

<b>For Cause Post-IRB Approval Monitoring</b>	Effective Date	02.26.2019
	Revisions Date	03.03.2022

- 1.0 Purpose:** In accordance with federal regulations, the UMCIRB has the authority to observe or authorize a third party to observe the consent process and the research. This authority allows protection of the rights and welfare of humans participating in research activities. This standard operating procedure establishes guidelines for directed, for-cause monitoring by the Post-IRB Approval Monitoring Program (PAM) at East Carolina University (ECU). The PAM Program functions independently of the University and Medical Center Institutional Review Board (UMCIRB). The aim of the Program is to ensure maximum protection of human participants involved in research activities and promotion of best practices in the conduct of human research. This aim will be achieved through post-IRB approval monitoring of studies and UMCIRB activities as well as education of investigators, research staff and the research community.
- 2.0 Human Research Affected:**
- 2.1** Research reviewed and approved by the UMCIRB (both single site and multi-center).
- 2.2** Research conducted at ECU or an ECU affiliate and reviewed and approved by an external IRB.
- 3.0 SOP:** To ensure the UMCIRB and ECU are meeting their obligations to protect human research participants the PAM program will:
- 3.1** Evaluate whether investigators conduct studies as approved by the IRB;
- 3.2** Evaluate whether the IRB adequately addressed applicable ethical and compliance issues; and
- 3.3** Identify and implement educational and training opportunities based on findings.
- 4.0 Definitions:**
- 4.1** Monitoring: As defined by Good Clinical Practice (GCP) guidelines monitoring is the act of overseeing the progress of a clinical trial, and ensuring that it is conducted, recorded, and reported in accordance with the protocol, Standard Operating Procedures, Good Clinical Practice, and the applicable regulatory requirement(s). For the purposes of this SOP this definition of monitoring may also be applied to other human subject research as well as clinical trials.
- 4.2** Good Clinical Practice: A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected. GCP guidelines are often cited as best practices and may also be applied to human subject research other than clinical trials.
- 4.3** Post-IRB Approval Monitoring: Overseeing the progress of a clinical trial or other human subject research after it has been approved by the IRB.
- 4.4** For-Cause Monitoring: Monitoring of studies where there are perceived or confirmed ethics or compliance violations. A for-cause monitoring visit may be requested by a department, study team member(s), UMCIRB staff, the IRB or other institutional officials. For cause monitoring visits are requested generally due to concerns regarding study compliance and/or subject rights and welfare. For-cause monitoring may also be initiated due to complaints, a lapse in IRB approval, repeated errors or a lack of responsiveness by the PI to IRB requests.
- 4.5** Source Documents: Original documents, data, and records related to human subject research (e.g. hospital records, office charts, laboratory notes, subject diaries, evaluation checklists, completed subject surveys, interview notes, pharmacy dispensing records, etc.).

## 5.0 Responsibilities:

- 5.1 The Principal Investigator (PI) is ultimately responsible for the overall conduct of the research, appropriate delegation of roles, responsibilities and tasks, as well as compliance with applicable laws and policies. In addition, the PI is responsible for fully cooperating with PAM personnel as well as providing, in writing, plans for corrective action if any have been recommended.
- 5.2 Key Study Personnel (sub-investigators, study coordinators, faculty mentors, other study team members) involved in supervising, managing, or conducting study-related activities are responsible for following the protocol and any standard operating procedures and executing tasks as delegated in compliance with regulatory requirements and institutional policies.
- 5.3 Post IRB-Approval Monitoring Director is responsible for coordination of monitoring activities including but not limited to:
- 5.3.1 Routine monitoring of selected IRB approved studies;
  - 5.3.2 Conduct of for-cause monitoring as indicated;
  - 5.3.3 Assessment of UMCIRB activities related to studies being monitored;
  - 5.3.4 Reporting findings from monitoring to the appropriate party(ies); and
  - 5.3.5 Development of educational and training programs and development and dissemination of materials such as study tools, templates, and guidance for use by investigators and key study personnel.

