SUNY Institute of Technology

SUBJECT – Institutional Review Board	EFFECTIVE DATE – February 12, 2013
TITLE – Continuing Review of Research	Approved BY – Deborah Tyksinski, Associate Provost; IRB Board

SCOPE - This policy applies to all members within or under the auspices of SUNYIT conducting research involving human subjects, and to the SUNYIT IRB Committee that oversees the conduct of that research.

PURPOSE – To define and establish guidelines and responsibilities for the continuing review of previously approved research.

POLICY – The Institutional Review Board (IRB) of State University of New York Institute of Technology (SUNYIT) conducts substantive and meaningful continuing review of all studies previously approved. HHS regulations at *45 CFR 46.109(e)* require that continuing review be conducted at intervals appropriate to the degree of risk, but must be accomplished at least annually. Approval for continuation must satisfy the requirements of *45 CFR 46.111* (and, where applicable,) *21 CFR 56.111* and *38 CFR 16.111*. The approval period cannot exceed one year. If IRB approval expires, the PI cannot enroll new subjects and must cease all research activities unless the IRB determines an overriding safety concern or ethical issue exists, or it is in the subject's best interest to continue in the research until the continuing review can be accomplished. Continuing review of research is authorized by the expedited review procedure if the research was initially eligible and continues to be eligible for expedited review. Expedited review is also authorized for research initially approved by the convened board in limited circumstances specified in *Categories 8 and 9 at 63 FR 60364-60367, November 9, 1998* as follows:

(a) The research is permanently closed to the enrollment of new subjects; all subjects have completed all research-related interventions; and the research remains active only for long-term follow-up of subjects; OR
(b) No subjects have been enrolled and no additional risks have been identified; OR
(c) The remaining research activities are limited to data analysis; OR
(d) The research involves the study of drugs and/or medical devices AND either does not require an Investigational New Drug (IND) and/or an Investigational Drug Exemption (IDE) and/or the device is approved for marketing and being used in accordance with the approved labeling. The IRB must also have determined and documented at a convened meeting that the research is no greater than minimal risk and no additional risks have been identified.

Guidance and Procedures

Continuing review is a federally mandated requirement and is the mechanism the IRB uses to ensure the continued safeguarding of participants' rights and welfare. Unless exempt from IRB oversight, the IRB must conduct continuing review of approved research at intervals appropriate to the degree of risk, but not less than annually. Review must be conducted at convened meetings unless the study qualifies for expedited review. Full board and expedited, continuing review must be substantive and meaningful and must be accomplished with the same diligence as initial review. Unless a study is terminated, continuing review is required for as long as the research is active, or for long-term follow-up, or for data analysis, even if the study is permanently closed to enrollment. Reviewers will have access to the full protocol binder including all documents from the initial review as well as those submitted after initial review, and any new documents submitted at the time of continuing review.

A **courtesy reminder** will be sent to the PI via email at least eight weeks prior to the approval expiration date. It is solely the responsibility of the PI to complete the continuing review report form and return all required documents to the IRB office to ensure timely review and re-approval.

Issues That Must Be Addressed During Continuing Review

The following issues will be discussed during the review:

1. The Continuing Review form and any supporting documentation
2. The current status of the study with respect to whether the study is open or closed to enrollment or open for follow-up or data collection
3. Recruitment, including the number enrolled and demographic information, and the number of subjects withdrawn or terminated from study and the reason for withdrawal or termination
4. Changes to the risk / benefit ratio based on study results or adverse events reports:
   (a) Summary of adverse events or unanticipated problems involving risks to subjects or others
   (b) Consider IND, IDE or other drug or safety reports (if applicable)
   (c) Consider DSMB or similar body report
   (d) Consider changes to research, including literature, amendments or modifications since last review.
5. Reports of injuries, unexpected events or unanticipated problems to subjects or others
6. Reports of protocol violations or protocol deviations
7. Statements of investigator non-compliance
8. Reports of complaint from subjects, employees, staff or others
9. Consideration of new financial or other conflicts of interest
10. Consideration of the accuracy and completeness of the current consent form including changes to risk-benefit ratio and new information that should be included or that could affect subjects' willingness to continue participation
11. Assess adequacy of the continuing review period with respect to degree of risk
12. Consider any new state laws or institutional policy affecting research
13. Any other information deemed necessary by the Board or submitted for consideration

Verification From Other Sources

The IRB may request additional information from sources other than the investigator in other to assess the completeness and accuracy of information submitted, and to verify that no material changes have occurred since the previous IRB review. The IRB makes this determination based upon any of the following criteria:

1. Randomly selected projects.
2. Complex projects involving unusual levels or types of risk to subjects.
3. Projects conducted by investigators who previously have failed to comply with the requirements.
4. HHS regulations or the requirements or determinations of the IRB
5. Projects where concern about possible material changes occurring without IRB approval have been raised based upon information provided in continuing review reports or from other sources.

