

Cornell University
Office of Research Integrity and Assurance
Human Research Participant Protection Program

SOP 3: INITIAL AND CONTINUING REVIEW BY THE IRB:
REQUIREMENTS FOR SUBMISSION OF APPLICATIONS, APPROVAL CRITERIA, AND
EXPEDITED AND CONVENED COMMITTEE REVIEW PROCEDURES

1. Subject of Policy & Procedure

If a Protocol Principal Investigator (Protocol PI) or ORIA determines that a research activity constitutes human participant research *and* requires IRB review and approval, the Protocol PI must complete and submit to ORIA the research protocol and all supporting documents required for IRB initial review and approval (research protocol application) under one of two processes: Expedited Review or Convened (full) Committee Review. Once approved and initiated, every research protocol is subject to Continuing Review. This means that every protocol must be submitted for review and continuation of IRB approval under the Expedited or Convened Committee process at an interval appropriate to the protocol's degree of risk, but not less than once per year. This Policy & Procedure sets forth the research protocol application submission requirements, criteria for IRB approval, and procedures for each review process.

2. Scope of Policy & Procedure

This Policy & Procedure applies to all on-going and future human participant research projects conducted by Cornell faculty, staff, or students or by anyone conducting a research activity supported by Cornell or on property maintained by Cornell.

3. Terms and Definitions

Employees (faculty and staff) and students should consult the IRB Glossary at <http://www.irb.cornell.edu/glossary/>.

4. See Also

Affected researchers and employees should also consult:

1. Cornell University Federal Wide Assurance Registration:
<http://www.irb.cornell.edu/regulations/fwa.htm>
2. The Belmont Report: <http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm>
3. National Academies Press Booklet: "On Being a Scientist: Responsible Conduct in Research":
<http://www.nap.edu/readingroom/books/obas/>
4. Initial Approval Request Form: Social and Behavioral Studies:
<http://www.irb.cornell.edu/forms/>
5. Initial Approval Request Form: Clinical and Medical Studies:
<http://www.irb.cornell.edu/forms/>
6. IRB Review Checklist (*to be developed*)
7. Continuing Approval Request Form: Social and Behavioral Studies:
<http://www.irb.cornell.edu/forms/>

8. Continuing Approval Request Form: Clinical and Medical Studies:
<http://www.irb.cornell.edu/forms/>
9. Request to Amend a Previously Approved Project: <http://www.irb.cornell.edu/forms/> (under Continuum of Approval)

5. Regulations and Guidance Applicable to Submission of Protocols & IRB Review Procedures

5.1. Federal Regulations

- 5.1.1. 45 CFR 46 (Protection of Human Subjects): Requirement for IRB review and approval of human participant research before its initiation
- 5.1.2. 45 CFR 46.109 & 21 CFR 56.109: IRB Review of Research
- 5.1.3. 45 CFR 46.111 & 21 CFR 56.111: Criteria for IRB Approval of Research
- 5.1.4. 21 CFR 56.108: IRB Functions and Operations, including for Expedited Review
- 5.1.5. 45 CFR 46.110: Eligibility and Procedures for Expedited Review
- 5.1.6. 45 CFR 46.108(b): Requirement for Convened Committee Review when Expedited Review is not used
- 5.1.7. 45 CFR 46.109(e): Continuing Review of research by IRB
- 5.1.8. OHRP Guidance on Continuing Reviews, July 11, 2002

5.2. Ethical Codes

- 5.2.1. The Nuremberg Code (1948)
- 5.2.2. The Belmont Report (1974)
- 5.2.3. Declaration of Helsinki (last revised in 2000)

6. Protocol Application Submission Procedures for Initial Review:

If the Protocol PI or ORIA determines that a research activity (a) constitutes human participant research,¹ **and** (b) is not eligible for exemption from IRB review,² the Protocol PI must submit the research protocol to ORIA for IRB review and approval under the Expedited Review or Convened Committee Review process, in accordance with the following procedures:

6.1. Training for Protocol PI:

Before the IRB can approve the research protocol, the Protocol PI, all co-investigators, and all key personnel must successfully complete the IRB online training addressing the appropriate conduct of human participant research.³ Proof of completion of this requirement by all investigators and key personnel is electronically generated and maintained in the protocol file by ORIA.⁴

¹ See SOP 1: Determining Whether a Research Activity Needs IRB Review or Exemption from IRB Review

² See SOP 2: Requirements for Submission of Research Protocols for a Determination by ORIA of Exemption from IRB Review

³ See Online Training at http://www.irb.cornell.edu/training/menu_soc.html.

⁴ The investigators and research staff may also familiarize themselves with the following materials pertinent to ethical standards governing the conduct of human participant research: Cornell University's Federal Wide Assurance Registration; the Belmont Report; and the National Academies Press Booklet: "On Being a Scientist: Responsible Conduct in Research. See Section 4 of this policy for online links.

