204.1 Protocol Review

The UH IRBs and the HSP, as delegated by its IRBs, oversee only human participant research in which UH is engaged or for research that has entered into an agreement with UH for UH IRB to be its “IRB of Record.”

All UH new human participant research (as defined in Section 201.5) and modifications to approved research (except to remove apparent immediate hazards to participants) must be prospectively reviewed and approved by the IRB, before research activities take place. Approved protocols and proposals must undergo continuing review if research activities are expected to continue beyond the approval period set by the IRB.

204.2 IRB Protocol Applications (eProtocol)

Most protocol and proposal submissions to the IRB are completed via an online web-based system called “eProtocol.” Forms available for online submission include:

- Protocol or proposal applications for:
  - New research
  - Modifications
  - Continuing Review
- Reports
  - Unanticipated Problems and Serious Adverse Events
  - Protocol Violations or Deviations
- Final Reports

See UH eProtocol Quicklink for more information on the UH eProtocol system for submitting research protocols and proposals.

Protocol applications include, but are not limited to, the following sections to be completed by the Investigator or Investigator’s designee:

- Research Personnel
- Study Location
- Funding
- Resources
- Collaboration/Multi-site
- Participant population
- Purpose, procedures, background
- Use of Drugs or Devices
- Recruitment methods and screening procedures
• Inclusion and exclusion criteria
• Vulnerable populations
• Potential risks and benefits
• Privacy and confidentiality
• Conflict of Interest
• Consent and assent
• HIPAA

Review Type

New protocol and proposal submissions are processed according to one of three levels of review:

1. **Exempt**: UH requires protocols and proposals qualifying for exemption from applicable, federal, state and local regulations to be submitted for IRB review and confirmation. Exempt review is performed by HSP staff who have the knowledge and authority to confirm exemption or refer the protocol or proposal for expedited or convened IRB review.

2. **Expedited**: Protocols that qualify for expedited review must meet the requirements set forth in 45 C.F.R. § 46.110 (i.e., the research involves not more than minimal risk and falls within the categories published in the November 9, 1998, Federal Register 63 F.R. 60367; F.R. 60356 HHS-FDA list of research eligible for expedited review).

3. **Convened IRB**: Research that does not qualify for exempt or expedited review is subject to convened IRB review.

Other Research or Special Situations

**Additional Requirements – Other Federal Agencies**: Depending on the source of support for the research, regulations from other agencies might apply. See GUIDE 617: Other Federal Agencies – Additional Requirements for these special considerations and for links to checklists to help ensure that all special considerations are met.

**Emergency Use of a Test Article: SOP 121**: Emergency Use of a Test Article describes the requirements for the emergency use of an investigational drug, device, or biologic under FDA regulations 21 C.F.R. § 56.104(c), and documentation to be submitted to the IRB.

204.3 Assignments of Protocols or Proposals For Review

Reviewer assignments are made with the objective of matching reviewer expertise and experience with the research subject matter (See Section 202.3). IRB members who are “non-scientists” assigned to review research are valued for the community perspective they bring to the review process for ensuring the protection of research participants.

Attempt is made to assign any modification requests and continuing review submissions to the same primary reviewer who reviewed the research when it was initially approved.
Full-Board -- Primary Reviewer System

The IRB utilizes a primary reviewer system, in which new protocols or proposals qualified for full-board review are assigned a primary reviewer who is responsible for performing a comprehensive review and presenting an assessment of the study at the convened meeting.

A secondary reviewer is also assigned. The secondary reviewer reviews the study and may present an assessment on the study. The secondary reviewer serves as the primary reviewer when the primary reviewer is absent at the meeting. The reviewers may contact the Investigator for any additional information, as necessary. HSP staff maintains anonymity of their Reviewers from the Investigators of research they are assigned, but Reviewers may waive their anonymity by contacting the Investigator.

Expeditied Research – Reviewer Qualifications

Only the IRB Chair or an experienced IRB member designated by the Chair may review research under an expedited review research. An IRB member is considered “experienced” when he/she has served the IRB for at least the last 6 months at the time of assignment and/or has had experience conducting human subjects research, or any other equivalent experience or expertise.