Criteria for Approving Continuation of Research

To approve the continuation of a research project, the IRB must determine that all of the criteria specified at 46.111 are satisfied. These criteria are listed on the *IRB Checklist: Criteria for Approval* which is distributed to all members when conducting initial and continuing review of research.

1. Risks to subjects continue to be minimized and reasonable in relation to anticipated benefits.

2. Selection of subjects continues to be equitable in relation to anticipated benefits.
3. The informed consent process continues to be adequate and appropriately documented.
4. Provisions for safety monitoring of the data are in place
5. Protections to ensure privacy of subjects and confidentiality of data are adequate.
6. Appropriate safeguards are in place for vulnerable populations.
7. There are no issues of noncompliance or conflicts of interest that have not been appropriately addressed.
8. Other issues the IRB determines appropriate to the study.

Range of Possible Actions

After discussion, the IRB Chairman, designated representative or the primary reviewer will request the board vote one of the following:

APPROVED FOR CONTINUATION – Continuation of the research is approved as submitted without requested modifications. The IRB Coordinator will send an approval letter to the PI along with a copy of the IRB date-approved consent form (if applicable).

APPROVED FOR CONTINUATION PENDING MODIFICATIONS – The IRB approved continuation of the study pending receipt of minor revisions which do not involve substantial issues. The IRB gives the Chair/designated representative authority to approve the revisions. The IRB Coordinator will notify the PI in writing describing the requested revisions. The PI will send the written responses to the IRB Coordinator who will review and then forward to the Chair /designated representative for review. The Chair / representative may approve it, request additional information from the PI or refer it back to the full board. The approval letter and IRB date-approved consent form will not be sent to the PI until approved by the Chair or full board.

TABLED/DEFERRED – Requires substantive clarifications or modifications regarding the protocol, consent documents or informed consent process that are directly relevant to the determinations required by the IRB as specified by HHS regulations at 46.111. The IRB Coordinator will notify the PI in Writing of the reason and describe the requested revisions. The PI may be requested to attend the next IRB meeting to discuss the IRB concerns.

DISAPPROVED – Questions about the research are so significant that approval is not possible. This outcome usually reflects the IRB's determination that the risks outweigh any possible benefits, or when the research does not meet the federal criteria for approval. The IRB Coordinator notifies the PI in writing. The study may be rewrite and resubmitted for full board review. In this case, a new application must be completed.

When the expedited review procedures is used for continuing review, the reviewer may exercise all of the authority of the full board except cannot disapprove continuing review. Only the full board can disapprove continuation of the research. The reviewer may make the following determinations:

Approved for Continuation;
Approved for Continuation Pending Modifications; or
Refer to Full/Convened Board.

Once a project is approved for continuation, changes or amendments to the protocol or consent form are not authorized without prior IRB review and approval.

Distribution for Continuing Review

Each member of the IRB must receive information in sufficient detail to make the determinations required by HHS regulations at 45 CFR 46.111. The following continuing review documents must be submitted to the membership (except where the primary reviewer is indicated) so as to receive it within seven calendar days of the scheduled meeting. Documents submitted by the PI for review that are received after the Agenda has been distributed may be distributed to the Board in the form of an Addendum. The IRB membership will review all documents sufficiently to be able to discuss the protocol at the meeting and be able to determine whether the research satisfies regulatory criteria for continuation approval.

1. The full protocol (primary reviewer or at least one member). Members not receiving the full protocol should receive the protocol summary.
2. The consent document for which approval is requested
3. Any amendments or modifications to the research since the last review, including interim findings, recent literature, multi-center trial reports or Data Monitoring Committee reports
4. *Investigator's progress report*
   (a) Number of subjects accrued
   (b) Summary of adverse events and any unanticipated problems involving risks to subjects or others
   (c) Withdrawal of subjects from the research or complaints about the research since the previous IRB review
   (d) Any other new or relevant information, especially information about risks associated with the research
5. The completed *Application for Continuing Review*
6. Checklists appropriate to assist board in completing review
7. The complete protocol file and other relevant documents, such as meeting minutes, shall be available to any member upon request.

