

Amendments to Currently Approved Human Subject Research	Effective Date	
	Revisions Date	01.21.2019

- 1.0 Purpose:** The purpose of this standard operating practice (SOP) is to ensure the UMCIRB and Principal Investigators (PI) meet the responsibilities associated with requests to amend previously IRB approved human research activities.
- 2.0 Research Protocols Affected:**
- 2.1 Human research activities reviewed and approved by the UMCIRB.
- 3.0 SOP:** Principal Investigators are responsible for submitting proposed changes to currently approved human research prior to initiating any such change. The requested change requires review and approval of the UMCIRB prior to the initiation of changes (this includes one-time protocol exceptions issued by a sponsor/funding agency). These changes are referenced as Amendments to the approved protocol. Changes that are immediately necessary to protect the safety and welfare of participants may be implemented prior to UMCIRB approval; however, the UMCIRB must be notified within 24 hours of implementing the change.
- The approval date for an amendment does not extend the approval period for the research study.
- 4.0 Definitions:**
- 4.1 **Amendment:** A PI or sponsor initiated request to revise currently approved human research activities.
- 4.2 **Human Subject:** A living individual about whom an investigator (whether professional or student) conducting research:
- (1) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
 - (2) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.
- 4.3 **Research:** A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this SOP, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities. The terms research, clinical research, clinical study, study and clinical investigation are deemed to be synonymous for the purposes of the FDA.
- 5.0 Minor changes:** The following are examples of when the IRB may review and approve amendments utilizing expedited mechanisms (i.e., review by one or more experienced IRB members who, at ECU, is typically the UMCIRB Chair, or designee) without subsequent review by the fully convened UMCIRB. The IRB Chairperson (or designee) may always elect to send the proposed change to the fully convened UMCIRB for review.
- 5.1 Changes that involve logistical, administrative, and/or editorial aspects of the research project;
 - 5.2 Addition of research activities that would be considered exempt or expedited if considered independent from the main research protocol;

- 5.3 Increase or decrease in proposed human research participant enrollment where the participants are not placed at increased risk;
- 5.4 Narrowing the range of inclusion criteria;
- 5.5 Broadening the range of exclusion criteria;
- 5.6 Alterations in drug administration (e.g., tablet to capsule, capsule to liquid) provided the dose and route of administration remain constant and participants are not placed at increased risk;
- 5.7 Decreasing the number or volume of biological sample collection provided the change does not affect the collection of information related to safety evaluations;
- 5.8 An increase in the length of confinement or number of study visits for the purpose of increased participant safety monitoring;
- 5.9 Alteration or liberalization of payment schedule with proper justification;
- 5.10 Improvement in wording and/or to correct typographical errors in the informed consent document;
- 5.11 Deletions of qualified key personnel if the responsibilities of the study team member(s) are appropriately shifted to other personnel;
- 5.12 Addition of qualified key personnel;
- 5.13 Deletion of study sites. If ECU or an ECU Affiliate is the primary site in a multi-center study, deletion of a participating site must include documentation that no participants have been enrolled at that site or are no longer enrolled at that site;
- 5.14 Addition of a study site (which may require confirmation of a Federal Wide Assurance (FWA) or other agreement between sites) with applicable off-site letters of approval;
- 5.15 Minor changes requested by other compliance committees;
- 5.16 Changes that do not alter the overall risk/benefit ratio of the study;
- 5.17 Change in the Principal Investigator (PI) provided the new PI has similar credentials to the previously approved PI.