6.2. Forms to be Completed and Submitted by Protocol PI:

The Protocol PI must complete and submit:

1. One of the two Initial Approval Request Forms, as appropriate, with signatures: Social and Behavioral Studies; or Clinical and Medical Studies. If the project is led by an undergraduate or graduate student, the faculty supervisor should sign the approval form.
2. An appropriate written consent form/assent form/information sheet or consent/assent script to be used with all human participants involved in the research activity, when appropriate. *See* SOP 9: Informed Consent Options, Processes, and Documentation.
3. External funding research proposal, if applicable.
4. Thesis or dissertation proposal, if applicable.
5. All recruitment materials.
6. All other study instruments including, but not limited to: (a) blank interview forms, (b) questionnaires or surveys, (c) sample contact letters, (d) instructions to interviewers/Research Assistants, (e) focus group guides, and (f) debriefing text. *and*
7. Permission letters from the appropriate authorities of all non-Cornell organizations from which the Protocol PI will be recruiting participants.

The Protocol PI may submit a copy of each required document either electronically or in hard copy format, to the IRB administrator.

6.3. Processing of Research Protocol Application by ORIA:

Upon receipt of the research protocol and supporting documents, ORIA will (1) verify that the research activity constitutes human participant research; (2) verify the completeness of the materials or coordinate with the Protocol PI to achieve completion; (3) review the protocol and attached materials to determine whether the Expedited or Convened Committee process is appropriate; (4) enter selected information from the Initial Approval Request Form into the research protocol tracking database; and (5) determine the need for all investigators and key personnel to complete training in the use of human participants in research.

After it has been determined that the research protocol application is complete, ORIA will submit the materials for IRB review and approval via the Expedited Review process or the Convened Committee Review process. *See* Sections 8 and 9 of this SOP for review procedures.

6.4. Possible Decisions Made Upon IRB Review:

No research activity shall be initiated until the Protocol PI has received written notification from ORIA that the protocol has been “approved” by the IRB.

The Protocol PI shall be notified by ORIA in writing that the IRB has made one of the following decisions after reviewing the research protocol application: (1) approved, (2) specific minor revisions required for approval, (3) tabled, or (4) disapproved. Within the IRB, *only the Convened IRB can disapprove a protocol*. While sponsors and/or other administrative review may override a decision by the IRB to approve the implementation of a research protocol, they may not override an IRB decision to disapprove a research protocol. All other decisions may be made under both the Expedited and Convened Committee Review processes. ORIA will draft, disseminate, and retain copies of all written notifications of IRB decisions. . If necessary, ORIA will review the content of a communication with the IRB Chair or a member of the IRB before transmitting it to the Protocol PI.

Approved: If the protocol is approved, ORIA will provide email notice of approval to the Protocol PI. Only after receiving the email notice of approval may the Protocol PI initiate the research activity.

Selective Observation: For approved research, the IRB has the authority to elect to observe, or to charge a third party to observe, either the consent process or the execution of any portion of the project.

Specific minor revisions required for approval: The Expedited Reviewer(s) or the Convened IRB may stipulate that approval of the research protocol will be granted only after the Protocol PI makes specific minor revisions to the protocol, informed consent documents and/or process, recruitment materials, etc. ORIA will send the Protocol PI a notification of the required changes. If the Protocol PI makes the revisions, he or she shall then submit them for review via the Expedited Review process. After all specific minor revisions have been approved, ORIA will send an email notice of approval to the Protocol PI. Upon receipt of the notice, the Protocol PI may initiate the research activity. If, however, the Protocol PI suggests or makes revisions that the Expedited Reviewer believes affect the risk-benefit ratio of the project, such revisions will be designated as major and referred for review by the Convened IRB.

The Protocol PI may request the IRB to review at a Convened meeting any specific minor revisions that were required during the Expedited Review process with which he or she disagrees. However, that research protocol cannot begin until all specific minor revisions have been satisfactorily addressed or the Convened IRB has reviewed and approved the research protocol.

Tabled: A protocol is tabled when the Expedited Reviewer(s) or the Convened IRB request additional information, substantive clarifications or modifications regarding the protocol, informed consent documents, etc. that are relevant to the evaluation of the risk/benefit ratio required for approval. The IRB may also table a protocol where it does not have a member with expertise adequate to the scope and complexity of the proposed research and thus seeks review by an expert in the appropriate field. The Protocol PI may suggest an expert to the IRB for this purpose.

A protocol requiring Convened Committee Review may be tabled for lack of appropriate expertise in attendance, lack of time, loss of quorum, etc. In the event a research protocol application is tabled for such administrative reasons, ORIA will assign it for review at a future meeting of the Convened IRB.

When a protocol is tabled, ORIA shall draft and transmit to the Protocol PI a memorandum setting forth the reasons for this action. The Protocol PI shall have up to approximately 90 days to respond to the concerns outlined in the memorandum and to make appropriate revisions to the documents in question. The Protocol PI will submit the revised documents to ORIA, which will assign them for Expedited Review or, if the revisions relate to the risk/benefit ratio of the research, for discussion at a Convened IRB meeting. After 90 days, the IRB will disapprove the protocol and the Protocol PI may be required to re-submit a new protocol.