Distribution – Primary Review System

SUNYIT IRB may use a Primary Reviewer System in which one or more members with the appropriate research subject matter expertise and IRB reviewer experience, are assigned, at the discretion of the IRB Chair in consultation with the IRB Coordinator, to review distributed materials. In this case, the Primary Reviewer will receive all of the above materials including a full protocol. The membership will receive:

1. *Application for Continuing Review*
2. Protocol Summary
3. Consent document for which approval is requested
4. IRB review Checklists
5. Recruit materials
6. The complete protocol file and other relevant documents shall be available to any member upon request

Distribution – Expedited Review

The IRB Chair or designated representative will receive the following materials as soon as it is known that an expedited review is required and appropriate:

1. *Application for Continuing Review of Research*
2. The complete protocol binder, including all relevant documents, such as past meeting minutes, amendments, and all other reports that are part of the protocol binder.
3. The Investigator's progress report, when applicable
4. Protocol Summary
5. The current consent form for which approval is requested
6. Appropriate checklists to assist in completing the review

Communicating Decisions / Actions to Investigators

Investigators will be notified promptly (usually within 5 business days) by email (followed by official letter) of all board decisions and actions.

1. Where research is approved a submitted, the certification letter will specify the approval period, including the expiration date as well as any instructions or other information the Board requires.
2. For Approvals pending modifications, the letter must discuss the modifications required.
3. For tabled or disapproved studies, the reason, as well as any appeals process, must be specified
   (a) If a previously approved study is suspended or terminated, the investigator, institutional official and the appropriate Department or Agency head shall be notified promptly.

The minutes shall reflect separate deliberations, actions and votes for each protocol undergoing continuing review by the convened IRB. A copy of the Board-approved minutes will be distributed to the Signatory Official and to all members of the board. Other entities will be notified as requested by the PI, IRB Chair or other regulating agencies.

Frequency of Continuing Review

1. The continuing review date is established at the time of initial review and begins with the initial approval date. For expedited review, the IRB Chairman or designated representative conducts the review and established the approval period, not to exceed one year of the date of final approval for the study.
2. At the time of continuing review, the Board determines if the frequency of review is adequate for the level of risk. The IRB should consider more frequent review when:
   a. The study involves vulnerable populations where more than minimal risk with no prospect of direct benefit to the participants;
   b. Unanticipated problems involving risks to participants or to others create new concerns regarding the need for closer scrutiny;
   c. Research involves serious risks to participants with no potential benefits;
   d. The clinical investigator's experience in conducting clinical research dictates;
   e. The IRB's previous history with a particular investigator or sponsor dictates;
   f. The degree of uncertainty regarding risks places subjects or others at increased risk.

Lapse in Review

Federal regulations require that continuing review of research be conducted at intervals appropriate to the degree of risk, but not less than once per year.

The PI is responsible for ensuring that the research is submitted to the IRB for continuing review in an appropriate time frame, in order to avoid a lapse of IRB approval.

If the PI fails to return the Continuing Review report form or the IRB has not reviewed and approved continuation of the study by the expiration date, research activities must stop and no new subject enrollment may occur.

EXCEPTION: Research activities may continue if the IRB determines upon review that it is in the best interest of individual subjects to continue participating in the research interventions or interactions.

An investigator who continues the research after the expiration date is in violation of federal regulations governing review of research. The IRB Coordinator will notify the PI via email and/or letter that approval for the study is about to or has lapsed and that research activities must cease.

If the PI is in the process of seeking approval for study continuation but could not respond to the IRB request for changes or amendments prior to the expiration date, the IRB can approve continuation of the study once the materials are received.

If the PI fails to return the CR report form or fails to respond to the IRB request for changes prior to the expiration date and subsequently submits the CR materials or the requested changes after the expiration date, the IRB will require the PI to submit a summary of events that occurred in the interim. If the PI submits the materials/revisions within 3 months of the end of the approval period, the IRB can review the materials and approve continuation of the study.

If the PI fails to return the CR report form or fails to respond to the IRB request for revision and the PI submits the CR materials/revisions more than three months after the end of the approval period, the IRB requires a new initial review application and a summary of events that occurred in the interim.

