

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

**1. Subject of Policy & Procedure**

If a Protocol Principal Investigator (Protocol PI) determines that a research activity constitutes human participant research *and* requires IRB review and approval, the Protocol PI must complete and submit to IRB 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 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 CCC-UPR faculty, staff, or students or by anyone conducting a research activity supported by CCC-UPR or where CCC-UPR is considered to be engaged in the research.

**3. Terms and Definitions**

Employees (faculty and staff) should consult the [IRB Glossary](#).

**4. See Also**

Affected researchers and employees should also consult:

1. CCC-UPR [Federalwide Assurance Registration](#)
2. [The Belmont Report](#)
3. National Academies Press Booklet: "[On Being a Scientist: Responsible Conduct in Research](#)"

4. Initial Application Form
5. Continuing Report Form
6. [Request to Amend a Previously Approved Project](#) (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,

### 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 2013)

## 6. Protocol Application Submission Procedures for Initial Review:

If the Protocol PI or IRB determines that a research activity (a) constitutes human participant research,<sup>1</sup> **and** (b) is not eligible for exemption from IRB review,<sup>2</sup> the Protocol PI must submit the research protocol 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 personnel named on the protocol must complete the CITI online training (Human Subject protection in research, HIPAA, Good Clinical Practices ) addressing the

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<sup>1</sup> See [SOP 1](#): Determining Whether a Research Activity Needs IRB Review or Exemption from IRB Review

<sup>2</sup> See [SOP 2](#): Requirements for Submission of Research Protocols for a Determination of Exemption from IRB Review

appropriate conduct of human participant research.<sup>3</sup> Proof of completion of this requirement by all investigators and key personnel is maintained in the protocol file by IRB.<sup>4</sup>

All researchers named on a protocol are required to renew their training every three (3) years unless the IRB grants an exemption or extension to this requirement as part of the protocol review or as a policy modification approved by a majority vote of the voting members of the IRB.

#### 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-CCC-UPR organizations from which, the Protocol PI will be recruiting participants.

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<sup>3</sup> See Online Training at <https://about.citiprogram.org/en/homepage>

<sup>4</sup> The investigators and research staff may also familiarize themselves with the following materials pertinent to ethical standards governing the conduct of human participant research: CCC-UPR's Federalwide 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 links.

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 IRB:

Upon receipt of the research protocol and supporting documents, IRB 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) Revise the Initial IRB Application Form; 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, the materials will submit 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 IRB that the protocol has been “approved” by the IRB.**

The Protocol PI shall be notified 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 another 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 and will be communicated in the form of written notifications.

***Approved:*** If the protocol is approved, IRB will send an email letter 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 after the Protocol PI makes specific minor revisions to the protocol, informed consent documents, and process, recruitment materials, etc. IRB 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; IRB 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, IRB will assign it for review at a future meeting of the Convened IRB.

When a protocol is tabled, IRB 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 any revisions and responses to the concerns or questions outlined in the memorandum, which will assign them for IRB review.

The IRB may make one of the following decisions concerning 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 the potential risk to participants or a lack of scientific validity to support the proposed research activities. IRB chair 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 writing. The IRB at a Convened meeting will review any written responses and decide 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, 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 about 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, by 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 obtain verification from sources other than the Protocol PI under the following circumstances:

1. The IRB has concerns about the 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 has been made aware of concerns expressed by research participants, employees, sponsors, regulatory agencies, and a member of the general public.

## **8. Procedures for EXPEDITED REVIEW:**

### **8.1. Expedited Reviewer Process:**

Expedited review of research subject to the revised Common Rule will be conducted using the procedures described in the CCC- UPR SOP Manual with the following variations:

1. The IRB shall apply the most current list of categories of research published in the Federal Register that may be reviewed using expedited review procedures [§\_\_.110(a)]
  2. Research that falls within the list of categories is presumed to be a minimal risk unless the IRB determines and documents that the research involves more than minimal risk. [§\_\_.110(b)(1)(i)]
- If the reviewer determines that the research involves more than minimal risk, it will be referred for review by the convened IRB
3. The limited IRB review that is required for certain exempt research (See Section 3) may be conducted using expedited review procedures [§\_\_.110(b)(1)(iii)]
  4. Continuing review of research is not required for research that qualifies for expedited review unless the IRB determines that is required and documents the rationale within the IRB record

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

The Chair of the IRB will select an IRB member with relevant expertise to served as the Expedited Reviewer for the protocol. The Expedited Reviewer will review the application using the IRB Review Checklist as a guide, and provide comments to IRB. IRB will email the Expedited Reviewer's comments, questions, and suggestions for revisions to the Protocol PI, who will respond in writing to IRB. 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,<sup>5</sup> *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

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<sup>5</sup> 45 CFR 46.111



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.<sup>6</sup> If the protocol is *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. Also, research protocols involving children must meet the standards outlined in [SOP 11: Informed Consent, Enrollment, and Other Considerations for Research Involving Children](#).