The IRB may make one of the following decisions with respect to a revised research protocol application: (1) approved, (2) specific minor revisions required for approval, (3) tabled, or (4) disapproved. This cycle will continue until the IRB issues a final decision—either approved or disapproved.

Disapproved: The IRB at a Convened meeting may elect to disapprove a research protocol when it identifies significant concerns about potential risk to participants or a lack of scientific validity to support the proposed research activities. ORIA will draft and transmit to the Protocol PI a written statement of the reasons for the IRB's decision. The Protocol PI will have the opportunity to respond in person or in writing. The IRB at a Convened meeting will review any written responses and make a decision about the appeal of the initial decision to disapprove the research protocol. As with all protocols, the Protocol PI may not initiate the corresponding research activity until the protocol has been approved by the IRB. The Protocol PI always has the right to submit a new protocol that addresses the concerns outlined during the initial review.

7. Criteria for IRB Approval upon Initial or Continuing Review:

7.1. Role of IRB:

The IRB evaluates each protocol application to assess the risk/benefit ratio and the methods used by the principal investigator and the research staff for protecting the rights of the research participants while allowing the research data to be collected for the benefit of society.

In making this assessment, the IRB will examine the initial protocol application, which consists of the protocol itself, outside approval letters, letters of support, recruitment materials, consent documents, any funding or thesis documents, and other supporting documents. The IRB will also consult the Protocol PI, as necessary, to gather additional information.

The goal of IRB review is to ensure approval only of research projects that meet the criteria listed in 7.2, delineating the parameters for adequate protection of the rights and welfare of human participants, as derived from (1) federal and state laws, (2) federal and state regulations, and (3) the principles of justice, beneficence, and autonomy articulated in applicable ethical codes like the Belmont Report and the Declaration of Helsinki.

7.2. Minimal Criteria for Approval of Research:

The IRB Expedited Reviewer(s) or the Convened IRB may approve a research project only when they find that the project fulfills all of the following conditions, their consideration of which shall be documented on the IRB Review Checklist.

Risks to participants are minimized: The protocol uses procedures that (1) are consistent with sound research design and (2) do not unnecessarily expose participants to risks without the informed consent of the participants.

Risks to participants are reasonable in relation to any anticipated benefits to participants and to the importance of any knowledge that is expected to result: When social or behavioral therapy or services are being provided to participants independent of their participation in the proposed research protocol, the Expedited Reviewer or the Convened IRB will (1) consider those additional risks and benefits; (2) review the Data Safety Monitoring Plan, when appropriate, to protect participants; (3) require that a Data Safety Monitoring Board (DSMB) be appointed, if appropriate; and (4) require that monitoring reports from the DSMB be submitted to the IRB at the time of Continuing Review.

Selection of participants is equitable: The IRB should consider the purposes of the research, the setting in which it will be conducted, and its inclusion/exclusion criteria, so as to maximize the equitable distribution of burdens and benefits. Moreover, the IRB should evaluate the recruitment practices and materials, as well as payments to participants. The IRB should consider particularly the special problems and additional safeguards posed by research involving vulnerable population participants such as children, prisoners, pregnant women, physically or mentally compromised individuals, or economically or educationally disadvantaged persons who may be vulnerable to coercion or undue influence in the context of the research. *See* SOPs pertaining to vulnerable populations.

Informed consent/assent: Informed consent or assent will be sought from each participant or his or her legally authorized representative and appropriately documented, in accordance with and to the extent required by local, state, and federal regulations. *See* SOP 9: Informed Consent Options, Processes, and Documentation.

Privacy and confidentiality: The protocol, if appropriate, will provide adequately for the protection of participants' privacy and the confidentiality of identifiable data.

The Expedited Reviewer(s) or the Convened IRB may request that ORIA obtain verification from sources other than the Protocol PI under the following circumstances:

1. The IRB has concerns about information provided by the Protocol PI.
2. The IRB has received information from the Protocol PI that is not consistent with other information known to the IRB and communication with the Protocol PI has not resolved the inconsistency.
3. The IRB is aware of previous or continuing non-compliance with Continuing Review requirements.
4. The IRB and/or ORIA have been made aware of concerns expressed by research participants, university employees, sponsors, regulatory agencies, and/or a member of the general public.

8. Procedures for EXPEDITED REVIEW:

8.1. Expedited Reviewer Process:

Only ORIA, the Chair of the IRB, or an experienced IRB reviewer who has been designated by the Chair of the IRB may make the determination that a research protocol application is *eligible* for Expedited Review and approval.