If the PI requests, the IRB may, if in the best interest of the individual subjects, or due to safety concerns or ethical issues, authorize the principal investigator to allow subjects currently enrolled to continue participation in the research until the study can be reviewed and approved.

Additional Procedures and Responsibilities

Principal Investigator

1. Respond to continuing review requirements in a timely manner.
2. Complete the Application for Continuing Review and submit it along with appropriate supporting documents according to the instructions on the form.
3. For questions or concerns about IRB recommendations for changes in the study, may submit response and justification in writing to the Office of the IRB or present the information in person by requesting to attend the next scheduled IRB meeting.

IRB Membership Responsibilities

1. Conduct continuing review at regularly scheduled meetings unless expedited review is authorized and accomplished.
   (a) During the meeting, any member with the appropriate expertise, having reviewed the materials, may summarize changes or critical issues for the other members, and lead the discussion, for example, by stating "*no / only minimal changes since the last continuing review date"* or "*AE*

reports are of the type and frequency as described in the current Investigator's Brochure, protocol version or informed consent document" or "*no changes are requested or necessary at this time".*

(b) For **expedited review**, the IRB Chair or designated reviewer will conduct the expedited review of studies where authorized by federal regulations.

2. Ensure that any member with a conflict of interest does not participate in the continuing review of a study except to provide information requested by the IRB.
3. Review the continuing review documents, including the *Application for Continuing Review of Research*, for each study prior to the meeting. All members have access to pertinent information for continuing review. Be able to discuss the study and determine if the protocol satisfies regulatory approval criteria. For controverted issues that do not meet approval criteria, formulate an appropriate resolution prior to voting activity.
4. Determine if any new information has emerged that may alter previous Board determinations or the participant's willingness to continue participation, with particular regard to risks or unanticipated problems involving risks to subjects or others. Additional considerations include:
   (a) Safety reports, including IND or IDE
   (b) Protocol violations and / or deviations
   (c) DSMB reports or reports from similar bodies
   (d) Complaints or subject phone calls
   (e) Reports of investigator non-compliance
5. Review the consent document for completeness and accuracy, and for any significant new findings that may relate to the subject's willingness to continue participation. Consider also, the adequacy of the process for obtaining informed consent.
6. Ensure adequate protections are in place when enrollment includes vulnerable populations.
7. Determine the final outcome of the review – approve continuation, approve pending modifications, table or disapprove continuation. The IRB may request the PI attend the next scheduled meeting to discuss remaining questions.
8. For expedited review, the IRB Chair or designated representative will complete the *Certification Form* and forward it to the IRB Coordinator
9. Determine the approval period appropriate to the degree of risk, but not less frequently than once per year.
10. For expedited review, the continuing review must occur within one year of the date the IRB Chair or designate gives final approval for the study.

IRB Coordinator Responsibilities

1. Remind the Principal Investigator approximately 8 weeks prior to expiration of the approval period via email. Include a copy of the *Application for Continuing Review of Research.*
2. Screen the submitted continuing review request application and supporting documentation to determine if it:
   (a) Qualifies for expedited review
   (b) Complies with selected federal requirements
   (c) Is consistent with IRB requirements

   Solicit additional information from the PI for incomplete applications. If the PI fails to respond, submit the Application as is to avoid expiration of study approval, and advise the IRB of the situation.

3. Forward the continuing review request along with the supporting documentation via email to the IRB membership as part of the Agenda at least 5-7 days prior to the meeting at which continuing review is scheduled.
4. Document separate deliberations, actions and votes for each protocol undergoing continuing review in the minutes and update the protocol file with the new information.
5. Notify the PI via written letter of the IRB decision and any required actions.

References

Bankert, E. A., & Amdur, R. J. (2006) *Institutional Review Board Management and Function, 2nd Ed*, Jones, and Bartlett Publishers, Sudbury MA.
Code of Federal Regulations: Title 45, Part 46
Code of Federal Regulations: Title 21, Part 56
OHRP Guidance on Continuing Review
PRIM&R – Public Responsibility in Medicine and Research (www.primr.org)
SUNY Binghamton IRB (www.research.binghamton.edu)
University of Kentucky IRB (www.research.uky.edu)
SUNY Upstate IRB (www.upstate.edu/researchadmin/compliance)