Administrative Changes to Expedited Research

Request for administrative changes to expedited research may be reviewed and approved by designated HSP staff. Examples of administrative changes to research include:

- Change in Project Title
- Principal Investigator’s contact information
- Changes to version number and/or revision date of study documents

204.4 Protocol/ Proposal Review

Criteria for Approval by an IRB

All proposed research must meet UH HRPP ethical standards governing the conduct of research (e.g., acceptable risk vs. benefit relationship, equitable selection, informed consent, protection of privacy, maintenance of confidentiality, and protections for vulnerable populations). The reviewers follow the approval criteria set forth in 45 C.F.R. § 46 and 21 C.F.R. § 50 in reviewing and approving a new protocol/proposal, continuing review, or review of a modification when the modification affects a criterion for approval. The IRB confirms that proposed Research Application, informed consent documents, and recruitment materials are accurate and complete.

The reviewers consider the regulations in reviewing and approving a protocol or proposal. They are facilitated in their consideration by the following several of HSP’s regulatory guidance and reviewer worksheets.
To approve research, an IRB must determine whether the following criteria are met:

1. Risks to subjects are minimized
   (i) by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and
   (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes;

2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB shall consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB shall not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

3. Selection of subjects is equitable. In making this assessment the IRB shall take into account the purposes of the research and the setting in which the research will be conducted and shall be particularly cognizant of the special problems of research involving members of vulnerable populations such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons;

4. Informed consent will be sought from each prospective subject or the subject's legally authorized representative according to Title 45, Section 46.116 in the Regulations;

5. Informed consent will be appropriately documented according to Title 45, Section 46.117 of the Regulations;

6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects; and

7. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain confidentiality of data.

### Review of Exempt Research

Continuing review is not required for exempt research. Modifications, however, are subject to review by HSP staff delegated by the IRB to conduct exempt review. Approval of the modification is required before implementing the change to the research. If a modification to an exempt research changes the review type appropriate for the research, the HSP staff will move the protocol or proposal to the appropriate review type status.

See Section 203.4 for information on exempt categories.

### Continuing Review

The IRB applies the same criteria for approval at continuing review as at initial review of new protocols or proposals.

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23 45 C.F.R. § 46.111(a).
Submission of a protocol or proposal for continuing review is required on all non-exempt approved research where its activities are ongoing, including but not limited to:

- Continuing recruitment and enrollment of participants;
- Research tests, procedures, and other interactions and interventions;
- Review of identifiable information;
- Data analysis; and
- Follow-up of previously enrolled participants.

The IRB determines whether the protocol or proposal needs verification from sources other than the researchers that no materials changes had occurred since previous IRB review.

Continuing review is not necessary only when:

- The research is permanently closed to the enrollment of new participants,
- All participants have completed all research-related interventions, and
- Collection and analysis of private identifiable information has been completed.

The continuing review application must be accompanied by the previously approved versions of the protocol or proposal’s supporting documents. (e.g., consent forms, advertisements, sponsor protocol). Modifications to the research at the time of continuing review shall be submitted separately as a modification request, and the continuing review shall reflect the protocol or proposal without the modification being requested.

**Modifications**

No modification to protocols may be implemented without prior approval of the IRB, except where necessary to eliminate apparent immediate hazards to participants. Investigators are required to complete a Modification request application that includes a summary of the proposed modification and indicate the change in the risks to participants associated with the modification (e.g., increase, decrease, no change).

Modifications involving changes to previously approved or submitted documents (e.g., consent forms, advertisements, and protocols) or the addition of new documents must be accompanied by the new documents and/or the proposed revised versions of the previously approved or submitted documents. Revised versions of previously approved documents must show its changes in track format.

In circumstances where a modification is made without prior IRB approval because it is necessary to eliminate apparent immediate hazards to participants, the Investigator must report this change to the IRB (see GUIDE 614: Events and Information that Require Prompt Report to the IRB). The IRB will determine whether the change was consistent with ensuring the participants’ continued welfare.

If significant new findings or information are submitted as part of a modification or continuing review, the IRB may require the reporting of this information to participants if the information could reasonably affect participants’ willingness to continue their participation.