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

Research that Commonly Undergoes Full Board Review

- (1) Research projects involving more than minimal risk
- (2) Classified research involving human participants;
- (3) Research involving prisoners;
- (4) Research involving mentally compromised individuals, when they are the focus of the research;
- (5) Projects that do not meet the Expedited Review (8.3 criteria) will automatically require Full Board Review.

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<sup>6</sup> Office of Human Research Protection, “Categories of Research that may be reviewed by the Institutional Review Board

(IRB) through an Expedited Review Procedure, Final document approved at SACHRP March 12-13, 2013

Common examples of projects that typically require Full Board Review include:

- (6) Research projects involving clinical trials and/or clinical interventions
- (7) Research projects that have special concerns or involves vulnerable populations
- (8) Research involving children, pregnant women or fetuses, prisoners, or people with mental impairment (depending on the nature of the study)
- (9) Research projects that involve the use of a medical device (in most cases)
- (10) Projects that involve possible coercion or undue influence that induces or entices consent (e.g., excessive compensation, inequitable relationship, etc.)
- (11) Sensitive information is being gathered (e.g., child abuse, violence, sexual conduct/misconduct, mental health/status information, AIDS, alcohol, compulsive disorders, etc.)
- (12) Projects involving deception (e.g., intentionally misleading subjects about their status, giving false information about the researchers or the research purpose)

### **8.2.3 Full Board Renewals**

Any active protocol that previously received a full board review must come back to the Full Board for its yearly renewal. However, a protocol that previously received Full Board review can go through an Expedited review (Category #8), so long as it meets one of the following three requirements:

- 1. the research is permanently closed to the enrollment of new subjects;
- 2. all subjects have completed all research-related interventions; and
- 3. the research remains active only for long-term follow-up of subjects; or where no subjects have been enrolled and no additional risks have been identified; or where the remaining research activities are limited to data analysis

### **8.3. Categories of Research Activities Eligible for Expedited Review**<sup>7</sup>

- 1. Clinical studies of drugs and medical devices only when one of this condition (a) or (b) is met.
  - a. Research on drugs for which an investigational new drug application (21 CFR 312) is not required. (Note: Research on marketed drugs that significantly

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<sup>7</sup> See <https://www.hhs.gov/ohrp/sachrp-committee/recommendations/2013-may-20-letter-attachment-a/index.html>

increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

- b. Research on medical devices where an investigational device exemption (IDE) application or an abbreviated IDE application for a non-significant risk (NSR) device (21 CFR 812) is not required.
2. The collection of blood specimens for research purposes using techniques consistent with routine clinical practice to minimize pain and risk of infection and within the following limits for volume:
- (a) from non-pregnant adults who weigh at least 50 kg, the amounts collected should not exceed 550 ml in an 8-week period; or
  - (b) from children and other adults, the amount of blood to be collected should not exceed the lesser of 150 ml or 3 ml per kg in an 8-week period.

Examples:

- a. Finger-stick, heel-stick, or ear stick with reasonable limits on frequency and with volumes consistent with clinical practice employing these methods.
  - b. Venipuncture with reasonable limits on frequency and with the total volume of clinical and research specimens limited as defined above.
  - c. Collection of blood from an in-dwelling peripheral venous catheter placed for research purposes with volume limits as defined above.
  - d. Collection of blood from an in-dwelling catheter already in place for clinical purposes, with the total volume of clinical and research samples limited as defined above.
3. Prospective collection of biological specimens, excluding blood, for research purposes by noninvasive or minimally invasive means. Examples:
- a. Tissues and fluids that the body produces continuously or sheds as a normal process, which are collected in a non-disfiguring manner.
  - b. Tissues and fluids if routine patient care indicates a need for removal or extraction.
  - c. Dental plaque and calculus.

- d. Tissues from non-facial, non-genital skin punch biopsies in adults that do not require sutures.
  - e. Specimens collected in adults by curettage, urethral, vaginal or rectal swabs.
  - f. Specimens collected from the external auditory canal or nares.
4. Collection of additional data and biological specimens, excluding blood specimens, for research purposes during procedures already being performed for clinical purposes, provided the additional collection does not entail more than a minimal increase in risk, pain or discomfort.

