IRBMED Guidance
Reporting Time-Sensitive Modifications

NOTE: *The following guidance does not apply to studies where IRBMED is relying on an external IRB for regulatory oversight ("ceding" IRB oversight). If your study is ceded, you must reach out to the IRB of Record for guidance and then submit an Amendment to IRBMED per the standard ceded study guidelines.*

General Overview

Per federal regulations, IRB review and approval is required before implementing any changes to IRB approved research (*an exception exists to eliminate an immediate hazard to subjects*). This guidance is intended to assist study teams by outlining the specific procedures for submitting time-sensitive or urgent changes to IRBMED approved research studies.

Generally, any submission received by IRBMED will be screened and triaged within 24 hours during normal business hours. When submitting time-sensitive submissions, study teams must follow the directions provided below. This process will ensure that the submissions are reviewed and approved promptly. Once submitted, the study team can also contact the staff owner of the submission in eResearch (via Post Correspondence activity, selecting IRBMED as a recipient) for a status update.

The following framework outlines specific reporting mechanisms based on the type of changes:

- To report time-sensitive **changes that are study-wide and/or permanent**, submit an Amendment in eResearch by following the directions provided below (Section I).

- To report time-sensitive **changes that are one-time and/or temporary** to accommodate one or two subjects (e.g., adjustment of enrollment criteria for a single participant), submit an ORIO in eResearch by following the directions provided below (Section II).

- To report time-sensitive **changes during the weekend or non-business hours**, contact the IRBMED Chair on Call by following the directions provided below. (Section III).

- To report **changes that were implemented without IRB approval** (*to eliminate apparent immediate hazards to the subjects*), submit an ORIO in eResearch by following the directions provided below (Section IV).

I. Study-wide and/or Permanent Changes (Amendment)

These are the changes that will usually impact the overall study and therefore should be submitted as an Amendment in eResearch.

- **Labeling:** Update the Amendment Title to indicate *"Time-Sensitive Changes" or "Urgent Changes" (or as appropriate to reflect the situation) along with any other indicators*. This will ensure that the submission is screened and triaged appropriately.
- **Include adequate details** in the Amendment to minimize the back and forth between IRBMED and the study team. For example:
    - Explain the time-sensitive nature in the Amendment coversheet (Section 01.4 or 01.5).
    - Clearly describe the proposed changes in the Amendment coversheet.

- Evaluate how the proposed changes will impact the current study procedures and participant risk level, and update the appropriate eResearch section(s) and study materials (protocol, recruitment, informed consent, etc.) as applicable.
- When updating and/or uploading the study materials, ensure that these are revised and uploaded appropriately (i.e., using the last IRB approved document from eResearch, enabling track-changes, uploading the track-changes document on top of the previous track-changes document, etc.)
- If the informed consent document is being updated, evaluate, and indicate whether or not subjects will be re-consented. See IRBMED guidance on "Seeking Reconsent from Research Participants"

NOTE: The standard eResearch Amendment process permits only one amendment to be in progress at the same time to assure version control of the IRB application/protocol. When an Amendment is already in progress and the study team must make additional study wide and/or permanent changes, contact the IRBMED staff owner for guidance. If possible, IRBMED staff will return the current amendment to make additional changes. If not possible, IRBMED staff will discuss other options.

II. One-time and/or Temporary Changes (ORIO)

The study teams may encounter situations where the intended change is one-time, impacts only one or two subjects, and is not a study-wide change. For these situations, the ORIO reporting process can be utilized to obtain IRB approval. As applicable and feasible, the sponsors and/or coordinating centers should be contacted for their concurrence. The study team should carefully evaluate whether the intended change is a one-time or a permanent study-wide change before using this ORIO process.

Example(s) of scenarios where this process may be permitted:

- A request to enroll a participant who does not meet the currently approved eligibility criteria:
  - Lab values slightly differ from those stated in the protocol
  - Participant age slightly varies from inclusion criteria (but not adding children and/or other new subject population)
- Making adjustments to the current study drug dosage (but not adding new drugs or devices)
- An amendment is already in-progress for study-wide protocol changes but the study team needs to implement specific protocol changes for one or two subjects. In this case, this is considered a temporary change that is limited to 1-2 subjects although there is a protocol amendment.
  - Example: Change in the consent process to utilize a different, institutionally approved, method of documentation, such as phone consent until the Amendment for the permanent change is approved.

Example(s) of scenarios where this process will NOT be accepted:

- Changes to the study procedures that will impact all or most of the subjects
- Adding a study team member as this requires assessments only available within the Amendment process
- Adding a vulnerable population (such as children or cognitively impaired adults) and/or additional research arms where the changes must be made via an Amendment to complete the required information in eResearch.