## 6.0 Procedures:

### 6.1 For-Cause Post-IRB Approval Monitoring

- 6.1.1 For-cause monitoring may be requested by a department, study team member(s), IRB staff, the IRB, institutional officials, study sponsors or others. For-cause monitoring may be triggered when there is a subject or staff complaint, there are multiple protocol deviations, numerous reportable unanticipated problems, other concerns about the conduct of the study such as a lapse in IRB approval or allegations of noncompliance. Prior to initiating a for-cause monitoring visit the PAM staff will gather all information available related to the concern or allegation. The PAM staff will determine whether the concern or allegation is related to a specific study or studies or if it is more general in nature. During for-cause monitoring the PI, study team and others involved will be interviewed for the purpose of obtaining information required to make a determination as to the concern(s) or allegation(s).
- 6.1.2 Investigators, their research staff, their Department Chair and Associate Dean of Research will be notified by email that a request for a for-cause monitoring visit has been received by the PAM staff. The email correspondence will contain the following information:
- 6.1.2.1 An explanation as to the reason for the request for the monitoring visit, unless, in the determination of the PAM Director, the UMCIRB Administrative Director and/or the UMCIRB Chairperson, the investigation would be jeopardized by doing so or the investigator was the person who identified and reported the potential concern or noncompliance.
  - 6.1.2.2 A request for available dates and times for the monitoring visit;
  - 6.1.2.3 An estimate of how much time will be required to complete the monitoring visit;
  - 6.1.2.4 A request for a location for the monitoring visit, that allows for convenient access to the study team and study records/files by the PAM staff;
  - 6.1.2.5 Notification of which study(ies) will be reviewed;
  - 6.1.2.6 Notification of documents that should be available for review;
  - 6.1.2.7 Notification that the PI and/or his/her designee should be available to answer

questions during the visit; and

**6.1.2.8** That an exit interview summarizing review findings will be conducted with the PI and any key study personnel selected by the PI.

**6.1.3** Prior to the for-cause monitoring visit PAM staff will review the IRB records of the study(ies) to which the concern or allegation is related. If the concern or allegation is of a more general nature, the PAM staff will review selected studies which are being conducted under the direction of the investigator. IRB record review may include but is not limited to the following:

**6.1.3.1** Profile of PI and key study personnel to determine if applicable required training is up-to-date and CVs are provided when required;

**6.1.3.2** Assigned roles and responsibilities to ensure they match the delegation of authority log if applicable;

**6.1.3.3** Identified conflict-of-interests (COI), associated management plan if applicable and whether the IRB-approved consent contains language addressing the COI if required;

**6.1.3.4** Whether or not quorum was maintained for all IRB votes, if applicable, on the study;

**6.1.3.5** Were changes approved by the IRB reflected in the study documents;

**6.1.3.6** Were consent forms date-stamped properly;

**6.1.3.7** If an IRB member had a conflict, did (s)he recuse;

**6.1.3.8** Was the study approval ever allowed to expire and if so were any participants enrolled during the period of expiration; and

**6.1.3.9** For studies reviewed and approved by external IRBs the following will be reviewed:

**6.1.3.9.1** The electronic submission study application to ensure it has been properly populated with all external IRB approvals and approved documents.

**6.1.3.9.2** Whether or not a fully and properly executed IRB Authorization Agreement (IAA) is in place.

**6.1.4** The for-cause monitoring visit will begin with an interview of the investigator and any other key study personnel deemed necessary. The purpose of this interview will be to explain the concern or allegation which has been raised and gather information from the investigator and key study personnel related to the concern/allegation.

**6.1.5** At the time of a for-cause monitoring visit, all research/regulatory documents for the study(ies) for which a concern/allegation has been raised must be available for review. If the concern/allegation is of a general nature, a study or studies may be selected for review and the documents for the selected study(ies) must be available. Depending on the nature of the concern/allegation, the list of items to be reviewed includes, but is not limited to:

**6.1.5.1** Current IRB approved protocol/research plan/grant and all previous versions;

**6.1.5.2** Current IRB approved informed consent document(s) and all previous versions;

**6.1.5.3** All original signed informed consent documents;

**6.1.5.4** Initial and all continuing review IRB submissions; corresponding requests for revisions/additional information and approval letters;

**6.1.5.5** All IRB regulatory documents including; Investigator's Brochure (if applicable);

**6.1.5.6** All amendments and/or revisions to the protocol/research plan, consent, study personnel and corresponding approvals;