An IRB member with relevant expertise will be selected by ORIA or the Chair of the IRB as the Expedited Reviewer for the protocol. The Expedited Reviewer will complete the IRB Review Checklist (*see* Attachment 3:G) and return it to ORIA. ORIA will email the Expedited Reviewer's comments, questions, and/or suggestions for revisions to the Protocol PI, who will respond in writing to ORIA. The response will be reviewed by the Expedited Reviewer or the Chair of the IRB. These communications may continue until the Expedited Reviewer or the Chair of the IRB approves the protocol or refers the protocol for review by the Convened IRB.

The Expedited Reviewer(s) may exercise all of the decisional authorities of the IRB,⁵ *except that Expedited Reviewer(s) may not disapprove the research protocol.* The Expedited Reviewer(s) may approve, require specific minor revisions, or refer the research to the Convened IRB for review and approval. If there are concerns about whether or not an individual research project meets the definition of minimal risk or if the project may involve procedures that cannot be reasonably reviewed via the Expedited Review process, the protocol will be submitted for consideration at a Convened IRB meeting.

8.2. Conditions of Eligibility for Expedited Review:

The Expedited Review process may be employed for new protocols, continuations of previously approved protocols, or amendments to approved protocols. The procedures in Section 8 apply to the Expedited Review of all three. Further information specific to Expedited Review of continuation applications and amendments is provided below in Sections 10 and 11 for Continuing Review and Review of Amendments, respectively.

8.2.1. To be eligible for approval via the Expedited Review process, a research activity **must always** meet **both** of the following conditions:

- (1) It must present no more than minimal risk to human participants; *and*
- (2) It must involve *only* procedures listed in one or more of the categories of research activities listed below in Section 8.3: Categories of Research Activities Eligible for Expedited Review.

In sum, inclusion on the list in 8.3 means only that the activity is *eligible* for review through the Expedited Review process **when** the specific circumstances of the proposed research involve no more than minimal risk to human participants.⁶ If the protocol is

⁵ 45 CFR 46.111

⁶ Office of Human Research Protection, "Categories of Research that may be reviewed by the Institutional Review Board (IRB) through an Expedited Review Procedure," p. 1: <http://www.hhs.gov/ohrp/humansubjects/guidance/expedited98.htm>.

eligible for review through the Expedited Review process but the Expedited Reviewer has additional concerns, the protocol will be submitted to the Convened IRB for review. In addition, research protocols involving children must meet the standards set forth in SOP11: Informed Consent, Enrollment, and Other Considerations for Research Involving Children.

8.2.2. The following types of protocols **will not** receive Expedited Review:

- (1) Those posing more than minimal risk to the participants;
- (2) Classified research involving human participants;
- (3) Those involving prisoners;
- (4) Those involving mentally compromised individuals, when they are the focus of the research;
- (5) Those where the activities of the participants fall outside the categories outlined in Section 8.3.

8.3. Categories of Research Activities Eligible for Expedited Review⁷

1. Clinical studies of drugs or medical devices that meet one of the conditions below:
 - a. Drug research that does not require an investigational new drug application (21 CFR Part 312), unless the research is on marketed drugs and significantly increases the risks or decreases the acceptability of the risks associated with the use of the product.
 - b. Research on medical devices that do not require an investigational device exemption application (21 CFR Part 812); or
 - c. Medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
 - a. From healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
 - b. From other adults, as well as children, considering their age, weight, and health, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.
3. Prospective collection of biological specimens for research purposes by noninvasive means, such as:
 - a. Hair and nail clippings in a non-disfiguring manner;
 - b. Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;
 - c. Permanent teeth if routine patient care indicates a need for extraction;

⁷ See <http://www.hhs.gov/ohrp/humansubjects/guidance/expedited98.htm>

- d. Excreta and external secretions (including sweat);
 - e. Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue;
 - f. Placenta removed at delivery;
 - g. Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
 - h. Supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;
 - i. Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
 - j. Sputum collected after saline mist nebulization.
4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves.
- a. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for Expedited Review, including studies of cleared medical devices for new indications.)
 - b. Examples include physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; weighing or testing sensory acuity; magnetic resonance imaging; electrocardiography; electroencephalography; thermography; detection of naturally occurring radioactivity; electroretinography; ultrasound; diagnostic infrared imaging; doppler blood flow; and echocardiography; moderate exercise; muscular strength testing; body composition assessment; and flexibility testing where appropriate given the age, weight, and health of the individual.
5. Research that does not meet the criteria for the categories of research eligible for exemption from IRB review,⁸ but involves materials (data, documents, records, or specimens) that have been collected, or will be collected, solely for non-research purposes (such as medical treatment or diagnosis).
6. Collection of data from voice, video, digital, or image recordings made for research purposes.
7. Research that does not meet the criteria for the exempt categories, but is on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or employs survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

⁸ See SOP 2: Requirements for Submission of Research Protocols for a Determination by ORIA of Exemption from IRB Review

9. Procedures for CONVENED COMMITTEE REVIEW:

9.1. Categories of Research Activities that Require Review by the Convened IRB:

1. Initial applications that appear to involve more than minimal risk or that otherwise do not meet the criteria for Exemption from IRB review (*see* SOP 2: Requirements for Submission of Research Protocols for a Determination by ORIA of Exemption from IRB Review, Section 6) or Expedited Review;
2. All other proposals that are determined by the IRB Chair or an Expedited Reviewer to require Convened Committee Review; and
3. Revisions to initial protocols that contain non-minor changes.

