit.

Investigational material accountability records are reviewed prior to the audit in order to identify any problems with accountability. There should be consistency among patient records, prescription forms, pharmacy receipt and return documents and pharmacy inventory logs. All unused investigational material must be returned to the sponsor or destroyed, whichever is required by the study protocol.


The study regulatory documents must be complete and current relative to the time the study was conducted. These documents include, but are not limited to: Form FDA-1572, signed protocol and amendments (if any), IRB approval notices and correspondence, IRB membership list, approved informed consent form, Investigator's Brochure, study personnel signature list, monitor's visit log, master patient list, CVs and certifications for all personnel named on the FDA-1572, pharmacy documents and study correspondence.

After the completion of the FDA site audit, the auditor writes an Establishment Inspection Report, or EIR. This document is not automatically provided to the site, but is eventually available through the Freedom of Information Act. EIRs are divided into three classifications:

NAI (No Action Indicated): No objectionable conditions or practices were found during the inspection.

VAI (Voluntary Action Indicated): Objectionable conditions or practices were found which represented departures from the regulations. A response by the investigator is usually warranted in the case of a VAI.

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OAI (Official Action Indicated): Objectionable conditions or practices were observed that represent significant departures from the regulations. A Warning Letter or other administrative or regulatory sanctions may be recommended in the case of an OAI.

Negative audit outcomes may result in such actions as closure of the site or IRB, or blacklisting of an investigator.

Documentation

Documentation for this procedure includes:

- Informed consent forms
- Patient charts
- Study progress notes
- Case report forms
- Test article accountability documents
- Pharmacy documents
- Regulatory documents
- Establishment Inspection Report (EIR)

Deviation Approval

The Director, MICHIR or designee, must approve deviation from this procedure. The Director, MICHIR or designee, must store documentation of the deviation approval.

Procedure Author

Manager, Research Support Core

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