Modifications and Amendments
Policy and Procedure

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I. Policy

A. Investigators may not initiate any minor or major changes in research protocol, procedures or consent form(s) without prior IRB review and approval, except where necessary to eliminate apparent immediate hazards to the subject. This includes single subject exceptions.

1. Administrative changes may be accepted by OIRB/OCR staff and do not require IRB review. Examples include (but are not limited to): Translations of approved consent forms and recruitment material, verification of media advertisements based on IRB approved scripts, minor changes to contact information, removal of a study sites, changes requested by affiliated institutions, changes that correct administrative errors made during previous IRB review.

2. Single subject exceptions require review and approval by the IRB. Examples include (but are not limited to): enrollment of a single subject who does not meet all eligibility criteria for a study, but the investigator and sponsor have agreed this subject should be enrolled.

3. Minor Changes require review and approval by the IRB. Examples include (but are not limited to): clarifications of procedures, new minimal risk procedures (not involving radiation), changes to recruitment methods/materials, new/modified safety monitoring procedures to decrease risks, etc.

4. Major Changes are reviewed by the convened IRB. Examples include (but are not limited to): major changes to study design, new/increased risks, change in the use of drugs, new vulnerable populations (when research is more than minimal risk), new more than minimal risk procedures, new/revised procedures involving radiation, reducing safety monitoring procedures, etc.

B. External IRB Modifications resulting in changes to the local site application when UTHSCSA IRB is not the IRB of record must be approved by the Office of Clinical Research (OCR). Examples include (but are not limited to): study staff changes, COI, safety committee approvals, local contact information in consent document, HIPAA language or waiver requests. (See the OCR Institutional Review Policy and Procedure.)

C. Changes related to Radiation safety or Biosafety – Approval to implement the changes will not be granted by the IRB until prior RSC or IBC approval is obtained.
D. Emergency Violations - If the investigator makes protocol changes without prior IRB approval to eliminate apparent hazards to the subject(s), investigators must promptly report the changes to the IRB using Prompt Report Form as outlined in the Deviations and Violations Policy and the UPIRSO Policy.

E. Investigators should promptly notify the IRB in writing of any change in a protocol’s status, such as discontinuation or premature/successful completion of a study. See the Continuation Review Policy and Procedure and the Study Inactivation Policy and Procedure for additional procedures on reporting an activity status change to the IRB.

II. Procedure – Modifications/Amendment requests are received, administratively reviewed and routed for appropriate review. (See Receiving, Routing, and Administrative Review of Submissions Policy and Procedure)

A. Administrative Actions taken by OIRB/OCR

1. Communication requesting the changes will be received by the OIRB. The request may originate from the PI, the IRB, or other institutional research offices.

2. The OIRB/OCR staff may review and accept administrative changes to research previously approved by IRB.

3. If the change is determined not to be administrative, the modification will be routed for Expedited review or Convened IRB review.

B. Single subject exceptions

1. An Exception Request Form is received by the OIRB from the PI including necessary documentation.

2. For greater than minimal risk studies, documentation of sponsor acknowledgement and/or approval is required for all applicable trials. Documentation of an independent assessment from another individual unrelated to the study must be obtained for all investigator initiated protocols without a sponsor and investigator sponsored protocols when enrolling subjects that do not meet inclusion/exclusion criteria. Requests will not be reviewed by a member of the IRB until appropriate documentation is provided.

3. Approval for additional Exceptions of the same type should be requested from the IRB with the submission of an amendment by the PI.

4. All Exception requests must include a confirmation from the Principal Investigator that the request does not affect the rights, safety, or welfare of the subjects or the integrity of the study data.

5. The OIRB staff will review and confirm whether the exception is considered a major or a minor change and will route to either Expedited Review or Convened IRB review as described in this policy.

C. Minor and Major Changes
1. An amendment request is received by the OIRB from the PI including the revised forms reflecting the changes.

2. The OIRB will review and determine the appropriate IRB review (expedited or convened IRB) for the request.

3. Minor changes may be reviewed by the Expedited Review Procedure or by the convened IRB.

4. Major changes are reviewed by the convened IRB.

5. For expedited research that was initially approved by expedited review, the following examples of minor and major changes are provided:

<table>
<thead>
<tr>
<th>Research initially approved by expedited review (expedited study)</th>
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</thead>
<tbody>
<tr>
<td>Examples of minor change</td>
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<tr>
<td>--- Modifications that are minimal risk and fit within the expended review categories 1 – 7</td>
</tr>
<tr>
<td>--- a modification that does not change the study's eligibility for expedited review</td>
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</tbody>
</table>

Note: Changes, which, in the opinion of the expedited reviewer do not meet the criteria or intent of a minor modification, will be forwarded to the convened IRB for review.