9.2. Primary Reviewer Process:

1. ORIA, in consultation with the IRB Chair, will assign each protocol two primary reviewers. The primary reviewers are always the IRB members with the applicable scientific and non-scientific expertise in the area of research. For studies that involve participants from vulnerable populations, one of the primary reviewers should have knowledge of or experience with that population. If one of the primary reviewers does not have such knowledge or experience, an appropriate consultant should be assigned.
2. If the Chair of the IRB determines that appropriate expertise for review is not available among the members of the IRB, the Chair may request that ORIA seek a consultant from within or outside the Cornell community.
3. ORIA will distribute to all primary reviewers and the IRB Chair all of the research protocol application materials in advance of an IRB meeting to allow for appropriate review. For protocols for which they are not primary reviewers, IRB members attending the Convened meeting will receive an abbreviated application package consisting of the protocol, recruitment materials, and consent forms 10 days before the IRB meeting. All members are expected to review and familiarize themselves with all protocols before the meeting.
4. The primary reviewers shall complete the IRB Review Checklist and email their comments to ORIA. ORIA will distribute these comments by email to the Protocol PI, the other primary reviewer, and the IRB Chair. The Protocol PI will have the opportunity to respond to these comments before the meeting and his or her comments will be included in the discussion of the research protocol by the Convened IRB. These communications may continue until the time of the IRB meeting.
5. Approximately ten days before the IRB meeting, each member will receive a packet containing abbreviated applications, the minutes from the last meeting, the primary reviewers' IRB Review Checklists, and any other pertinent materials. At the IRB meeting, members will also receive an agenda for the meeting. This agenda will include a list of protocols that have been approved under the Expedited Review process since the last IRB meeting.

At the IRB meeting, the primary reviewers will provide a brief summary of each study, identify significant concerns, and report on the status of the Protocol PI's resolution of

these concerns. All members are expected to discuss the significant concerns outlined by the primary reviewer, identify additional concerns, provide necessary clarifications, and/or propose solutions or modifications. The ORIA representative (usually the IRB Administrator) will keep minutes of the meeting, including key discussion points and IRB decisions.

9.3. Quorum Requirements for Votes on Convened IRB Decisions:

A Convened IRB meeting is one at which a quorum is present (or participating via teleconference), which means that a majority (more than half) of the members of the IRB are present, including at least one member whose primary concern is in a non-scientific area. For studies that are FDA-regulated, the quorum must include at least one physician. Members attending by telephone- or video-conference count towards the quorum and may vote providing they have received all pertinent material prior to the meeting and they can participate actively and equally in the discussion of the protocols. The IRB minutes should document that these two conditions are met.

Approval of research is by a majority vote of the full IRB, minus the Chair, who does not vote except to break a tie.

A quorum can fail during a Convened meeting, by *inter alia* loss of a majority through recusal of members with conflicts of interest, early departures, or the absence of a non-scientist member. In the case of quorum failure, the remaining group may continue discussion of protocols, but may not take further actions unless and until the quorum can be restored.

10. Procedures for CONTINUING REVIEW:

The IRB will conduct Continuing Review of all ongoing research protocols in order to ensure that the protection of human participants is consistent throughout the execution of the research project and that the research protocol is revised, as appropriate, to include new knowledge generated since the last Continuing Review. Continuing Review shall not occur less frequently than once per year, but may occur more frequently depending upon the perceived risk of the research activity and the uniqueness of the specific research protocol.

Neither the collection of prospective research data nor the performance of research-related procedures can occur after the approval date until a Continuing Approval Request form has been reviewed and approved under the Expedited or Convened Committee Review process, as appropriate. Data collected after the previous approval date and before the approval of the continuation shall not be eligible for use in the research protocol.

Continuing Review is required as long as the research project remains active for long-term follow-up of participants, even when the research is permanently closed to the enrollment of new participants and all participants have completed all research-related interventions. Continuing Review is required even when the remaining research activities are limited to analysis of private identifiable information.

10.1. Intervals for Continuing Review:

Research activities are approved for a finite time period and use of any data after the approval period is considered unapproved research. The IRB will conduct Continuing Review of all ongoing research protocols at intervals relevant to the degree of risk involved, but not less than once per year. The purpose of the Continuing Review is to ensure the continuing protection of human participants in the research and the modification of the research, as appropriate, to reduce risk and incorporate any new knowledge that has been identified since the last Continuing Review. Not less than once per year means that the research must be reviewed and approved on or before the one-year anniversary of the previous IRB review date (*i.e.* the date of expiration of the approval period), even though the research activity may not have been initiated until some time after the IRB granted approval. Under most conditions, it is assumed that the approval period will be 364 days from the date of initial IRB approval or 363 days when approval occurs in a leap year, unless the IRB determines at the time of initial review and approval that the degree of risk attendant to the protocol requires a shorter approval period. The approval period will be specified in the approval notice given to all Protocol PIs and no research can be conducted outside of the time period identified in the approval notice.