Examples:

- a. Collection of additional bodily fluids (e.g., peritoneal fluid, bone marrow or cerebrospinal fluid)
  - b. A reasonable extension of anesthesia, sedation or operating room time to allow collection of additional data or specimens.
  - c. Tissue collected from pap smears.
5. Collection of data through noninvasive or minimally invasive procedures (not requiring the addition of general anesthesia or sedation for research purposes) routinely employed in clinical practice. Examples:
- a. Physical sensors that are applied either to the surface of the body or at a distance.
  - b. Weighing or testing sensory acuity.
  - c. Magnetic resonance imaging.
  - d. Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography.
  - e. Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing.
  - f. Allergy skin-testing in subjects not known or suspected to have serious allergies to the allergen being tested.

- g. Procedures in adults involving a single exposure to ionizing radiation with an effective dose not exceeding 0.1 mSv (the amount typically associated with a chest x-ray) provided appropriate shielding techniques are employed.
- 6. Secondary use of materials (data, documents, records, or biological specimens) that have been or will be collected for purposes other than the currently proposed research project.

Examples:

- a. Secondary use of data collected from another research study provided the use is compatible with the original terms of consent if any.
    - 1. Secondary use of clinical or educational records.
    - 2. Use of banked specimens in biorepositories.
- 7. Activities at statistical and data coordinating centers or biospecimen repositories that are not responsible for the primary oversight of the study and are not involved in the primary collection of data or specimens, which may be ongoing at other sites.

Example:

A multicenter clinical trial where data are gathered under separate IRB approval(s) for the performance sites, but received and managed by a central coordinating center that does not otherwise participate in the clinical intervention or interact directly with subjects.

- 8. Collection of data from voice, video, digital, or image recordings made for research purposes.
- 9. Surveys, interviews, self-reports, direct and indirect observations of individual and group behavior, other verbal or computer-assisted interactions or assessments, non-invasive physical or behavioral tasks, manipulation of the subject's environment and similar methods commonly used in cognitive, behavioral, social, ethnographic, educational, health, and epidemiologic research.

Examples

- a. Measures of performance on cognitive, perceptual, neuropsychological, behavioral and other related tasks employing non-invasive technologies (e.g., paper and pencil assessment, computerized tasks, remote data collection using mobile devices).
  - b. Interviews, questionnaires, surveys, focus groups, and internet-based data collection on personal experience, identity, language, relationships, attitudes, beliefs, and practices.

- c. Psychiatric diagnostic or symptom assessments in healthy or mentally ill populations conducted by clinicians or trained interviewers (with appropriate mechanisms for clinical back-up or referral).
  - d. Measures of symptoms, mobility, range of motion, quality of life and activities of daily living patient and non-patient populations by clinical or other trained personnel (e.g., nurses, physicians, social workers).
  - e. Methods used in ergonomics and human factors research including cognitive, human-computer, physiological and bio-mechanical measures in consumer, industrial, and biomedical settings.
  - f. Qualitative and quantitative data collection through observation, participant observation and interaction with groups in naturalistic settings (including the internet).
  - g. Surveys on personal and family finances, consumer preferences and decision-making.
  - h. Assessments of compliance with medication or treatment regimens.
  - i. Surveys to establish the effectiveness of public health interventions.
10. Establishment of subject recruitment databases.

Examples:

- a. Collection of identifiable information to establish subject pools.
- b. Disease-specific patient registries.
- c. Screening protocols including interviews, questionnaires and physical assessments that could be expedited under one of the categories listed above.

### **Expedited Continuing Review of Previously Approved Research**

1. Research previously approved by the convened IRB and now subject to continuing review where one of the following conditions apply:
  - a. The research is permanently closed to the enrollment of new subjects, (ii) all subjects 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
  - d. a non-significant risk (NSR) determination was initially made by a convened IRB for research involving medical devices, and the research was determined to present no greater than minimal risk to the subject; or

- e. 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.

## **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 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. 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 nonscientific 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 seek a consultant from within or outside the CCC-UPR community.
3. IRB coordinator 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 review the protocol using the Protocol Review checklist as the guide, and send their review comments to IRB. IRB Coordinator will distribute these comments 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. Before the IRB meeting, materials relevant to the meeting, including an agenda, protocol documentation for those protocols that are under review, the minutes from the previous meeting, a report on expedited protocols that were processed since the last IRB meeting, and any other materials for voting and/or discussion will be made available to each committee member.

