Post-Approval Monitoring Program Description

Objective
The goal of post-approval monitoring of studies involving human subject research is to confirm by observation and documentation comparison, an accurate and consistent protocol performance, conducted in accordance with an Institutional Review Board (IRB)-approved protocol. An additional goal of the program is to provide education to the investigators on best practices for conducting their human subject research study in compliance with their IRB-approved protocol, Iowa State University (ISU) IRB policies and guidance, and federal regulations. The program is also designed to help investigators, their teams, and the University prepare for external audits by granting, regulatory, and accreditation agencies.

Roles
The purpose of the IRB is to help researchers ensure that the rights and safety of human participants in research are protected and that research is conducted in compliance with relevant regulations. To achieve this, the IRB (1) advises investigators in the design of research projects that minimize potential harm to participants, (2) reviews all planned research involving human participants prior to initiation of the research, (3) approves research that meets established criteria for protection of human participants, and (4) monitors approved research to ascertain that participants are being protected. The IRB has the authority to approve, require modifications, disapprove, suspend, or terminate all human subject research activities at ISU. The IRB may determine whether a post-approval monitoring visit is needed. The IRB is administratively housed within the Office for Responsible Research (ORR), under the oversight of the Vice President for Research.

The Director, Office for Responsible Research (DORR), provides oversight and management of the Post-Approval Monitor (PAM) and the post-approval monitoring program and assures that the IRB and the Institutional Official receive reports or updates on items of concern.

As part of ISU’s post-approval monitoring program, the IRB Chair and IRB Co-chair, in consultation with the DORR, may determine if a post-approval monitoring visit is needed. This is considered a “directed” visit. Additionally, the IRB Chair and Co-chair review PAM reports in consultation with the DORR to determine if additional follow-up is needed.

The PAM is not a member of the IRB. The role of the PAM is to meet with investigators and/or their teams and confirm by observation and documentation comparison that research activity is performed in accordance with approved IRB protocols. The PAM reviews study records, observes research activity, prepares reports, provides recommendations for maintaining compliance, provides training or information on training options when needed, and assists in execution of corrective and preventative actions.

Protocol Selection
All studies, even those determined to qualify for exempt status, are subject to monitoring. Studies chosen for monitoring visits are primarily randomly selected. However, emphasis may be placed on monitoring studies involving vulnerable populations, deception, confidentiality concerns, waivers granted by the IRB.
(e.g., waiver of informed consent or waiver of documentation of informed consent), studies with more than minimal risks to subjects, or studies conducted by investigators with past IRB concerns.

Monitoring visits may also be “directed” by the IRB, the DORR, IRB Chair, or Co-chair as needed (e.g., to assist in verification of findings in cases of potential noncompliance, to provide verification of implementation of corrective actions implemented in response to noncompliance, to assist the IRB in monitoring studies requiring more frequent review, etc.).

A PI may also request an on-site review to help keep records and procedures in compliance with federal regulations and institutional policies or to prepare for an external audit by a sponsor or federal agency. Visits of this nature are encouraged, as the goal of post-approval monitoring is to assist investigators in conducting compliant research. During these PI-requested visits, the PAM focuses on areas of improvement, and, if protocol deviations are found, counsels the PI on self-reporting the issue to the IRB, along with submitting a protocol modification if needed.

**Monitoring Process**

The PAM schedules the visit with PI(s) and their staff, making every attempt to accommodate schedules. At the time the visit is scheduled, the PI is provided a copy of the “PI Self-Assessment” (Appendix) that may be used to prepare for the visit. “Directed” monitoring may or may not be scheduled.

During the post-approval monitoring visit, the PAM compares procedures being conducted in the laboratory or study area with those listed in the IRB-approved protocol and any approved modifications. This may include reviewing study records, visiting with the PI to review procedures being followed, observation of the consent process, etc. Documented discrepancies between observed and approved activities are brought to the attention of the PI.