6.0 Major changes: A proposed change in a research study which could possibly introduce increased risk to the safety and welfare of research participants or might adversely affect the willingness of current participants to remain in the study, require full UMCIRB review and approval of the proposed change(s). Requested amendments that must be reviewed by the convened UMCIRB include, but are not limited to:

- 6.1 A recognized increase in risks to participants;
- 6.2 A change in the research design or methodology of greater than minimal risk studies;
- 6.3 Unfavorable changes in the qualifications of the research team (e.g., PI or research staff loses license to practice medicine);
- 6.4 A change and subsequent inability of the facilities to support safe conduct of the research;
- 6.5 Broadening the range of inclusion criteria;
- 6.6 Narrowing the range of exclusion criteria;
- 6.7 Alterations in dosage or route of administration of a drug;
- 6.8 Extending the duration of exposure to a test material or intervention;
- 6.9 Addition of procedures that would require full board review, if considered independent from the main protocol;
- 6.10 Deletion of laboratory tests, monitoring procedures, or study visits directed at the collection of information for safety evaluations;
- 6.11 Addition of serious unexpected adverse or unanticipated events that must be included in a revised informed consent document;

- 6.12 Addition of a facility or a population for which the IRB Chairperson or designee is not familiar;
- 6.13 Any change that may alter the risk/benefit ratio;
- 6.14 Changes that may affect a participant's decision to continue;
- 6.15 Any change to the research procedures, recruitment, enrollment, or informed consent, which in the opinion of the UMCIRB Chairperson or designee does not meet the criteria or intent of a minor change;
- 6.16 Any change/revision requested by the UMCIRB that requires anything other than verification by the IRB Chairperson or designee (i.e., additional information for which a determination of appropriateness must be made in order to issue approval).

7.0 Amendments Implemented Immediately for Safety Reasons: Amendments that must be made immediately to ensure research participant safety are an exception to the requirement for IRB approval prior to implementation. The PI is expected to use his/her judgment when determining if an amendment must be implemented immediately to ensure research participant safety. If this occurs, the IRB Administrative Director or IRB Chairperson or designee must be notified immediately; an amendment request must follow within 24 hours. The request may be considered by the fully convened IRB to determine whether each change was consistent with ensuring the participant's continued welfare. Following review of the requested amendment, the PI will be notified of UMCIRB approval, any required modifications, clarifications or conditions, or disapproval. If changes to the informed consent form have been approved, a copy of the revised informed consent form will be available in ePIRATE along with the approval notification. Amendments for any other reason cannot be implemented without prior, final approval from the UMCIRB. If the change is required for only a single individual under a special circumstance, then the action should be submitted to the UMCIRB following the instructions for a protocol deviation.

8.0 Previously deemed Expedited Research: If an amendment to a protocol previously approved under expedited review procedures causes the protocol to no longer qualify for expedited review, the UMCIRB staff will schedule the protocol to be reviewed by the convened UMCIRB.

9.0 Previously deemed Exempt Research: Any proposed or anticipated changes in a study that was previously declared exempt from IRB review must be submitted to the IRB for approval prior to initiation of the change. The proposed amendment will then be evaluated for appropriate IRB review. Should the proposed change cause the research to no longer qualify for exempt certification, a notice will be sent to the PI requesting that a more complete application be submitted for review and approval.

10.0 Responsibilities:

10.1 Principal Investigator (PI) is expected to provide the IRB with all relevant information regarding the conduct of the research including:

10.1.1 Completed and submitted Amendment;

10.1.2 Ensuring other study team members or subinvestigator(s) being added have current human research protection education certification;

10.1.3 Modified document(s) must clearly indicate the changes that have been made by uploading a version with changes tracked (e.g., "red lined" or "tracked changes") and a final "clean" version (without changes indicated) of the modified document(s) to be approved;