At the IRB meeting, the PI or the primary reviewers will provide a 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 propose solutions or modifications. The IRB coordinator representative 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 least **5** IRB member are present, including at least one member whose primary concern is in a non-scientific area (community member). 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 to provide they have received all pertinent material before 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 *among other things* 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 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 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 first 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 sometime after the IRB approved. 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 period identified in the approval notice.

Following the guidance provided by the OHRP on this topic, CCC-UPR IRB recognizes the logistical advantages of keeping the IRB approval period constant from year to year throughout the life of each project. When continuing review occurs annually, and the IRB performs continuing review within 30 days before the IRB approval period expires, the IRB may choose to retain the anniversary date as the date by which the continuing review must occur.

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

***Receipt of Reminder Notice:***

Investigators are responsible for maintaining their IRB approval and for submitting a continuation and amendment application to the IRB, as appropriate. As a courtesy and service to the PI, IRB will send an email reminder to Protocol PIs, 6-8 weeks before the protocol expiration date, requesting that they complete and submit a Continuing Approval Request form for IRB review or request for the project to close if no research with human participants is expected to continue past the expiration date.

***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 IRB in sufficient time to allow review and approval of the application before the expiration date. The Protocol PI is required also to submit to IRB the following documents, which together with the Continuing Approval Request form, will constitute the complete protocol continuation application: (1) the informed consent oral scripts or a copy of an actual written signed consent form, even if identical to the version(s) submitted and approved the previous year; (2) any proposed 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 CCC-UPR.

***Continuation Review Process:***

The revised Common Rule modifies when continuing review is required. Unless CCC-UPR IRB determines otherwise, continuing review of research is not required for research subject to the revised Common Rule in the following circumstances:

1. Research eligible for expedited review in accordance with §\_\_.110;
2. Research reviewed by the IRB in accordance with limited IRB review;
3. Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:
  - a. Data analysis, including analysis of identifiable private information or identifiable biospecimens, or
  - b. Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care

CCC-UPR IRB may determine that continuing review is required for any research protocol that falls within the above criteria. (The following is not required but provided as an example of

factors an IRB may take into consideration.) For example, the IRB may determine that continuing review is required when:

1. Required by other applicable regulations (e.g., FDA);
2. The research involves topics, procedures, or data that may be considered sensitive or controversial;
3. The research involves particularly vulnerable subjects or circumstances that increase subjects' vulnerability;
4. An investigator has minimal experience in research or the research type, topic, or procedures; and/or
5. An investigator has a history of noncompliance

When the CCC-UPR IRB determines that continuing review is required for such research, it will document the rationale in the IRB record and communicate the requirement to the investigator in the IRB determination letter.

Upon receipt of the continuation report, IRB will verify the completeness of the materials or coordinate with the Protocol PI to achieve completion; review the application to determine whether the Expedited or Convened Committee Review process is appropriate; and Initiate the review process for the application.

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

- (1) a protocol that falls within one of the 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.

IRB 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 IRB that the protocol has been “approved for continuation” by the IRB. Such notification will send by email. Please refer to the preamble of Section 6.4, above, for general procedures for transmittal of IRB decisions.**

**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, IRB will send to the Protocol PI a written notification 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 after the Protocol PI implements specific minor revisions. The required revisions will be communicated to the Protocol PI and must be completed or otherwise resolved before the protocol can be approved. Upon approval of the continuation request, IRB will send a written notification of approval to the Protocol PI. 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. An Expedited Reviewer may decide that the Convened IRB should review a continuation application. In this event, IRB 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, IRB shall draft a memorandum outlining the required changes and send it to the Protocol PI, who must respond to the concerns outlined in this memorandum, make appropriate revisions and send them to IRB. IRB 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.

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.

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 the potential risk to participants or a lack of scientific validity to support proposed research activities. The IRB 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 writing. The Convened IRB will review any written responses. If the Protocol PI chooses to alter or to replace the research activity following 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.

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.

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 IRB for further information.

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.

### **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 to amend a Previously Approved Project form and submitting it to IRB. 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, IRB 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 IRB 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.**

*Approved:* If the amendment is approved, IRB will provide email notification 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 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 after the Protocol PI makes specific minor revisions to it. IRB 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, IRB 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, IRB will assign it for review at a future meeting of the Convened IRB.

When an amendment is tabled, IRB shall draft and transmit to the Protocol PI a memorandum setting forth the reasons for this action. The Protocol PI will respond to the concerns outlined in the memorandum and make appropriate revisions to the amendment in question and submit the revised amendment to IRB, 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.

The IRB may make one of the following decisions concerning 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 the potential risk to participants or a lack of scientific validity to support the amendment. IRB 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 writing. The IRB, at a Convened meeting, will review any written responses and decide 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.