

## Part 12 - Quality Assurance and Research Compliance

*This section describes the University's quality assurance, quality improvement, and enforcement activities.*

### I. QUALITY ASSURANCE: ASSESSMENT AND IMPROVEMENT

#### A. Performance Measurement and Quality Assessment

Refer to [HRPP OM Part 12.I.A](#)

#### B. Quality Improvement

Refer to [HRPP OM Part 12.I.B](#)

### II. COMPLIANCE OVERSIGHT

#### A. Response to Complaints or Allegations of Noncompliance

Refer to [HRPP OM Part 12.II](#)

If information brought to the attention of the IRBMED, through any source, indicates the possibility that research subjects or others are exposed to unnecessary or excessive risks, or that the requirements of the IRBMED are not being met, the IRBMED shall collect any additional information necessary to evaluate the credibility or accuracy of the information and determine whether further action [such as education of the Principal Investigator (PI) or Principal Investigator's research staff, or suspension or termination of the project] appears necessary. In some circumstances, in consultation with the IRBMED, the Principal Investigator may place a voluntarily "hold" on new subject accrual or research-related interventions during the fact-finding period, unless to do so would place subjects in immediate harm or otherwise jeopardize their well being.

Under institutional authority and federal regulations (45 CFR 46.103[b][5], 45 CFR 46.113, 21 CFR 56.113), the IRBMED is responsible for overseeing the safety of human subject research participants and has the authority to suspend or terminate human subject research that is (1) not being conducted in accordance with the federal and IRBMED's requirements or (2) has been associated with unexpected serious harm to subjects.

In the event of a credible allegation of noncompliance with applicable law or University policy, including these procedures, the matter will be handled consistent with University policies.

1. Should the allegation of noncompliance pose immediate risk to subjects, the IRBMED Director will notify the IRBMED Chairs, the Medical School Associate Dean for Regulatory Affairs, the Health System Legal Office, and the Office of the Vice President for Research (UMOR) immediately.
2. Allegations or other indications of fabrication or falsification of research results will be reported to the Medical School Associate Dean for Regulatory Affairs, the Health System Legal Office, and the UMOR.

An IRBMED staff member initiates a review of any complaint or allegation of noncompliance made to the IRBMED. If assistance with the review is desired, the IRBMED Chairs will make a written request to UMOR (usually via the IRBMED Director) to request assistance from OHRCR. The purpose of the review is fact-finding, and may involve examination of study records, including, but not limited to, source documentation, informed consents, and the study protocol. Where appropriate, the IRBMED staff member may engage in discussion with the research team, research participants, the complainant (if known), and others.

Initial fact-finding may include, but is not limited to, any or all of the following:

- Providing IRBMED with copies of or access to:
  - Signed informed consent documents
  - Study files
  - Drug dispensement logs/IDS logs
  - Patient records
  - Lab tests
  - Delegation logs
- Observation of study activity (e.g., witnessing the informed consent process)
- Review of study by an outside auditor
- Interviews of study personnel
- Interviews of research subjects

Upon completion of the review, the report is provided to the Chairs in the context of a Chairs and Director Meeting (CDM). The Chairs review the information and determine whether the complaint or allegation of noncompliance constitutes potentially serious and/or continuing noncompliance. If so determined, the matter is referred to the convened board with oversight for the study in order to make a final determination as to the nature of the noncompliance.

The IRBMED shall notify the Medical School Associate Deans for Research and Regulatory Affairs and the UMOR of any complaints or allegations of noncompliance, as required in [HRPP OM Part 12](#). If necessary, the UMOR will notify any applicable Federal Agency.

During the course of investigating an allegation of noncompliance, the IRBMED may request assistance from the OHRCR through the UMOR or the Health System Legal Office.

#### **1. Local Reports**

The IRBMED staff maintains records of all complaints and allegations of noncompliance that come to the attention of the IRBMED. These records include communications with the complainant and other parties providing information to the IRBMED, copies of source documents and other information gathered during the fact-finding activity, analysis of the fact-finding results for presentation to IRBMED Chairs and board members, notes and minutes of Chair and board member deliberations and determinations, and communications with the PI and relevant study personnel.

