I. Definition

A review is considered “for-cause or directed” 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. OHRCR receives direction to initiate a for-cause review for possible noncompliance from UMOR (e.g., the Human Research Protections Program (HRPP) 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 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.
- To provide risk mitigation oversight to ensure all corrective actions have been implemented.

III. The Overall OHRCR Review Process

OHRCR receives direction to initiate a for-cause/directed review for possible noncompliance from UMOR, (e.g., the Human Research Protections Program (HRPP) Director). U-M IRBs forward concerns about noncompliance and requests for OHRCR review to UMOR. The IRB may request a review after identifying concerns with the study during committee review of a modification or renewal submission. Multiple submissions of unanticipated problems may also trigger this type of review. However, concerns about noncompliance may also come from any source. (see OM Part 12.II.B.2, Flow Diagram: Review of Complaints or Concerns about Human Subjects Research). All complaints and concerns related to the HRPP or to the conduct of individual studies are reviewed by the IRB or the HRPP Director, however, they will not all involve noncompliance or OHRCR review (see OM Part 12, II).
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).

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 OHRCR 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.

IV. Procedures

Investigator notification and scheduling
1. The principal investigator (PI) will receive a letter of notification from the OHRCR director.
2. The assigned OHRCR reviewer will email the PI and describe the nature of the review.
3. The review is usually expected to begin within one week of OHRCR’s initial investigator contact.
4. The PI is expected to facilitate the review, including:
   a. Cooperation in scheduling
   b. Attendance at interviews or meetings requested by OHRCR

Review preparation
1. OHRCR reviews the eResearch application and IRB approved study documents prior to any on-site meeting or discussion.
2. OHRCR may request additional information such as confidentiality protections or enrollment numbers.
3. The PI should ensure that all subject study records are available for review. Study binders will be requested for FDA-regulated studies.
4. The PI should provide adequate space for the onsite review

On-site review
1. When necessary OHRCR may contact internal U-M or external experts to provide consultation or assistance with complex questions or interpretations that arise during a review.
2. 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 OHRCR reviewer.
3. 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.
4. 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.

5. Any safety issues that could result in an immediate risk of harm to study participants are reported promptly to the IRB.

**OHRCR Report and Close out**

1. OHRCR develops a draft report of factual observations noted during the review and any corrective actions. This draft is vetted with the U-M HRPP Director and with the IRB to ensure report information is clearly written and to provide the PI corrective actions consistent with HRPP and IRB expectations.

2. To ensure report facts are accurate, the draft is then shared with the PI for feedback. PI feedback is requested within five business days. When the PI has returned their feedback, the final report is prepared and disseminated to the investigator, to the IRB, to the UMOR Vice President for Research, and to the school or college Research Associate Dean (RAD) and may include the school or college director.

3. When there are corrective actions, OHRCR will monitor progress completing the actions and will follow up until all corrective actions have been completed. Generally, corrective actions are expected to be completed within 30 days.

4. The review is satisfactorily completed when all corrective actions have been completed and all IRB related corrective actions have received IRB approval. OHRCR will send the investigator an email indicating all corrective actions have been satisfactorily completed. This email will also include the fact that OHRCR reserves the right to revisit the study at any time.