See SOP 115: Submitting Modification Requests to the IRB for more information on the procedures for requesting approval of modification requests to IRB-approved research.
Status/Final Reports

Upon completion of a research project Investigators may be required to submit a Final Report notifying the IRB of the completion of the project.

Final Reports are required for:

- Research that was subject to a full-board review and involved enrolled participants.

Final Reports are not required for:

- Research subject to expedited or exempt review, or
- Research projects subject to full board review but never commenced or never enrolled participants.

204.5 Full-Board Review

New Protocol or Proposal

Along with assigning a new protocol or proposal to a primary and secondary reviewer, external expert reviewers may be asked to review to the research, when applicable (e.g., Data Governance if project involves request and use of institutional data). The primary reviewer may also contact a consultant to assist with the review of a study prior to the convened meeting.

If there is not at least one person on the IRB with the appropriate scientific or scholarly expertise, or other expertise or knowledge, to adequately conduct an in-depth review of the research, the IRB defers the application to another meeting or to another IRB, or obtains consultation. The convened IRB can determine whether a consultant is needed.

Modification Requests

The following modifications are subject to full-board review and are assigned by the IRB Coordinator to one reviewer who reviews and presents the modification request at the convened meeting:

- **Major (or “substantive”) modification** is a change that may increase the level of risk to participants or a greater than minor modification in any of the following:
  - Informed consent
  - Research design or methodology
  - Participant population enrolled in the research
  - Qualifications of research personnel
  - Facilities used to support the safe conduct of research
  - Any other issues that would warrant review of the proposed changes by the full-board IRB

- **Substantive modifications or clarifications** are requested by the convened IRB, and are directly relevant to required IRB determinations.
Continuing Review

For all protocols or proposals initially subject to full-board review, the continuing review application undergoes full-board review, unless it meets the criteria for expedited review (see below). Those that must undergo full-board review are assigned to one reviewer who reviews and presents the continuing review application at the convened meeting.

Other Reports

See Section 203.7 on Unanticipated Problems, and
See Section 203.6 on Non-Compliance

IRB Notification to Organizational Offices and Officials

The HSP notifies organizational offices and officials in writing, of the IRBs’ findings and action and provide a copy of the minutes to the Vice President for Research and Innovation.

204.6 Expedited Review

See OHRP Guidance Categories of Research That May Be Reviewed by the Institutional Review Board (IRB) through an Expedited Review Procedure for human participant research that qualifies for expedited review.

Additional requirements may apply depending on the type of research project, or the sources of support or funding for the project or institution at which the study will be conducted. See GUIDE 617: Other Federal Agencies – Additional Requirements.

Only the IRB Chair or an experienced IRB member designated by the Chair may review research under an expedited review procedure. See Section 204.3 for information on reviewer qualifications.

New Protocol or Proposal

Protocols and proposals subject to expedited review follow a single reviewer process and are assigned by the IRB Coordinator either to the IRB Chair or to a qualified IRB member.

Modification Requests

Modifications (minor) eligible for expedited review must meet all of the following criteria, based on the judgment of the IRB reviewer:

1. Any increase in risk is less than minimal risk.
2. All additional activities or procedures would have been eligible for expedited review had they been included in the initial protocol or proposal review.
3. Either the research is minimal risk or the proposed changes do not alter the study design.
If the modification changes the review type appropriate for the research, the HSP staff will move the protocol or proposal to the appropriate review type status. The IRB reviewer makes the final determination of whether changes to the research are “major” or “minor.”

### Continuing Review

Protocols and proposals subject to expedited continuing review are assigned to one reviewer and are not presented at a convened meeting.

#### For Protocols or Proposals Initially Subject to Full-Board Review

For a protocol or proposal initially subject to full-board review, the continuing review undergoes expedited review if:

- Under Expedited Category 8:
  - (i) The research is permanently closed to 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
  - No subjects have been enrolled and no additional risks have been identified; OR
  - The remaining research activities are limited to data analysis,
- Or under Expedited Category 9:
  - For continuing review of research, not conducted under an investigational new drug (IND) application or investigational device exemption (IDE) where categories two (2) through eight (8) do 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.

#### For Protocols or Proposals Initially Subject to Expedited Review

For a protocol or proposal initially subject to expedited review, the continuing review undergoes expedited review if:

- It does not include an modifications, OR
- If modifications are included, the proposed modifications would have been eligible for expedited review had they been part of the initial protocol or proposal.