The IRBMED Chairs and Medical School Associate Deans for Research and Regulatory Affairs are provided with any copies of case reports that are prepared for submission to the UMOR.

The IRBMED shall promptly notify the UMOR of (1) any unanticipated problems involving risks to subjects or others or any potentially serious or continuing noncompliance with institutional policy; and (2) any suspension or termination of IRBMED approval for a project. In certain instances of alleged or apparent noncompliance, the IRBMED may choose to provide an early preliminary report to the UMOR (i.e., where the noncompliance may pose immediate risk to subjects) prior to a determination of serious or continuing noncompliance. As described in the [HRPP OM Part 12](#), the UMOR may choose to further investigate the reports of serious or continuing noncompliance or to ask for additional review by the Office for Human Research Compliance Review (OHRCR). For situations reported to the UMOR for additional review and/or reporting, the Vice President for Research makes and reports the institutional conclusions and imposes any institutional sanctions or remediation requirements. Summaries of non-serious or non-continuing noncompliance concerns are reported by IRBs to the UMOR on a quarterly basis, as a way of monitoring the need for attention to policy or to education.

#### **2. Institutional Reports**

Refer to [HRPP OM Part 12.II.H](#) which describes the obligations of the University to make additional reports outside the institution to sponsors and government authorities with jurisdiction.

## B. Noncompliance Review Procedures

Refer to [HRPP OM Part 12.II.B](#)

### 1. Definitions

Refer to [HRPP OM Part 12.II.B.1](#)

### 2. Process Summary

Refer to [HRPP OM Part 12.II.B.2](#)

### 3. Rights of Faculty, Staff, or Others Accused of Noncompliance

Refer to [HRPP OM Part 12.II.B.3](#)

### 4. Assurances of Confidentiality

Refer to [HRPP OM Part 12.II.B.4](#)

### 5. Policy Against Retaliation for Reporting

Refer to [HRPP OM Part 12.II.B.5](#)

## C. How Compliance Concerns Are Brought Forward

Refer to [HRPP OM Part 12.II.C](#)

Reports or allegations of noncompliance are brought forward by, but are not limited to, the following means:

- Telephone
- Via electronic mail (e-mail) communications
- Anonymous communications (telephone, mail, e-mail)
- UM Compliance Hotline (1-866-990-0111)
- Through staff or faculty of the UM

## D. Receipt and Initial Handling of Allegations of Noncompliance

Refer to [HRPP OM Part 12.II.D](#)

## E. Chair and Board Considerations and Determinations

Refer to [HRPP OM Part 12.II.E](#)

If, according to the results of the IRBMED fact-finding, the alleged noncompliance is determined by the IRBMED Chairs or Director to be credible and potentially serious or continuing, the case is presented to the IRBMED Co- and Vice-Chairs collectively at the next available Chairs and Directors Meeting, not later than thirty (30) days from the fact-finding determination. In reviewing the alleged noncompliance, the Chairs may request a meeting with the PI and others to discuss the concerns and provide an opportunity for the study team to correct or clarify the fact-finding information.

The Chairs determine by vote whether or not the activity has (1) possibly caused injury or an unanticipated risk to subjects or others; or (2) possibly constitutes serious or continuing noncompliance with IRBMED determinations or federal regulations. Documentation of the outcome of a decision by the Chairs to refer the matter to the convened IRB will be sent to the Medical School Associate Deans for Research and Regulatory Affairs, the Health System Legal Office, and the PI.

If the convened IRB determines that the noncompliance was not serious and/or continuing, the Medical School Associate Deans for Research and Regulatory Affairs, the Health System Legal Office, and the PI will be notified. A finding of serious and/or continuing noncompliance as determined by the convened IRB will be sent to the PI, the Department Chair and Associate Chair for Research (if applicable), the Medical School Associate Deans for Research and Regulatory Affairs, the Health System Legal Office, and the UMOR. If, at the request of the Medical School or the UMOR, there is additional information or investigation needed, UMOR may request the assistance of OHRCCR. Any request for additional information or investigation will be assessed by OHRCCR for the amount of staff resources, time required, and the depth of review. The outcome of this assessment will be reported to the requesting party.