10.2. Procedure for Submitting a Research Protocol for Continuing Review:

Receipt of Reminder Notice: The ORIA database tracks approval and expiration dates and generates monthly reports for ORIA listing the Continuing Reviews due by the month of protocol expiration dates.

Investigators are responsible for maintaining their IRB approval and for submitting a continuation and/or amendment application to the IRB, as appropriate. ORIA will send email reminders to Protocol PIs, requesting that they complete and submit a Continuing Approval Request form for IRB review. *See* Attachments 3:H and 3:I. Protocol PIs whose protocols were approved under the Expedited Review process will receive the email reminder 6 weeks before their protocol expiration date, while those whose protocols were approved under the Convened Committee Review process will receive the email reminder 2 months before the protocol expiration date. Subsequent reminders to the Protocol PI may be sent by email and/or telephone. All reminders are designed as a *courtesy* to Protocol PIs; investigators are responsible for maintaining their approval and for not conducting research outside of the review period.

Documents Constituting Protocol Continuation Application: The Continuing Approval Request form must include the signatures of all investigators and the faculty supervisor (if applicable). Protocol PIs must return the completed Continuing Approval Request form to ORIA by the due date stated in their reminder notice, which will be approximately 2 weeks before the next IRB meeting. The Protocol PI is required also to submit to ORIA the following documents, which together with the Continuing Approval Request form, will constitute the complete protocol continuation application: (1) the informed consent document(s) or oral scripts, even if identical to the version(s) submitted and approved the previous year, if participants are still being recruited for the project; (2) any new or revised advertisements or other recruitment materials or wording; (3) any available funding review comments pertinent to the human participant research component of a grant; (4) documents pertaining to funding sources procured after the previous IRB review and approval, and (5)

the results of all reviews by IRBs not affiliated with Cornell University. The Protocol PI should also provide a copy of revised informed consent document(s) or oral scripts and all revised advertisements or other recruitment materials, highlighting the proposed changes. These documents can be submitted either electronically or in hard copy format.

Continuation Review Process: Upon receipt of the continuation application, ORIA will (1) verify the completeness of the materials or coordinate with the Protocol PI to achieve completion; (2) review the application to determine whether the Expedited or Convened Committee Review process is appropriate; and (3) enter selected information from the Continuing Approval Request form into the research protocol tracking database.

The following types of protocols will receive Continuing Review under the Expedited process:

(1) a protocol that falls within one of the seven categories of research activities eligible for Expedited Review set forth above in Section 8.3; *OR*

(2) a protocol that was reviewed and approved previously under the Expedited process *and* to which no non-minor changes have been made that render it appropriate for Convened Committee Review; *OR*

(3) a protocol that was reviewed and approved previously under the Convened Committee process, *but* meets the following conditions:

- a. (i) the research is permanently closed to the enrollment of new subjects; (ii) all participants have completed all research-related interventions; *and* (iii) 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

(4) research, not conducted under an investigational new drug application or investigational device exemption, where categories 2 through 7 in Section 8.3 (Categories of Research Activities Eligible for Expedited Review) and item (3) above does not apply, but the IRB has determined and documented at a Convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

Any protocol which poses or has been revised to pose more than minimal risk will be reviewed under the Convened Committee process. And, generally, protocols that initially required Convened Committee Review will receive Continuing Review under the same process.

ORIA will attempt to assign continuation applications to the protocol's original Expedited Reviewer or primary reviewers. The Continuing Reviews for the Convened IRB will be added to a future meeting agenda, and every member of the IRB will receive the complete continuation applications, not abbreviated packages.

10.3. Consequences of Failure to Submit Research Protocol for Continuing Review:

There is no grace period extending the conduct of the research beyond the expiration date of the approval period. Extensions beyond the expiration date are not granted. If the continuation application is not received as required, and continuation of the research has not been approved, the Protocol PI must terminate the research on the date of expiration unless the safety of the research participants would be compromised. Principal Investigators should consult with the IRB on the process for withdrawing human participants from the research protocol when there is concern about their safety. *See* SOP 6: Suspensions and Terminations of IRB Approval of Research Protocols.

10.4. Possible IRB Decisions Upon Continuing Review:

No research activity shall continue past the expiration date until the Protocol PI has received written notification from ORIA that the protocol has been “approved for continuation” by the IRB. Such notification will be sent by email. Please refer to the preamble of Section 6.4, above, for general procedures for transmittal of IRB decisions by ORIA.

If a Protocol PI believes that the suspension of all human research-related activities will result in a risk to participants, he or she should work with the IRB to develop and implement a plan to withdraw the participants in ways that would minimize the risk to them.

Audit: As part of the Continuing Review, the Expedited Reviewer or the Convened IRB may elect to audit the research records of the Protocol PI.