### Final Reports

Final Reports prior to closure of research project are subject to expedited review and are assigned by the IRB Coordinator to one reviewer and are not presented at a convened meeting (see APP 08: Study Closure Form).
204.7 IRB Decisions

Protocols/Proposals Subject to Full-Board

The IRB systematically evaluates each protocol or proposal to ensure the protection of research participants and reach a decision. The IRB consider the approval criteria set forth in 45 C.F.R. § 46.111 and 21 C.F.R. § 56.111 in reviewing a research protocol or proposal.

The possible decisions are:

1. **Approval** means approval of the study as submitted. The study may commence once the Investigator receives the approval letter from the HSP.

2. **Approval with Stipulations** is acceptance of the study with requests for clarification or modifications as a condition for final approval. The IRB adopts this action only when minor changes are requested. The Investigator may not begin the study before the approval date on the final written approval from the HSP.

3. **Recommendations.** The IRB may make recommendations to the Investigator, often to clarify the protocol or informed consent documents. Unlike stipulations, they are NOT required changes.

4. **Deferral** of an application requires a written response from the Investigator to substantive questions raised by the IRB during its review. Those questions are directly related to the Criteria for Approval by an IRB. The response from the Investigator must be reviewed by a convened IRB. An IRB adopts this action when substantive changes are required.

   An IRB votes on the action of deferral because deferral is one of the allowable actions by an IRB besides approval, which includes approval without and with stipulations, and disapproval.

5. **Disapproval** of an application indicates that the study does not meet the Criteria for Approval by an IRB and the study, as presented, may not be performed at the UH or by a UH faculty member, staff, or student. This action does not apply to a study under expedited review.

6. **Tabled** applications are deferred to a future convened meeting for review, and are usually done because the IRB lacks the appropriate expertise to adequately review the protocol or proposal or the IRB finds it necessary to seek external consultation. Tabled applications do not require voting, as this is not an official IRB action.

Protocols/Proposals Subject to Expedited Review

The reviewer(s) of protocols or proposals subject to expedite review act on behalf of the IRB and have the authority to approve, require modifications (to secure approval) or request full–board review of the research. Expedited reviewers consider the approval criteria set forth in 45 C.F.R. § 46.111 and 21 C.F.R. § 56.111 in reviewing a research protocol or proposal.
The possible decisions are:

1. **Disapproval Not Allowed.** An expedited reviewer may not disapprove research. Research may be disapproved only after a convened IRB review. It can be returned to the Investigator if incomplete, or referred to the convened IRB if the reviewer does not approve the research.

2. **Allowable Types of Actions.** An expedited reviewer may adopt one of the following actions:
   a) **Approval** if all criteria for IRB approval are met,
   b) **Approval with stipulations** (equivalent to “approval with conditions” as termed by federal regulations) in which the Investigator must address certain questions or concerns about the application prompted by the expedited review; application is not approved until reviewer has reviewed and approved the Investigator’s response, or
   c) **Referral** to the convened IRB if the expedited reviewer finds that the protocol or proposal warrants a full-board review or disapproval.

### 204.8 Approval Date and Determination of Expiration Date

#### Approval Date

The “approval date” is the date when the Investigator may start to conduct the study.

**How Is the Approval Date Determined?**

- **If the Study Is Approved Without Stipulations,** the approval date is the date when the research is approved by expedited review or the date of the convened review.

- **If the Study Is Approved With Stipulations,** the approval date is the date when the Chair or the Chair's designee determines the stipulations have been met.

#### Expiration Date

The HSP does not fix the anniversary date of research. The IRB sets the expiration date at the time of approval.

**Definition:**

The expiration date is the last day that the study is approved, which means the Investigator may conduct the study on the expiration date. Continuing review of the study must occur by or on the expiration date.

