SECTION: For-Cause

SUBJECT: Purpose and Review Processes

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I. Definition

A review is considered "for-cause" when allegations, indications or possible concerns of human subjects related noncompliance are received from UMOR, IRBs, ancillary committees, research administration, research subjects, faculty, research support staff, or funding or regulatory agencies. ORCR receives requests to initiate a for-cause review for possible noncompliance from UMOR (e.g., the Human Research Protection Program (HRPP) Associate Director).

II. Purpose

The purposes of for-cause reviews may be one or more of the following:

- To determine whether or not there is noncompliance in a study being conducted;
- To analyze the frequency and nature of any alleged, or actual noncompliance;
- To determine whether or not, or to what extent, subjects may have, or could have been, harmed by noncompliance;
- To examine the seriousness and/or continuing nature of noncompliance for consideration by the IRB or institutional official of possible findings of serious and/or continuing noncompliance (See OM, Part 12, II.B.1);
- To recommend corrective actions, to provide remediation, and to prevent future noncompliance. Corrective actions are coordinated with other HRPP units, as appropriate;
- To determine root causes of any noncompliance and recommend remediation of the causes.

III. The Overall ORCR Review Process

ORCR receives requests to initiate a for-cause review for possible noncompliance from UMOR, (e.g., HRPP Associate Director). A for-cause review typically includes an in-depth examination of all aspects of a study and study protocol. During the course of the review, the ORCR reviewer may expand the review to include additional documents or documentation related to the study or study protocol in order to ensure a thorough review has been completed.

The U-M Operations Manual describes the circumstances under which allegations of noncompliance may, and must, be reported and describes the process for reporting, the protections afforded individuals who make reports, and the process for investigating and responding to reports (see OM Part 12, II).

IV. Procedures

Investigator notification and scheduling

a) The principal investigator (PI) will receive a letter of notification from the ORCR director.
b) The assigned ORCR reviewer will email the PI and describe the nature of the review.
c) The review is usually expected to begin within one week of ORCR's initial investigator contact.
d) The PI and study team members are expected to facilitate the review, including:

a. Cooperation in scheduling;
b. Attendance at interviews or meetings requested by ORCR;
c. Providing access to study records (electronic and hard copies).

Review preparation

1. ORCR reviews the eResearch application and IRB approved study documents prior to any on-site meeting or discussion.
2. ORCR may request additional information related to confidentiality protections or enrollment numbers.
3. When necessary, ORCR may contact internal U-M or external service units and study monitors to provide consultation or assistance with complex questions or interpretations that arise during a review.
4. The PI should ensure that all subject study records are available for review. Study binders will be requested for FDA-regulated studies.
5. The PI should provide adequate space for the on-site review.

On-site review

1. The study review generally includes a discussion meeting and on-site research record review. The length of time set up for the review may vary depending on the complexity of the research study and is determined by the ORCR reviewer.
2. Adherence to the IRB approved protocol is evaluated including subject records of recruitment, enrollment, informed consent, observations or procedures, study visits and any subject follow up activities.
3. Research records selected for review are based on the nature of the for-cause review and study risks. The review may include a complete review of all subject study records or portions of a subject study records. In addition, it may include study level tracking documents such as training logs, adverse event tracking logs, excel spreadsheets, etc. The extent to which all records or a portion of records will be reviewed is made on a case-by-case basis and may change as the review progresses, based on ongoing issues that are identified.
4. Any safety issues that could result in an immediate risk of harm to study participants are reported promptly to the IRB.

ORCR Report and Close out

1. Report Development
   ORCR develops a draft report of factual observations noted during the review and any recommended corrective actions. This draft is vetted with the U-M HRPP Associate Director and with the IRB of Record to ensure report information is clearly written and provides the PI with recommended corrective actions consistent with HRPP and IRB expectations. Feedback is requested within 10 business days.

2. Report Distribution
   To ensure report facts are accurate, the draft is then shared with the PI for feedback. The PI is informed that he or she may share the draft report with any other individuals or units that have

been involved in the review. PI feedback is requested within 10 business days. When the PI has returned his/her feedback, the final report is prepared and disseminated to the investigator, the IRB Director and Chairs, the HRPP Associate Director, the Executive IRB Director, the school or college Research Associate Dean (RAD), and/or Associate Chair for Research/Department Chair.

3. CAPA Development
   The IRB works with ORCR and other involved units to develop a CAPA plan, as necessary, based on ORCR's recommendations for corrective action. The CAPA plan will include two parts: substantive change and other minor corrections to ensure that the PI receives one plan.

4. CAPA Delivery and Monitoring
   The IRB delivers the CAPA to the PI. IRBMED's compliance coordinator monitors the completion of the corrective actions, as needed.

5. Closeout
   The review is satisfactorily completed when all corrective actions have been completed and all IRB related corrective actions have received IRB approval. At that time, IRB sends a close-out note to the investigator indicating that all corrective actions have been satisfactorily completed, including ORCR on the communication.