Approved: If the Expedited Reviewer or the Convened IRB approves the continuation application without revisions, ORIA will send to the Protocol PI a written email notification of approval, as well as the clean copy of the informed consent documents/oral scripts featuring a stamp of approval. If the date of expiration has passed before the date of approval of the continuation application, the Protocol PI may re-initiate the research project on the approval date for the continuation of the research protocol.

Specific minor revisions required for approval: The Expedited Reviewer or the IRB may stipulate that approval of the continuation will be granted only after the Protocol PI implements specific minor revisions. The required changes will be communicated to the Protocol PI in an email from ORIA. The Protocol PI must make these changes and certify the changes as complete to ORIA before the expiration date. If the changes are not made before the expiration date, ORIA will provide the Protocol PI with a notice of expiration. Upon receipt of such a notice, the Protocol PI must suspend all human research-related activities for that protocol until he or she receives a new approval email with a new approval period. If the Protocol PI suggests or makes revisions that the Expedited Reviewer believes affect the risk-benefit ratio of the project, such revisions will be designated as major and referred for review by the Convened IRB.

An Expedited Reviewer may decide that the Convened IRB should review a continuation application. In this event, ORIA will assign the continuation application to a future IRB meeting agenda.

Tabled: The Expedited Reviewer or the Convened IRB may decide to require substantive clarifications or modifications to the protocol or informed consent documents. In this event, ORIA shall draft a memorandum outlining the required changes and send it to the Protocol PI, who shall have up to approximately 90 days to respond to the concerns outlined in this memorandum and to make appropriate revisions and send them to ORIA. ORIA will assign the revisions for Expedited Review or, if the revisions relate to the risk/benefit ratio of the research, for discussion by the Convened IRB at a future meeting. After 90 days, the IRB will disapprove the continuation of the protocol and the Protocol PI may be required to re-submit a new protocol. If the date of expiration passes during the 90 day period, ORIA will issue a letter of expiration to the Protocol PI who shall suspend all human research-related activities for that protocol until approval is obtained.

Where Convened Committee Review is required, a protocol may be tabled for lack of appropriate expertise in attendance, lack of time, or loss of quorum. Again, if approval is not granted before the expiration date, ORIA will provide the Protocol PI with a notice of expiration. Upon receipt of such a notice, the Protocol PI must suspend all human research-related activities for that protocol.

The IRB may make one of the following decisions for the revised protocol: (1) approved, (2) specific minor revisions required for approval, (3) tabled, or (4) disapproved. This cycle continues until the IRB issues a final decision—either approved or disapproved.

Disapproved: The Convened IRB may elect to disapprove a continuation application when it identifies significant concerns about potential risk to participants or a lack of scientific validity to support proposed research activities. On behalf of the IRB, ORIA will provide the Protocol PI a written statement of the reasons for the IRB's decision. The Protocol PI will have the opportunity to respond in person or in writing. The Convened IRB will review any written responses. If the Protocol PI chooses to alter or to replace the research activity in accordance with any IRB recommendations for major revisions to the protocol, the Protocol PI may submit an entirely new research protocol application for that revised/replacement research activity.

11. Procedures for REVIEW of AMENDMENTS:

A Protocol PI may not implement an amendment to a previously approved research project during the approval period, even if requested by a sponsor, unless and until the IRB reviews and approves it under the Expedited or Convened Committee Review process, except where necessary to eliminate apparent immediate hazards to human participants. An amendment is necessary for all modifications or changes to the research protocol. The IRB will review the amendment in the context of the entire research protocol and will approve the amendment before it is incorporated into the approved research protocol.

11.1. Definition of Modifications and Corresponding IRB Review Requirements

There are two types of modifications: minor modifications and non-minor modifications.

Minor modifications to previously approved research protocols are those that meet all of the following criteria: (1) Involve the addition of no more than minimal risk *or* reduce a risk that was reviewed and approved previously by the Convened IRB; *and* (2) Involve the addition of

procedures or activities that would be exempt from IRB review or eligible for initial review under the Expedited Review process if they were considered independently of the previously approved research protocol.

Minor modifications may be eligible for Expedited Review.

Modifications that do not meet both of these criteria are non-minor modifications, which require IRB review and approval under the Convened Committee process.

Examples of minor modifications include, but are not limited to: (1) minor increases or decreases in the number of participants; (2) changes in remuneration; (3) changes to improve the clarity of statements or to correct typographical errors in informed consent documents or debriefing texts, provided that the changes do not alter the content or intent of the statements; and (4) additions or deletions of co-investigators or key personnel. A non-exhaustive list of examples of amendments that require IRB review and approval is provided on the IRB website, at <http://www.irb.cornell.edu/forms/amendmentGuidance.htm>. However, if a Protocol PI has any question as to whether a change or modification to a previously approved protocol requires IRB review and approval, he or she should contact ORIA for further information.