**How Is the Expiration Date Determined?**

**The Regulation.** An IRB must conduct continuing review of a study not less than once a year.²⁴

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²⁴ 45 C.F.R. § 46.109(e).
Projects Requiring More Frequent Review. In determining which projects require review more often than annually, the IRB will consider the degree of risk of the study, the risk/benefit ratio (i.e., the higher the perceived risk, the earlier the IRB may set the expiration date of the approval), the participation of vulnerable subject populations (if any), investigator experience, and other pertinent factors including, but not limited to, whether:

- The study involves unusual levels or types of risk to the participants;
- The investigator has failed previously to comply with HRPP policies and procedures, applicable federal regulations or IRB requirements;
- The IRB has concerns about possible material changes occurring without IRB approval.

Initial Review.
- Approval Period. If the study is approved during the initial review, the approval period will be counted from the approval date.

- The expiration date. If the study is approved for one year, the expiration date is the day before the approval date in the next calendar year. If the approval period is less than a year, the expiration date is the last day within the approval period from the approval date.

Continuing Review.
- Approval Period. If the study is approved during continuing review, the approval period will be counted from the date of review, the date of expedited review if the study was under expedited review or the convened-IRB meeting if the study was under convened-IRB review.

- The Expiration Date. Counting approval period from the date of review makes a difference in the expiration date only when the study is approved with stipulations during continuing review. If a study is approved with stipulations for one year during continuing review, the expiration date is one year from the date of review, not the approval date. The next continuing review must occur by or on the expiration date.

Notification from the HSP about Expiration of Approval

About sixty (60) days before the expiration date, the HSP notifies the Investigator by email that the research’s expiration date is approaching and the research would be closed if the Investigator fails to apply for continuing review within three (3) months after the expiration date. This notification is considered a courtesy provided to Investigators. Investigators are expected to track their study approval and to promptly apply for re-approval to avoid a lapse.

Lapse of Research

In general, a lapse occurs when the IRB has not approved the research by or on the expiration date. If research lapses,

- all research activities involving human subjects must stop until the IRB reapproves the research, with the exception of already-enrolled participants described below; and
- the Investigator may not enroll new participants.

Note: The Regulations only governs research involving human subjects. Thus, when research lapses,

25 OHRP Guidance on Continuing Review.
26 Id. at H.
all research activities involving human subjects must stop, but it does not mean all research activities must stop.

The HSP will close the research file if the Investigator fails to apply for continuing review within three months after the expiration date.

If research lapses, the Investigator must stop all research activities involving human subjects until the IRB reapproves the research, except if the Investigator determines to be in the best interest of already-enrolled participants for them to continue participating in the research. The exception applies, for example, when the research interventions hold out the prospect of direct benefit to the participants or when withholding those interventions poses increased risk to the participants. The Investigator, in consultation with the participants’ treating physicians if the Investigator is not the treating physician, may determine whether continuing the research is to the best interest of the subjects. The Investigator shall submit the determination as soon as possible to the IRB to seek confirmation. The IRB Chair, a member or group of members designated by the IRB Chair, or the convened IRB may make the confirmation. If the IRB does not confirm the determination, the Investigator must stop all research activities involving human participants.

A research lapse does not warrant reporting to OHRP or other federal agencies, but, if an Investigator frequently fails to submit applications for continuing review or an IRB frequently fails to approve research before the expiration date, the HSP Director and IRB Chair, as appropriate, determine whether noncompliance exists and needs to be reported to the IO, funding agencies, and the OHRP.27

Communication of IRB Actions

Notifying the Investigator

The HSP notifies IRB actions to the Investigator in writing.

If the IRB defers the research, the IRB must provide the Investigator the questions raised by the IRB during the review that require the Investigator’s response.

If research is approved, the notification must clearly state28:
• the approval date;
• the approval period;
• the expiration date by or on which continuing review must occur, and
• stipulations of the approval, if any.

If the IRB disapproves research, the IRB must include a statement regarding the reasons for the decision and provide the Investigator an opportunity to respond in person or writing.29 Any response from the Investigator will be reviewed by a convened IRB. The Investigator is allowed to revise the protocol/proposal and resubmit for IRB review and approval as a new application.

Notifying the Institutional Official (IO)

The HSP notifies the IO of the IRB findings by emailing meeting minutes to the official.

27 45 C.F.R. § 46.103(b)(5); OHRP Guidance on Continuing Review, at H.
28 OHRP Guidance on Continuing Review, at I.
29 45 C.F.R. § 46.109(d); OHRP Guidance on Continuing Review, at I.