- 10.1.3.1 UMCIRB requires that amendments be incorporated into the protocol, ePIRATE Smartform, and applicable documents, to ensure that the all study documents are valid in their entirety.
 - 10.1.4 Rationale for any delays in submitting amendments to a research study (specifically amendments that are originated by a sponsor).
 - 10.1.5 Any other relevant study documentation that will allow the IRB to review the science and ethics of the proposed amendment and make a determination regarding approval.
 - 10.1.6 Providing any additional information or clarification requested by the fully convened IRB, IRB Chairperson or designee, or UMCIRB staff in a timely fashion, to assist in the determination of approval.
- 10.2 University and Medical Center Institutional Review Board Office Staff:
- 10.2.1 Advise PI and research staff in the preparation and completion of the amendment submission process.
 - 10.2.2 Conduct a pre-review of the submission and supporting documents to identify any issues.
 - 10.2.3 Ensure all applicable documents have been provided.
 - 10.2.4 Submit concerns to the study team for incomplete submissions, clarifications or minor changes to allow for review by the fully convened IRB or the IRB Chairperson or their designee.
 - 10.2.5 Confirm study type (e.g., expedited or full board) is appropriate as submitted by the PI and request changes in accordance with federal regulations, state and local laws and institutional policies and procedures.
 - 10.2.6 Schedule amendments requiring review by the convened UMCIRB committee to the next available IRB meeting.
 - 10.2.7 Assign full board submission(s) to reviewer(s).
 - 10.2.8 Ensure the UMCIRB committee has adequate representation during the evaluation of the proposed human research activities.
 - 10.2.9 Ensure IRB members with a COI on a research study are not present during its discussion and vote.
 - 10.2.10 Assign expedited submissions to the IRB Chairperson or designee for review.
 - 10.2.11 Prepare and send IRB correspondence to the investigator via the electronic submission system.
 - 10.2.12 Include reporting of approvals of expedited submissions in the UMCIRB minutes.
- 10.3 Convened IRB Committee (for full board review):
- 10.3.1 Are provided with all materials submitted by the PI in order to conduct their review and have access to all study related material.
 - 10.3.2 Determine whether the proposed change to the human research activity continues to meet the federal criteria for approval through the reviewer checklist.
 - 10.3.3 When some or all of the participants are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, the UMCIRB Committee ensures additional safeguards have been included in the study to protect the rights and welfare of these participants.
 - 10.3.4 Primary Reviewers:

- 10.3.4.1 The UMCIRB utilizes a primary reviewer system for amendments requiring approval by the full committee meaning that one individual is primarily assigned to complete the review of the amended materials submitted for consideration on a research study, and then presents the amendment to the UMCIRB committee for discussion, review and approval.
- 10.3.4.2 Have the authority and should make recommendations to the fully convened, IRB. These recommendations can be accepted as presented, modified, or rejected by a motion and passed by a majority.
- 10.3.5 Have the authority to vote on the final determinations of those recommendations.
- 10.3.6 The IRB Chairperson will request a motion, call for discussion and vote on each agenda item.
 - 10.3.6.1 Amendments that increase the risk or are created as a result of unanticipated problems involving risks to participants or others may require a shorter approval period with a more frequent continuing review interval to protect the safety and welfare of participants
- 10.3.7 The IRB, makes the following determinations and PIs are notified in writing.
 - 10.3.7.1 Approval: The PI is not required to change any aspect of the proposed amendment. The approval date is the date of the IRB meeting or the date approved by the IRB Chairperson or designee (if expedited). The approval is valid for the time remaining on the study approval period, unless the UMCIRB designates a shorter period due to the details of the amendment.
 - 10.3.7.2 Approved with Contingencies: Minor stipulations are required for approval (e.g., require simple concurrence or modifications from the PI and do not require substantive judgment by the IRB Committee). The UMCIRB may vote to authorize the UMCIRB Chairperson or designee to approve the response submitted by the PI unless the investigator does not provide the minor revisions requested. Should the UMCIRB Chairperson or designee feel that the response is not adequate or requires review by the fully convened UMCIRB, the amendment would be added to the next available agenda for the committee that originally conducted the review. The PI may not implement the requested changes until IRB approval is granted. The requested changes should be made within 30 days of the date issues were communicated by the UMCIRB. The research staff can request an extension, otherwise the amendment will be withdrawn, and a new submission will be required for the amendment.
 - 10.3.7.3 Deferred: There are substantive issues regarding the proposed amendment to the research that must be addressed. This action is taken if substantial modification or clarification is required, or insufficient information is provided to judge the proposed research amendment adequately (e.g., the risks and benefits cannot be assessed with the information provided). UMCIRB approval of the proposed amendment will not occur until subsequent review of the additional material has occurred. If the submission is deferred, the research staff will be notified of the reason and any information or changes that are required should be submitted to the UMCIRB within 60 days. The research staff can request an extension, otherwise the application will be withdrawn, and a new submission will be required for the amendment.

