

IRBMED Guidance Time-Sensitive Research Modifications During COVID-19 (Procedures for Urgent Amendments)

Per federal regulations, IRB review and approval is required before implementing proposed changes to IRB approved research (an exception exists for immediate hazard to subjects). In order to assist study teams with procedures for submitting time-sensitive or *urgent amendments* to research studies (especially as it relates to COVID-19 circumstances), this document consolidates IRBMED guidance in a single location.

I. URGENT MODIFICATIONS FOR SUBJECT SAFETY (One-time event, not a permanent change)

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. *These protocol changes may impact the risk level to the subjects and thus may be considered more than minimal risk.*

Eliminating immediate hazards may include reaction to a perceived hazard or an event that exceeds the parameters set in the approved IRB application. Note that these types of changes are generally expected to be rare. Investigators should use their best judgment in determining to proceed without IRB approval in these scenarios. Note that permission/advice of sponsors may be necessary for evaluating modifications for investigational agents. IRBMED can be contacted at IRBMED@umich.edu for consultation.

If a study team determines it is necessary to make a protocol modification to eliminate apparent immediate hazards to subjects, 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. NOTE: Additional reports to FDA may be needed if the U-M PI is also IND/IDE holder. Contact [MICHMIAPIAP](#) for assistance.

When submitting the ORIO, please follow the below instructions:

- In the ORIO title, indicate “COVID Protocol change without IRBMED approval” along with any other indicators related to change
- Select “Protocol Deviation” sub-type
- In 6.1, select “Deliberate protocol departure for subject’s safety”
- In 6.3, describe the protocol change(s) that were made. Also, indicate if any changes to the study documents (protocol, informed consent, etc.) are required. Provide enough 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: If the modification is a permanent change to the research study, an Amendment must also be submitted in eResearch.

II. TIME-SENSITIVE MODIFICATIONS NOT IMPACTING SUBJECT SAFETY

If there is no apparent immediate hazard to subjects but the intended change is time-sensitive (changes to lab criteria to enroll a subject, changes to the study team, timing of study visit, changing from in-person visits to telephone visits, etc.), researchers must obtain IRB approval before any changes in the study procedures can be implemented. Consider the strategies below for these situations. *These protocol changes may not impact the risk level to the subjects and thus must be considered minimal risk.*

A. eResearch Amendment (Standard process)

- Submit an Amendment in eResearch and note the time-sensitive nature by appropriately labeling the submission

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- Indicate “COVID Time-Sensitive” or “COVID Urgent” (or as appropriate to reflect the situation) in the amendment title
- Explain the time-sensitive nature in the Amendment coversheet (Section 01.4).
- This will allow IRBMED to identify and appropriately triage the submission.
- The study team can also contact the IRB staff owner of the study (or, the general email ID at irbmed@umich.edu) for a status update and/or to notify the time-sensitive nature of the Amendment.
- **IRBMED is currently resourced to address these requests promptly. Submissions received by IRBMED will be screened and triaged within 24 hours during normal business hours. During the weekend, these will be checked periodically.**
 - eResearch permits only *one* amendment at a time in the submission and review process. In most situations, IRBMED will be able to support these requests by prioritizing the Amendment so it is reviewed and approved promptly. If it is necessary to open a simultaneous second amendment, see below for a temporary, alternative approach for minor changes.

B. eResearch ORIO (Temporary COVID-19 process)

- The standard eResearch Amendment process permits only one amendment to be in progress at the same time in order to assure version control of the IRB application/protocol. This may create challenges when two unrelated modifications require evaluation at the same time (e.g., a complex amendment is undergoing full board evaluation and a minor but time-sensitive amendment such as a study team change is also required).
- For these situations, IRBMED policy is altered to temporarily accept certain minor modifications via the eResearch ORIO submission. It is important to note that *these changes must be minor and qualify for expedited review according to regulatory criteria*. Changes that are not minor will not be accepted via this route.

Urgent modifications that ARE eligible for approval through eResearch ORIO

- 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 but would not be expected to increase risk to the participant
 - Participant age slightly varies from inclusion criteria (but not adding children and/or other vulnerable subject population)
- Changing from in-person visits to telephone ‘visits’. This could be a one-time change for a single subject or a group of subjects.
- Payment related changes where the amount or the process is being slightly adjusted to accommodate the changes in study procedures

Urgent modifications that are NOT eligible for approval via the eResearch ORIO process

- A request to enroll a subject who does not meet the currently approved eligibility criteria:
 - Adding a new participant population such as children
 - Lab values significantly different from those stated in the protocol
- Increasing investigational drug dosage
- Adding new drugs, medical devices, or invasive study procedures
- Consent form changes

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- When submitting the ORIO:
 - In the ORIO title, indicate “COVID time-sensitive change”
 - Select “Protocol Deviation” sub-type (this selection must be chosen in this work-around)
 - In the ORIO submission, describe the change(s) that will be made and provide enough information for IRBMED to acknowledge that the changes will meet the criteria for minor changes. Also, if any changes to the study documents (protocol, informed consent, etc.) are required, upload the revised documents in the Supporting Documentation section of the ORIO.
 - Upload any additional supporting documentation (such as sponsor’s approval or other similar documentation)
 - NOTE: If the modification is a permanent change to the research study, an Amendment must also be submitted in eResearch.
- **Submissions received by IRBMED will be screened and triaged within 24 hours during normal business hours. During the weekend, these will be checked periodically.**

III. RESOURCES

1. FDA’s March 2020 [Final Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic](#)
2. FDA’s May 2001 Final Guidance: [Changes or Modifications During the Conduct of a Clinical Investigation](#)
3. IRBMED Guidance on Time-Sensitive Research Modifications During COVID-19: [Workflow Chart](#)