#### F. Actions of the Institutional Official

Refer to [HRPP OM Part 12.II.F](#)

#### G. Response to Determinations of Noncompliance

Refer to [HRPP OM Part 12.II.G](#)

The IRBMED Co-Chairs will convey the board's decision by telephone or e-mail to the Principal Investigator at the conclusion of the board meeting and vote as to whether or not the noncompliance constitutes serious and/or continuing noncompliance. A formal letter will be sent to the Principal Investigator outlining the reasons for the board's decision and any requested remediation, e.g., attendance at a designated IRBMED educational workshop(s).

#### **Monitoring Activities**

##### 1. Special Requirements for Monitoring the Conduct of Human Research

The IRBMED may monitor studies both for-cause (e.g., suspected noncompliance) and not-for-cause (e.g., random or risk-based review for quality assurance purposes). Monitoring may include, but is not limited to, accessing and reviewing any or all of the following:

- Signed informed consent documents
- Study files (protocol, approval letters, advertisements, etc.)
- Drug dispensement log/IDS logs
- Patient records
- Lab tests
- Observation of study activity (e.g., witnessing the informed consent process)
- Review of study by an outside auditor
- Interviews of study personnel
- Interviews of research subjects
- Study personnel logs

##### 2. Considerations for Imposition of Special Monitoring Requirements

The IRBMED may impose special requirements or restrictions on either a PI or a particular study. These may be imposed because of risk level, safety issues, conflict of interest issues, or because of findings of noncompliance.

#### **Examples of Special Monitoring Requirements**

Requirements or restrictions imposed on a PI, study team member or project may include, but are not limited to, any or all of the following:

- Requirement for education, certification in the conduct of clinical research, i.e., the Association of Clinical Research Professionals (ACRP) or the Society of Clinical Research Associates (SoCRA), and re-certification of PEERRS
- Less than one year approval of the research project

- Submission of reports to the IRBMED at specific time intervals (in addition to the study's scheduled continuing review submission for renewal of IRBMED approval)
- Submission of reports to the IRBMED at specific increments of subject participation (e.g., after every third subject completes the trial or after the first three doses of an agent)
- Restriction on location of study activities
- Requirement for additional supervision of overall study or aspects/activities of the study
- Prohibition, permanently or for a period of time, from obtaining informed consent from subjects
- Prohibition, permanently or for a period of time, from conducting certain types of research
- Prohibition, permanently or for a period of time, from serving as a PI or study team member

#### H. Institutional Notification and Reporting Requirements

Refer to [HRPP OM Part 12.II.H](#)

### III. OTHER REPORTABLE EVENTS (ADVERSE EVENTS, UNANTICIPATED PROBLEMS INVOLVING RISKS TO SUBJECTS OR OTHERS) AND SUSPENSION OR TERMINATION OF IRB APPROVAL

Refer to [HRPP OM Part 12](#) and the information below.

#### A. Background

Refer to [HRPP OM Part 12.III.A](#)

#### B. Roles and Responsibilities

Refer to [HRPP OM Part 12.III.A.1](#)

##### 1. Researchers

As noted in the OM, guidelines and reporting procedures for reporting Adverse Events (AEs), Other Reportable Information or Occurrences (ORIOs), including those AEs and ORIOs that are also unanticipated problems involving risks to subjects or others, are posted on the [IRBMED website](#). This guidance is also referenced within the help feature in eResearch. It provides the timelines and process for submitting reports. Researchers are responsible for understanding and following these guidelines and reporting procedures. The IRBMED offers workshops that review the guidelines and will consult with study teams as needed in order to assist PIs in understanding the reporting requirements. Failure to follow these guidelines may require the IRBMED to halt the study and/or the institution to report the noncompliance to government agencies or study sponsors.

As noted in the guidelines and the OM, PIs should be aware of their option to submit a "Study-Specific AE Reporting Plan" to the IRBMED, either with their initial IRBMED application or via an amendment on an approved study. If approved, a study-specific plan would be used to determine the required AE reporting and timing of reports, instead of the requirements in the [Standard AE Timetable](#), which applies the most stringent reporting required by the FDA (21 CFR 312 and 812), NCI and NIH. Researchers who initiate an approved study using a standard adverse event reporting plan and then modify the project to a study-specific AE reporting plan must follow the standard reporting guidelines until the IRBMED approves the modification.