10.3.7.4 **Disapproval:** The proposed research amendment, as designed, is inherently flawed, and the UMCIRB cannot recommend approval. The reason for disapproval is communicated to the study team in writing via the electronic submission system. Once an amendment has been disapproved, it can be resubmitted by the study team as a new amendment to the UMCIRB for further consideration if the new submission has been changed to address the UMCIRB's concerns. All resubmissions of disapproved amendments must be reviewed by the fully convened IRB. Resubmission of applications must be substantially modified to address all previous concerns outlined by the IRB prior to being reconsidered by the fully convened board.

10.3.8 Have the authority to require notification to current or previous research participants of any significant new findings that may affect the participants' willingness to continue participation and the re-consent of study subjects.

10.3.8.1 Notification can occur by:

10.3.8.1.1 Letter to subjects;

10.3.8.1.2 Phone call to subjects (promptly); and/or

10.3.8.1.3 Re-consent of subjects at next study visit or promptly.

10.4 **UMCIRB Chairperson or designee (for expedited reviews):**

10.4.1 The UMCIRB Chairperson (or designee) serves as the primary reviewer for expedited amendment submissions and has the authority to approve or request modifications to amendments that qualify for expedited review:

10.4.1.1 Changes needed for a study to be approved will be communicated to the study team via the electronic submission system.

10.4.1.2 Once the study team submits changes or answers to questions, the study will be sent back to the UMCIRB Chairperson (or designee) for confirmation that final approval can be granted.

10.4.1.3 An expedited study amendment can only be disapproved by the convened UMCIRB.

10.4.2 Is provided with all the material submitted by the PI in order to conduct his/her review and has access to all study related material.

10.4.3 Determines whether the proposed amendment to the human research meets the federal criteria for approval.

10.4.4 All expedited amendments approved by the Chairperson (or designee) will be reported to the UMCIRB committee on the next available meeting minutes and the PI is notified via the electronic submission system.

11.0 Appeal: Should the UMCIRB make a decision the PI believes to be unduly restrictive, the PI may appeal the decision of the UMCIRB. The UMCIRB will consider appeal(s) based upon new information provided about the disapproved proposed amendment. The PI should appeal to the UMCIRB in writing. The PI may first discuss the matter with the UMCIRB Chairperson or designee and/or the UMCIRB Administrative Director or designee, taking care to provide a full explanation. The PI may attend the subsequent UMCIRB meeting where the disapproved amendment and appeal are reviewed to address issues raised by the UMCIRB committee. The PI will not be permitted to remain in attendance during the UMCIRB deliberation and vote on the study. Appeals of UMCIRB determinations must be made within 30 days of the PI receiving written notice of the IRB determination.

12.0 Notification: All findings and actions taken on Amendments to existing research studies are recorded within the UMCIRB minutes. These minutes are available to all IRB members, ex-officios and institutional officials within the electronic submission system.

Revision History:

Date	Change	Reference Section(s)
7.30.2013	Updated to stand-alone document.	All
01.21.2019	Common Rule revisions and update of ORIC name	3.0-4.0, 10.0, 12.0

References:

FDA. Code of Federal Regulations:

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?CFRPart=56>

DHHS, OHRP. Code of Federal Regulations:

<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html>