When submitting the ORIO:

- **Labeling:** *When creating the ORIO, update the ORIO title to indicate "Time-Sensitive Change" or "Urgent Change" (or as appropriate to reflect the situation) along with any other indicators*. This will ensure that the submission is screened and triaged appropriately.
- Select the "Protocol Deviation" sub-type in eResearch ORIO 1-2.1
- **Include adequate details** in the ORIO submission to minimize the back and forth between IRBMED and the study team. For example:
    - Indicate why the ORIO is being submitted instead of an Amendment.
    - State how the proposed changes will impact the current study procedures and participant risk level, and clarify whether or not the study materials (informed consent document or other) will be updated. If updated, upload them within the ORIO submission.
    - If the informed consent document needs to be updated:
        - Use the most recent document from eResearch Section 10-1 to make changes
        - Add a note in the consent document footer (right-hand side) to indicate that this is a one-time urgent change and include the ADV submission ID for tracking purposes. *Note: IRBMED will not be able to include its approval stamp in the header.*
        - Evaluate, and indicate whether or not subjects will be consented or re-consented.
    - As applicable, state or clarify whether the sponsor and/or the coordinating center has been contacted about the proposed changes.
    - Also, upload any additional supporting documentation (such as sponsor approval or other similar documentation)

Once submitted, the ORIO will be reviewed by IRBMED staff to ensure that the proposed changes are in compliance with this guidance. The submission will then be assigned for either expedited (if the changes meet the regulatory definition of "minor") or full board review (if the changes are substantial and/or may impact subject safety).

NOTE: If IRBMED notes that a study team is submitting frequent one-time/urgent ORIOs for an individual IRB application, IRBMED may require a protocol amendment to permanently address inclusion/exclusion criteria or protocol procedures that are not addressing current/recurrent circumstances.

III. WEEKENDS or NON-BUSINESS HOURS (Chair on Call)

The IRBMED Chair on-call can be contacted directly if there is a time-sensitive situation or a submission that is one-time and/or temporary **and** requires immediate IRBMED attention during the weekends or non-business hours. This method can also be utilized if there are any extenuating circumstances during which the study team cannot obtain IRBMED approval via an eResearch submission.

For scenarios/examples, review the examples outlined under the "Section II. One-time and/or temporary changes (ORIO)" heading above.

Create and submit an ORIO in eResearch as outlined above under Section II. Once the ORIO is submitted, notify the IRB Chair on-call via an email with the submission ID and **follow-up with a page.**

When sending the email:

- Indicate in the subject title "Urgent Changes, requesting IRBMED Chair On-Call approval"
- Copy IRBMED@umich.edu on the email
- Provide the submission ID (ADV000…./HUM….)
- Include a telephone number for the chair to contact the PI

The IRBMED Chair on-call may take one of the following actions:

A. If the changes are **not** impacting subject safety and **meet the regulatory criteria to be "minor changes,**" the IRBMED Chair on-call may approve the proposed changes.
   - If approving, the Chair on-call will provide their approval or acknowledgment via the Post Correspondence activity to the study team and the IRBMED staff in eResearch. Later, IRBMED staff will issue the formal IRB approval letter.
   - If the IRBMED Chair on-call determines that changes are required, the Chair will provide specific contingencies and communicate this to the study team and via the Post Correspondence activity in eResearch.
   - It is the responsibility of the study team to provide adequate information to the IRBMED Chair on-call and document IRBMED approval.
   - If the changes are also intended to be permanent and/or study wide, an Amendment must also be submitted and approved.

B. If the changes impact subject safety **and/or** do not meet the regulatory criteria to be "minor changes" the changes are **not eligible for approval** by the IRBMED Chair On-call. For these situations, the study team should carefully evaluate the intended changes and act accordingly:
   - If the intended change is to eliminate an imminent apparent hazard to the subjects, the change can be implemented without IRB approval but a follow-up ORIO submission is needed. See Section IV below for additional details.
   - If the intended change is NOT to eliminate an imminent apparent hazard to the subjects, the study team must submit an Amendment or ORIO as described above in this guidance document (see Section I or Section II).

IV. Changes to Eliminate Imminent Hazards (ORIO afterward)

Federal regulations (HHS 45 CFR 46.108(a)(3)(iii) and FDA 21 CFR 56.108(a)(4)) and IRBMED Standard Operating Procedures permit researchers to immediately implement a protocol change without IRB approval ONLY when the change is intended to eliminate an apparent immediate hazard to subjects.

Note that these types of circumstances are expected to be rare. Investigators should use their best judgment in determining to proceed without IRB approval. As applicable and feasible, permission/advice of sponsors may be necessary for evaluating modifications for investigational agents. Study teams are strongly encouraged to contact IRBMED for consultation (email IRBMED at IRBMED@umich.edu during normal business hours **or** contact the IRBMED chair-on-call during weekends or non-business hours).

If a study team determines it is necessary to make a protocol modification to eliminate apparent immediate hazards to subjects and there is no adequate time to obtain IRB approval, these modifications

can be made without prior IRBMED approval but must be reported to the IRBMED **within 5 calendar days** via the ORIO reporting mechanism.

When submitting the ORIO:

- In the ORIO title, indicate "Changes Implemented without IRB approval" along with any other indicators related to the change.
- Select "Protocol Deviation" sub-type in eResearch ORIO 1-2.1.
- In eResearch ORIO 6.1, select "Deliberate protocol departure for subject's safety"
- In eResearch ORIO 6.3, describe the protocol change(s) that were made.
    - Indicate if any changes to the study documents (protocol, informed consent, etc.) are required.
    - Provide adequate information for IRBMED to acknowledge that the changes were intended to eliminate an apparent immediate hazard to subjects.
- Upload any supporting documentation such as sponsor's approval or other similar documentation.

NOTE(s):

1. If the modification is a permanent or study-wide change, an Amendment must also be submitted.
2. Additional reports to the FDA may be needed if the U-M PI is also the IND/IDE holder. Contact MICHR MIAP for assistance.