For studies that do not involve investigational agents, and particularly for studies that are minimal risk, a study-specific plan is recommended. [Guidance for developing a study-specific plan](#) can be found on the IRBMED website.

2. The IRBs (Members, Consultants, and Staff)

Refer to [HRPP OM Part 12.III.A.2](#)

a) AEs, ORIOs and Unanticipated Problem Involving Risks to Subjects or Others (UaPs/UPIRSOs) Review Decisions

An essential element of human subject protection is identifying, analyzing the causes of, and responding appropriately to expected and unexpected AEs, as well as to UaPs/UPIRSOs. Principal Investigators are required to identify and help analyze the events and to formulate responses.

Adverse Events are events that involve physiological, social, legal, financial, or psychological harm to subjects or risks of harm to additional subjects or others. Adverse Events include expected and unexpected harmful effects, as well as unexpected risks of an interaction or intervention.

**Adverse Events may be caused by:**

- The test article or test procedure
- Other aspects of the interaction or intervention
- The subject's underlying condition
- The subject's concurrent standard treatment

**IRBMED board members consider the following when reviewing an AE report:**

- Principal Investigator's assessment of the AE and concurrence or disagreement with that assessment. The reviewer and board will consider:
  - Causality and relatedness of the event to the research, not just to an investigational agent that is part of the research
  - Seriousness
  - Expectedness
  - Whether the event constitutes an UaP/UPIRSO
  - Whether urgent communication with the PI, IRBMED director, UM Office of General Counsel, UMOR, or other authority or unit (e.g., whether risk management is required)
  - Safety of subjects (including whether the study should be halted or modified)
  - Risk/benefit assessment of the study
  - Impact of AE on subjects' willingness to participate in the study

**For AEs not described in the currently approved informed consent document (ICD), the review will consider:**

- Whether AE/SAE type should be added to the ICD
- Whether previously enrolled subjects should be notified and/or re-consented

**IRBMED board members consider the following when reviewing an ORIO report:**

- Principal Investigator's assessment of the ORIO and concurrence or disagreement with that assessment. The reviewer and board will consider:
  - Causality and relatedness of the event to the research, not just to an investigational agent that is part of the research
  - Whether the event constitutes an UaPs/UPIRSOs
  - Whether remediation is required (e.g., education of the study team or referral to risk management)

- Whether urgent communication with the PI, IRBMED director, Office of General Counsel, Co- or Vice-Chair, UMOR or other authority is required
- Whether the report indicates that serious or continuing noncompliance may have occurred
- Whether the report indicates that an UaP/UPIRSO has been identified
- Safety of subjects (including whether the study should be halted or modified)
- Risk/benefit assessment of the study
- Impact of ORIO on subjects' willingness to participate in the study

**For ORIOs not described in the currently approved ICD the review will consider:**

- Whether event or information should be added to the ICD
- Whether previously enrolled subjects should be notified and/or re-consented

**IRBMED Board Members consider the following when reviewing an UaP/UPIRSO. Is the event:**

- Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
- Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research);
- Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

**The list of problems that require reporting in accordance with the above definition. Include:**

- Internal AEs that are unexpected, involve new or increased risks, and are related to the research.
- External AEs that are UaPs/UPIRSOs.
- Changes made to the research without prior IRB approval in order to eliminate apparent immediate harm.
- Other unanticipated information that is related to the research and indicates that subjects or others might be at increased risk of harm. For example:
  - Information that indicates a change to the risks or potential benefits of the research. For example:
    - An interim analysis or safety monitoring report indicates that frequency or magnitude of harms or benefits may be different than initially presented to IRBMED.
    - A paper is published from another study that shows that the risks or potential benefits of your research may be different than initially presented to IRBMED.
    - A breach of confidentiality.
    - Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.
    - Change to the protocol taken without prior IRBMED review to eliminate an apparent immediate hazard to a research subject.
    - Incarceration of a subject in a protocol not approved to enroll prisoners.
    - Event that requires prompt reporting to the sponsor.
    - Sponsor imposed suspension for risk.
    - Complaint of a subject when the complaint indicates unexpected risks or cannot be resolved by the research team.
    - Protocol violation (meaning an accidental or unintentional change to the

IRB approved protocol) that harmed subjects or others or that indicates subjects or others may be at increased risk of harm.

