

## Monitoring

### Introduction:

Principal investigators and research staff are responsible for ensuring compliance with Federal regulations governing human subject research and the conduct thereof, as well as with IRB and institutional policies and procedures. The Center for Clinical Research and Technology (CCRT) provides investigator support services to promote research integrity. This includes assistance to investigators with protocol submissions, research compliance monitoring, and responsible research conduct education. Research compliance support is provided to promote continuous quality improvement through participation in prospective monitoring. A primary goal of the monitoring process is to educate the UHCMC research community regarding responsible conduct of research and to evaluate the understanding of ethical standards governing research. These services are primarily provided by the Office of Research Compliance and Education.

A program of retrospective clinical research chart review was established in 1999 in compliance with Joint Commission of Accreditation of Health Care requirements for clinical research standards. The retrospective monitoring program reviews informed consent documents and compares them with source documentation to ensure compliance. This process also provides monitoring of IRB review and approval of the required elements of consent. The prospective monitoring program is designed to assist and educate investigators in the responsible conduct of research and to provide ongoing evaluation of the Human Research Protection Program (HRPP).

### Definitions:

**Good Clinical Practice (GCP)** is an international standard for the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting of clinical trials. It ensures that data reported are credible and accurate, and that subjects' rights and confidentiality are protected. The [Good Clinical Practice Program](#) is the focal point within the FDA for issues arising in human research trials regulated by the FDA.

**Monitoring** is the process of reviewing human subject research studies to ensure proper conduct of the study, as stated in the IRB approved protocol. It also involves the review of clinical research standard operating procedures, Good Clinical Practices, and regulatory requirements.

**Non-Compliance:** Any action or activity associated with the conduct or oversight of research involving human subjects that fails to comply with local, state and federal regulations pertaining to human research protections. Non-compliance actions may range from minor to serious, be unintentional or willful, and may occur once or several times. The degree of non-compliance is evaluated on a case-by-case basis and will take into

account such considerations as the degree of harm to subjects (actual or potential) and willfulness of the noncompliance.

**Suspension** is when research on an approved protocol is partially or completely stopped pending future action by the IRB. Examples include: an unanticipated problem in research involving greater than minimal risks to subjects or others; unexpected serious harm to subjects; or when the IRB is investigating a research protocol for possible issues of human subject non-compliance or continuing non-compliance with federal regulations, or with the determinations of the IRB. Suspended protocols remain open and require continuing review.

**Termination** is when the IRB permanently stops some or all research procedures associated with an active approved protocol.

### **Policy:**

As a means of evaluating responsible conduct of research compliance, the Office of Research Compliance and Education staff will conduct monitoring visits and compliance reviews, which are designed to identify standards of excellence and potential areas for improvement in order to promote a solid foundation for the conduct of human subjects' research. Compliance monitoring is conducted in the form of **directed** (for cause) and **prospective** (routine) reviews.

### **A) Research Compliance Monitoring**

All human research approved by the IRB and/or conducted at UHCMC (including cancer protocols) may undergo monitoring in order to assure the protection of human research participants and compliance with Federal regulations, state and local law, IRB policies and procedures, and UHCMC's Federalwide Assurance with OHRP. The purpose of a monitoring visit is to:

- Assess adherence to Federal regulations as defined by OHRP and FDA;
- Assess adherence to UHCMC IRB policies and procedures;
- Assess adherence to UHCMC research policies;
- Assess adherence to Federal Privacy rule regulations under HIPAA via the Office of Civil Rights;
- Assess adherence to local and state laws and regulations;
- Assess adherence to regulations as defined by the Office of Research Integrity regarding Research Misconduct;
- Determine that the rights and safety of human research participants have been properly protected; and
- Provide education to investigators.

External research compliance monitoring may also be conducted in the form of prospective and directed monitoring at affiliated UH sites or where the UHCMC IRB serves as the IRB of Record.

**Prospective Monitoring:** Routine **proactive** monitoring is conducted to assess the investigator's compliance with Federal, state and local law, and UHCMC and IRB policies. Protocols are selected for routine visits by performing a query of the IRB database, reviewing IRB minutes, or may be requested on a voluntary basis by the principal investigator, Department or Clinical Chair. The prospective research compliance monitoring may include, but is not limited to, the following:

- Examining the entire research project.
- Assigning observers to the sites where the informed consent process is being conducted.
- Interviewing investigators, research staff, or research participants.
- Monitoring advertisements and other recruiting materials.
- Monitor conflict of interest concerns.
- Assure the consent documents include the appropriate information and disclosures.
- Requesting progress reports from Investigators.
- Other monitoring or auditing activities deemed appropriate.

**Directed Monitoring:** Directed monitoring occurs when the CCRT, usually through the IRB, identifies a concern or issue and requests additional review of IRB approved research. The CCRT and/or the IRB may request directed monitoring for any reason including, but not limited to, the following:

- Notification of an FDA or other sponsor initiated audits;
- A response to an externally initiated complaint (OHRP, FDA or sponsor) of potential protocol violations or non-compliance;
- A response to a complaint or concern from a participant, a participant's family member, the public or anonymous sources;
- A response to a concern raised by an employee;
- An IRB directive or concern;
- An investigator with a history of poor adherence to research policies and procedures.