**6.1.5.7** If applicable to the study; all FDA required documentation and correspondence;

**6.1.5.8** If applicable to the study; all sponsor required documentation and correspondence such as monitoring and audit reports, etc.;

- 6.1.5.9 Documentation of all unanticipated problems involving risks to participants and others as well as IRB notification of such;
  - 6.1.5.10 Documentation of all study violations/deviations as well as IRB notification of such;
  - 6.1.5.11 Data Safety Monitoring Board reports as well as IRB notification of such;
  - 6.1.5.12 All other UMCIRB Correspondence;
  - 6.1.5.13 Investigator and research staff training and certification logs if applicable; and
  - 6.1.5.14 Other applicable study logs (i.e. screening logs, enrollment logs, consent logs, etc.).
- 6.1.6 For studies where participants have been enrolled, participant records will need to be available for review as well. The review of participant records may include but is not limited to:
- 6.1.6.1 The informed consent documents, inclusive, when applicable, of parental permission/consent documents, assents, and HIPAA authorization(s);
  - 6.1.6.2 Documentation of informed consent;
  - 6.1.6.3 Inclusion/exclusion criteria documentation;
  - 6.1.6.4 Source documentation and data collection forms; and
  - 6.1.6.5 The participant's medical record (if applicable to the study)
- 6.1.7 During the for-cause monitoring visit, PAM staff may request to observe the consent process using procedures which may include, but are not limited to:
- 6.1.7.1 Witnessing administration of informed consent to potential participants
  - 6.1.7.2 Surveying research participants enrolled in the study; the survey will include, but may not be limited to, the following questions:
    - 6.1.7.2.1 What information was provided during the informed consent process;
    - 6.1.7.2.2 Were you given the opportunity to ask questions;
    - 6.1.7.2.3 Were you given enough time to make a decision;
    - 6.1.7.2.4 Who originally administered the consent process?
- 6.1.8 During the for-cause monitoring visit PAM staff may request a tour of the facility to verify/confirm security of documents/records; verify/confirm control of storage and accountability of investigational products devices and specimens, if applicable to the study.
- 6.1.9 At the end of the monitoring visit; an exit interview will be conducted with the PI; and at the investigator's discretion, select study personnel. During this interview the PAM staff will provide an overview of the findings as well as an explanation as to the details related to follow-up of the monitoring visit such as possible corrective action plan(s), timeframe for PI's response to findings, etc.
- 6.1.10 PAM staff will generate a draft report of findings outlining the concern/allegations that prompted the monitoring visit, the findings of the monitoring visit, any required corrective actions and the time frame within which the corrective actions should be addressed, and recommendations for best practices. The draft report of findings will be disseminated to the following people within two weeks of completion of the monitoring visit:
- 6.1.10.1 Principal Investigator;
  - 6.1.10.2 Principal Investigator's Department Chair and Associate Dean of Research; and
  - 6.1.10.3 UMCIRB Administrative Director
- 6.1.11 Upon receipt of the draft report of findings, the PI will be required to provide a response outlining the status of each item requiring corrective action as well as the status of each item

where best practice recommendations are made. If the PI chooses not to implement the best practice recommendation(s) they must provide a rationale for this decision. The draft report of observations will contain the deadline for the PI's response to the PAM office.

- 6.1.12** Once the PAM Office receives the PI's response to the draft report of findings, a final copy of the report with the PI's response attached will be emailed to the PI, their Department Chair and Associate Dean of Research as well as the UMCIRB administrative director. This will signify that the file for the for-cause monitoring visit is complete.

**Revision History:**

<b>Date</b>	<b>Change</b>	<b>Reference Section(s)</b>
02.26.2019	Written as a free-standing SOP; separating out for-cause monitoring from routine monitoring SOP	All Sections
05.24.2019	Providing specific example of when for-cause monitoring might be initiated – a lapse in IRB approval	4.4; 6.1.1
03.03.2022	Revised title, revision to sections 6.1.10, 6.1.11, 6.1.12 based on recent Internal Audit consultation, addition of language to 6.1.8 and 6.1.9, and minor grammatical corrections	6.1.8, 6.1.9, 6.1.10, 6.1.11, 6.1.12

**References**

21 CFR 56.109

38 CFR 16.109

45 CRF 46.109

OHRP Institutional Review Board Written Procedures: Guidance for Institutions and IRBs (2018)