11.2. Procedure for Submitting an Amendment for IRB Review:

Documents to Submit: The Protocol PI must submit an amendment request to the IRB in writing by completing the Request to Amend a Previously Approved Project form and submitting it to ORIA. The Protocol PI should attach to the form all amended instruments and consent/assent form/information sheets, etc and should highlight the proposed modifications. These documents will comprise the amendment application.

Selection of Expedited or Convened Committee Review: Upon receipt of the amendment request form, ORIA will evaluate the amendment and its risk level to determine whether it is appropriate for review under the Expedited or Convened Committee Review process. If there is doubt as to whether an amendment qualifies for Expedited Review, it should be reviewed by the Convened IRB.

If the amendment is suitable for Expedited Review, that review will take place under the same Expedited procedures outlined above in Section 8.1. If the amendment requires Convened Committee Review, or is referred for such review by the Expedited Reviewer, that review will take place under the same Convened Committee Review procedures outlined above in Section 9.2, except that the primary reviewers and the rest of the IRB members all will receive the amendment application. Full documentation for the previously approved protocol will be made available to the primary reviewers.

11.3. Possible IRB Decisions Regarding IRB Amendment:

No amendment shall be implemented until the Protocol PI has received written notification from ORIA that the amendment has been “approved” by the IRB. Please refer to the preamble of Section 6.4, above, for general procedures for transmittal of IRB decisions by ORIA.

Approved: If the amendment is approved, ORIA will provide email notice to the Protocol PI. Only after receiving the email notice of approval may the Protocol PI implement the amendment.

However, the Protocol PI is always charged with safeguarding the health and safety of all research participants. Therefore, in working with a particular participant, he or she may implement an amendment that reduces a risk to the physical or emotional health of that participant. This deviation from the approved research protocol must be submitted to the IRB for its review using the amendment application process in 11.2. Moreover, before enrolling other participants, the Protocol PI is responsible for submitting the amendment to the IRB for its review and approval.

Specific minor revisions required for approval: The Expedited Reviewer(s) or the Convened IRB may stipulate that approval of the amendment will be granted only after the Protocol PI makes specific minor revisions to it. ORIA will send the Protocol PI a notification of the required changes. If the Protocol PI makes the revisions, he or she shall then re-submit the amendment for review via the Expedited Review process. After all specific minor revisions have been approved, ORIA will send an email notice of approval to the Protocol PI. Upon receipt of this notice, the Protocol PI may implement the amendment. If, however, the Protocol PI suggests or makes revisions that the Expedited Reviewer believes affect the risk-benefit ratio of the amendment or the project as a whole, such revisions will be designated as major and referred for review by the Convened IRB.

The Protocol PI may request the IRB to review the required specific minor revisions at a Convened meeting. However, the amendment cannot be implemented until all specific minor revisions have been satisfactorily addressed or the Convened IRB has reviewed and approved the amendment.

Tabled: An amendment is tabled when the Expedited Reviewer(s) or the Convened IRB request additional information, substantive clarifications or modifications regarding some aspect of its substance or implementation that is relevant to the evaluation of the risk/benefit ratio required for approval. The IRB may also table an amendment where it does not have a member with expertise adequate to its scope and complexity and thus seeks review by an expert in the appropriate field. The Protocol PI may suggest an expert to the IRB for this purpose.

An amendment requiring Convened Committee Review may be tabled for lack of appropriate expertise in attendance, lack of time, loss of quorum, etc. In the event an amendment application is tabled for such administrative reasons, ORIA will assign it for review at a future meeting of the Convened IRB.

When an amendment is tabled, ORIA shall draft and transmit to the Protocol PI a memorandum setting forth the reasons for this action. The Protocol PI shall have up to approximately 90 days to respond to the concerns outlined in the memorandum and to make appropriate revisions to the amendment in question. The Protocol PI will submit the revised amendment to ORIA, which will assign it for Expedited Review or, if the revisions relate to the risk/benefit ratio of the research, for discussion by the Convened IRB. After 90 days, the IRB will disapprove the amendment and the Protocol PI may be required to re-submit a new amendment request if he or she wishes to amend the approved protocol.

The IRB may make one of the following decisions with respect to a revised amendment application: (1) approved, (2) specific minor revisions required for approval, (3) tabled, or (4) disapproved. This cycle will continue until the IRB issues a final decision—either approved or disapproved.

Disapproved: The Convened IRB may elect to disapprove an amendment when it identifies significant concerns about potential risk to participants or a lack of scientific validity to support the amendment. ORIA will draft and transmit to the Protocol PI a written statement of the reasons for the IRB's decision. The Protocol PI will have the opportunity to respond in person or in writing. The IRB, at a Convened meeting, will review any written responses and make a decision about the appeal of the initial decision to disapprove the amendment. As with all protocols, continuations, and amendments, the Protocol PI may not initiate the corresponding amendment until it has been approved by the IRB. The Protocol PI always has the right to submit a new amendment that addresses the concerns outlined during the review of the previous version of the amendment.