Upon completion of the directed monitoring activities, the results will be reported to the Vice President for Research and Technology, the IRB Chair and the IRB Committee (if applicable). The CCRT has the responsibility and authority to report issues to other corporate departments or officers of UHCMC as applicable.

For both directed and prospective research compliance monitoring, the principal investigator and contact person as identified with the IRB will be contacted regarding the upcoming monitoring visit. Prior to the visit, the principal investigator or contact person will be asked to schedule a mutually agreeable time with the Research Compliance

Specialist (RCS) during which the monitoring visit will occur. The individuals who should be present during the monitoring visit include, but not limited to: any individual knowledgeable about the roles and responsibilities of the research team; and any individual obtaining informed consent. The principal investigator is not required to attend the monitoring visit, unless otherwise indicated. The principal investigator or contact person will be asked to provide the number of participants currently enrolled to the RCS for reference prior to the monitoring visit.

On the day of the monitoring visit, the RCS will interview the individuals present to: better understand the process flow and conduct of the research; identify the roles and responsibilities of the research team; understand the informed consent process, including how and when potential participants are identified for the study and how informed consent or assent is obtained; and ask any additional questions that may be necessary to evaluate the conduct of the research.

The following information will be reviewed during the monitoring visit: regulatory binder; informed consent document(s); HIPAA Authorizations; participant research records; source documentation; inclusion/exclusion criteria; study procedures as approved by the IRB; drug accountability if managed by the study site; and occurrence and reporting of adverse events, unanticipated problems and protocol deviations. At the conclusion of the on-site visit, the RCS will review any observations with the PI or study staff, if they are available. If additional time is needed to complete the review, the PI or study staff will be notified.

After the onsite monitoring visit is complete, the following additional areas may be reviewed, if applicable: Investigational Drug Services; Clinical Research Unit; Grant, Grant Account and Contract. The review of these additional areas will occur after the onsite monitoring visit, on a day mutually agreeable by all parties.

If additional information is needed, or questions arise after the review of the ancillary areas, or after compiling the observations from the on-site monitoring visit, additional on-site monitoring may be requested.

The PI will be informed of any findings subsequent to the monitoring visit. This process includes discussion with the Investigator and the research team, followed-up with written documentation of the findings. Once all observations for all areas are compiled, and a report has been finalized in consultation with the IRB Chair or designee, the Principal Investigator and contact person will receive a summary of findings discovered while monitoring the protocol. Additionally, results of all monitoring reviews, both prospective and directed, are reported to the Vice-President for Research (or designee) and a copy of the summary will be placed in the IRB file.

The Investigator will be asked to respond to the monitoring observations within 30 days of receiving the final report. Failure to respond to the observations could be considered an issue of non-compliance. The investigator will be notified if the response is acceptable or if additional information is needed.

**Monitoring of the Informed Consent Process:** Considering the importance of the informed consent process the IRB may require special monitoring of the process by an impartial observer (consent monitor) in order to reduce the possibility of coercion and undue influence.

Such monitoring may be particularly warranted where the research presents significant risks to subjects, or if subjects are likely to have difficulty understanding the information to be provided. Monitoring may also be appropriate as a corrective action where the IRB has identified concerns associated with a particular investigator or a research project.

If deemed appropriate as a result of routine or for cause audit findings, or if otherwise justified by the nature of the research and/or the subject population, special monitoring of the consent process will be required for either a set time period or set number of subject enrollments as determined by the IRB committee or the IRB Chair working in conjunction with the IRB Administration Office. The IRB will include in the written communication to the Principal Investigator the need to have the consent process monitored, the justification for this decision, and any other relevant details. The Principal Investigator will be instructed to inform the RCS of all upcoming scheduled visits which might reasonably include efforts to enroll new subjects into the study. The RCS will arrange to be present during the consent process, and will be informed of the particular issues which warrant special monitoring of the consent process. After the monitoring, the RCS will provide a written report of the observation to the PI and individual obtaining informed consent.

In all cases, the report will be shared with the leadership of the CCRT, the IRB Chair and frequently with a convened board, which will determine if the process is adequate or if a corrective plan of action is required. The board's decision will be communicated to the Principal Investigator per normal mechanisms.

Monitoring of the consent process may also be requested as part of prospective, not-for-cause, monitoring. Such monitoring will allow the RCS to provide guidance or suggestions to the individual obtaining informed consent after the observation is complete, and to help promote good research conduct by educating the research staff. After the observation, a written report of the observation will be given to the individual observed.

## **B) Unanticipated Problems/Protocol Deviations/Non-Compliance Allegations**

If any of the above monitoring activities (UHCMC and non-UHCMC sites) find that participants in a research study have been exposed to unexpected serious harm or that non-compliance with human subjects' research regulations has occurred, such findings will be promptly reported to the IRB Administration Office for further review

### **References and/or Regulatory Citations:**

[21 CFR 50](#)

[21 CFR 56](#)

[21 CFR 312](#)

[21 CFR 812](#)

[45 CFR 46](#)

[45 CFR 160 and 164](#)

[FDA Good Clinical Practice Program](#)

### **Related Policies:**

[IRB Policy, Non-compliance Involving Human Subjects' Research](#)

[IRB Policy, Administrative Hold, Suspension, or Termination of IRB Approval](#)