The PAM reviews and assesses areas such as, but not limited to the following:

- Research team composition and training
- Recruitment procedures
- Screening procedures
- Consent process
- Study procedures
- Publications from the study
- Current enrollment and verification of informed consent
- Reports of adverse events
- Storage of study documents and data
- Privacy and confidentiality issues
- Subject payment
- Questions and concerns from the PI and research team

One of the primary goals of the post-approval monitoring program is education. The PAM is able to explain the IRB process, the importance of following the approved IRB protocol, and what is expected from investigators and their team. Additionally, the PAM is a resource for investigators, providing best practice ideas for conducting their human subjects research in compliance with ISU IRB policies and educating the research team on IRB guidance documents, policies, and federal regulations.

The PAM also assists the principal investigator in identifying any protocol deviations and/or unanticipated problems, provides guidance for self-reporting any deviations or unapproved changes to the IRB protocol and implementing any necessary actions, such as submitting a protocol modification. The vast majority of potential noncompliance found during post-approval monitoring visits is a result of lack of understanding of the roles and responsibilities of individuals involved in research and inadequate
training of staff. *In many cases, minor discrepancies observed during PAM visits can be addressed through modification of an existing protocol or reverting to procedures that were originally approved; however, protocol deviations and/or unanticipated problems are reported to the DORR and IRB (see process below).*

**Information Sharing Process and Follow-Up**

Following completion of the post-approval monitoring visit, the PAM discusses observations with the PI and/or their staff prior to leaving the office/laboratory. If the PI is unavailable, a time is scheduled to discuss the results of the visit. Issues that pose an immediate threat to research participants or that may constitute serious noncompliance are brought to the immediate attention of the DORR, the IRB Chair, and Co-chair as needed.

A written report of the post-approval monitoring visit is prepared by the PAM. The goal of this report is to outline any discrepancies from the IRB-approved protocol and offer suggestions or recommendations for areas of improvement, including any suggested protocol modifications identified during the visit. A draft copy of the report will be shared with the PI for their comments and review. Following review by the PI, the report is finalized and a copy is shared with the PI for their records. The final report is then shared with the DORR, the IRB Chair, and Co-chair who review the report to determine whether additional follow-up is needed. If warranted, the DORR contacts the PI to investigate any potential noncompliance found during the PAM visit.

Following this investigation, the DORR prepares a report of potential noncompliance to share with the IRB. The IRB discusses both the PAM report and the potential noncompliance report (if warranted) at a regularly convened IRB meeting. Any determinations of noncompliance or for additional follow-up are made at this time.

In the case of noncompliance or protocol deviations, additional monitoring visits may be necessary to ensure that required corrective and precautionary actions have been taken to prevent protocol deviations in the future, or as directed by the DORR, IRB Chair(s), and IRB as needed.

The ORR IRB staff assists investigators, if needed, in completion of required actions resulting from the PAM visit or IRB-determined corrective actions. Assistance may include providing guidance with protocol modifications and/or direction to appropriate training.

**Appeal Process**

If a PI disagrees with the findings of the post-approval monitoring visit or required actions, they are invited to address these concerns with the PAM during the discussion at the end of the visit. If a satisfactory resolution has not been determined, the PI may then contact the DORR to discuss these issues within 30 days. Again, if no satisfactory resolution is agreed upon, the PI may address the IRB in writing within a second 30-day period.

**Recordkeeping**

A copy of the final post-approval monitoring visit report is kept by the PAM and by ORR with study files.

**Appendix**

PI Self-Assessment
APPENDIX: PI Self-Assessment

The goal of post-approval monitoring of studies involving human subject research is to confirm by observation and documentation comparison, an accurate and consistent protocol performance, conducted in accordance with an Institutional Review Board (IRB)-approved protocol. An additional goal of the program is to provide education to the investigators on best practices for conducting their human subject research study in compliance with their IRB-approved protocol, Iowa State University (ISU) IRB policies and guidance, and federal regulations. The program is also designed to help investigators, their teams, and the University prepare for external audits by granting, regulatory, and accreditation agencies.