The review of problems reported by investigators. In this description, specify the following:

- The individual or individuals (by position or title) who are responsible for making an initial determination about whether a reported event is an UaP/UPIRSO.
- The information that reviewers receive to determine whether a reported event is an UaP/UPIRSO.

**IRBMED staff will consider the following when reviewing an AE, ORIO or UaP/UPIRSO report:**

- Whether urgent notification of the IRBMED Director, Health System Legal Counsel, a Co- or Vice-Chair, the Medical School Associate Deans for Research and Regulatory Affairs, UMOR, or other authority is required (e.g., whether to notify Co- or Vice-Chair of subject incarceration report)
- Completeness
- Whether necessary supporting documents are included
- Whether submission occurred within the required timeframe
- Whether the event or information is described in the currently approved informed consent document (when applicable)

Events that are unexpected, related, or linked in a significant way to the research, and indicate risks that were previously unknown or unrecognized, will be flagged to enable the reviewer to assess whether the event represents a UaP/UPIRSO.

**b) AEs, ORIOs, and UaP/UPRISOs Triage, Timelines, and Type of Review**

The workflow for review of AEs and ORIOs is described [here](#).

The workflow for possible UaPs/UPRISOs is found [here](#).

**The timelines for completion of review are dependent upon:**

- Whether the report is a UaPs/UPIRSOs
- The seriousness of the report
- Completeness of the report
- Openings on IRBMED meeting agendas for full-board reviews or Single IRB Member review workload

Generally, IRBMED staff open submissions for initial assessment within three (3) but no more than ten (10), business days from their arrival in the staff in-box. Requests for incomplete reports to be completed by the study team should be sent in a timely manner from the date of the initial assessment. However, if an incomplete report raises serious concerns, it may be sent to a designated reviewer while the missing information is being collected. Serious reports identified as possible UaP/UPIRSO will receive full board review as soon as possible, usually at the next available full-board IRB meeting. Non-serious reports identified as possible UaP/UPIRSO will receive standard assignment of a full-board meeting based on the available members and open agenda slot of that reviewer. Required changes to the submission or research, if any, will be communicated to the researchers. If a Single IRB Member reviewer of an AE or ORIO report requires changes to the research based upon that report, or if the report is judged to include potential UaPs/UPIRSOs, the submission must be sent for convened full-board review. UaP/UPIRSO problems will be reported to UMOR as soon as possible, but not later than seven (7) days from IRBMED's Board determination.



All AEs and ORIOs review decisions for eResearch projects are documented electronically.

**3. University of Michigan Office of Research (UMOR)**

*Refer to [HRPP OM Part 12.III.A.3](#)*

**4. Office of Human Research Compliance Review (OHRCR)**

*Refer to [HRPP OM Part 12.III.A.4](#)*

**IV. QUESTIONS AND CONTACT INFORMATION**

Questions are answered by phone by the IRBMED Receptionist or staff designee. The receptionist or designee will take the pertinent information and route the message to the most appropriate person to answer the question.

Principal Investigators and study team members may request representatives from the IRBMED office to meet with them to discuss a research project or regulatory question by contacting the Office Reception number listed below.

**A. IRBMED Director and Office**

- Director and Office Reception: (734) 763-4768
- E-mail: [irbmed@umich.edu](mailto:irbmed@umich.edu)
- US Mail: IRBMED, 2800 Plymouth Rd., Building 200, Room 2086, Ann Arbor, MI 48109-2800

**B. Questions Concerning University Policies and Procedures**

- The Office of Research: (734) 615-1332
- The Office of Regulatory Affairs: (734) 647-1576
- The Office of the Vice President for Research: (734) 763-1289
- The Health System Legal Office: (734) 764-2178