*Perhaps the most effective way to prepare for a PAM visit is to carefully and objectively read your approved protocol and make sure that you and your staff are performing the research activities as described and approved by the IRB. Many variables can play into the need for adjustment in the design, procedures, etc., of your protocol. The main thing to remember is any changes to the IRB-approved protocol must be approved by the IRB prior to implementation. It is easy to get caught up in the progress of research and forget to submit a modification. Likewise, an issue may seem trivial to a researcher, but it may be of great concern to the IRB, federal regulators, or auditors.*

*The staff of the ORR is always willing to assist in answering questions or to help facilitate modifications to your protocol. They can be reached at 515-294-4566 or irb@iastate.edu.*

**General Tips**

- How many participants are currently enrolled in the study? Is the number enrolled in line with the number approved? Is a modification to add participants needed?
- Are key personnel performing duties as described and approved? Are modifications needed?
- Have there been early withdrawals from the study? Have they been reported during continuing review?
- Have there been any adverse events? Were they reported?
- Who is responsible for conducting study procedures? Are procedures in accordance with what was approved by the IRB?
- Have any changes been made to the approved materials (recruitment fliers, questionnaires, interview questions, etc.)? Has IRB approval been sought prior to implementing these changes?
- Who is responsible for training study personnel on IRB protocol-specific procedures? Are records of training maintained?
- Are all research team members who have contact with participants or the participants’ data listed as Key Personnel on the IRB-approved protocol? Is a personnel modification needed?
- Is there a copy of the IRB-approved protocol on file? Including any continuing reviews and modifications? Are all personnel (i.e., PIs, co-PIs, research staff) aware of all approved modifications?
- Do you have a copy of the approval letter on file?
- Is the informed consent document being used the current version? Does it have the IRB stamp?
- ORR strongly recommends the addition of “Printed Name” lines to informed consent documents for each person signing (i.e., if required: child assent, parental consent, person obtaining consent).
- Are you using the IRB-stamped advertisements?
- Are study documents (i.e., applications for approval, approval letters, informed consent) maintained for 3 years?
- Are documents stored as outlined in the IRB-approved protocol?
- ORR strongly recommends creating a file for each participant containing all study documents (i.e., consent, surveys, debriefings, etc.) when applicable.
Common Findings

Below are examples of common findings from post-approval monitoring visits:

- The informed consent document on file is not complete (i.e., only the page containing the signature is on file).
- The IRB-approved version of the informed consent or assent document is not used.
- Dates:
  - Informed consents are not dated by participants or those obtaining consent (in real time).
  - Dates are added in by persons other than those giving or obtaining consent.
  - Dates of consent occur after study procedures have begun.
  - Dates of consent occur prior to receiving IRB approval of study.
- Signature problems (when applicable):
  - No real time signatures by individuals obtaining consent (missing, or postdated).
  - Signatures are illegible; this is particularly important when determining if individual giving consent for minors is authorized to do so (i.e., parent or legal guardian, not a grandma, uncle, aunt, sibling, etc.) Again, ORR recommends “Printed Name” lines in informed consent documents.
- Changes have been made to the IRB-approved survey questions or interview questions:
  - Questions have been added prior to IRB review or approval.
  - Questions have been removed prior to IRB review or approval.
- Recruitment methods have been changed prior to IRB review or approval.
- Survey methods have changed (e.g., from paper versions to online versions).
- Compensation plans have been changed prior to IRB review or approval.
- Study Records
  - Study records are not STORED as indicated (i.e., storing other than removal for working on them, stored unsecured).
  - Persons reviewing study records who are not approved or trained to do so.

If you have identified discrepancies between your current practices and those outlined in the approved protocol and these questions, please make the appropriate corrections. This may require submitting a modification to your protocol or simply implementing better documentation practices.

Remember, the goal of post-approval monitoring is not to “catch” you doing something you aren’t supposed to be doing. Rather, it is designed to facilitate research by making sure it is conducted in a manner where the conditions of federal regulations and University policy are met and by assisting researchers to identify and correct any deficiencies.