6. For research that was initially approved by the convened IRB (i.e., not eligible for expedited initial review), the following examples of minor and major changes are provided:

<table>
<thead>
<tr>
<th>Research initially approved by the convened IRB/not eligible for expedited initial review</th>
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<tbody>
<tr>
<td>Area of study affected by modification</td>
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<tr>
<td>Elements of consent</td>
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<tr>
<td></td>
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<tr>
<td>IRB Approval 46.111 – Risks minimized</td>
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| IRB Approval 46.111 – Risks reasonable relative to benefits | -- Modifications with no effect on the risks or benefits |
| -- Modifications that improved the acceptability of the risks in relation to the harms; |
| -- Addition of a direct benefit to the subjects enrolled; |
| IRB Approval 46.111 – equitable selection of subjects | -- Addition/modification of recruitment procedures or materials; |
| -- Addition/modification of payments to subjects that will not unduly influence the subject; |
| -- Addition of children under 46.404; |
| IRB Approval 46.111 – adequate safety monitoring | -- Addition/modification of safety monitoring plan that will likely improve the safety of subjects; |
| IRB Approval 46.111 – adequate protection of privacy and maintenance of confidentiality | -- Addition/modification of privacy or confidentiality safeguards that will likely improve the protections; |
| Qualification of the research team | -- Changes in study staff requiring training for specialized procedures |
| Facilities available to support safe conduct of the study | -- Changes in study sites |

Note: Changes, which in the opinion of the expedited reviewer do not meet the criteria or intent of a minor modification, will be forwarded to the convened IRB for review.

7. If the OIRB staff determines the changes are minor, then the review follows the expedited procedures listed below.

8. If the OIRB staff determines the changes are not minor, modification request is scheduled for review at a convened IRB following procedures outlined in the Receiving, Routing, and Administrative Review of Submissions Policy and Procedure.

D. Expedited Procedures

1. The IRB may use the expedited review procedure to review minor changes in previously approved research during the period (of one year or less) for which approval is authorized. In all cases, the modifications are reviewed by the IRB Director, IRB Chair, Expedited Reviewer or another experienced IRB member designated by the Chair (designee) (collectively referred to as the Expedited Reviewer(s)).

2. The OIRB Expedited Reviewer performs most of the expedited reviews of modifications. Depending on the study, workload, availability of other reviewers and other factors, other reviewers may be included or substituted in the process. The review is conducted outside of a convened meeting. If any of the assigned expedited reviewers are not available or have a conflict of interest, the OIRB contacts a secondary reviewer to conduct the review. In general,
3. The expedited reviewer conducts the review, using standard expedited review procedures and is provided all information that would be reviewed by the convened IRB. The expedited reviewer exercises all of the authority of the IRB except that the reviewer may not disapprove the modification. The IRB is notified of the expedited approvals by providing a report of Expedited actions to the members of IRB 1, 2 and 3 as part of each convened meeting’s agenda. During the meeting, the members are reminded that they can request additional information related to the expedited approvals.

4. If the Expedited Reviewer would prefer or requires additional expertise during the review, an IRB consultant may be requested. Documentation of the consultant’s review will be recorded with the Expedited reviewer’s documentation to support the determination.

5. When the modification involves the addition of categories of subjects vulnerable to coercion or undue influence, the Expedited Reviewer considers whether consultation is necessary for review of the research involving vulnerable human subjects (IRB Approval of Research Policy and Procedure).

6. The Expedited Reviewer documents the determination regarding whether the convened IRB or expedited review procedures are appropriate on the Expedited Approval/Administrative Review Documentation.

7. The expedited reviewer documents the applicable approval determinations regarding expedited review eligibility, whether the research meets the criteria for IRB approval, and whether any research categories of the currently approved protocol are affected by the proposed modification on the Expedited Approval/Administrative Review Documentation.

E. Convened IRB Review Procedures

1. The OIRB staff may invite the PI to attend the IRB meeting if the modification is unusually complex, the staff anticipates a controverted issue will arise during the review, or at the request of the reviewing IRB member. The full IRB reviews the modification proposal following procedures outlined in the Initial Review of Research Policy and Procedure and apply the federal criteria for approval as applicable to the request (IRB Approval of Research Policy and Procedure).

   a) The HSC has designated all IRBs operated by the HSC to review non-exempt human research conducted under its Federalwide Assurance (FWA).

   b) Review of modifications to previously approved research may be performed by any of the designated IRBs.

2. The OIRB staff sends packets to IRB members scheduled to attend per Initial Review of Research Policy and Procedure, a copy of the Amendment Form and all tracked changes versions of the modified documents are included in the Primary/Secondary Reviewer packets. These documents are made available to all other IRB Members scheduled to attend the IRB meeting. Other documents may be added to the submission for all members as determined appropriate.
3. The primary reviewer is responsible for reviewing the proposed modification and rationale for the change, determining whether the modified research continues to fulfill the criteria for IRB approval, and documenting his/her determinations on the Reviewer Worksheet. The primary reviewer reports recommendations to the IRB at a convened meeting. The primary reviewer makes recommendations on issues which he/she determines are not meeting the federal criteria for approval, involving controverted issues, or where additional information is necessary. If the primary reviewer is unable to attend the meeting, the Secondary Reviewer or Regulatory Specialist provides the Primary Reviewer’s written comments or recommendations to the IRB at the convened meeting.

4. When the IRB reviews research that involves categories of subjects vulnerable to coercion or undue influence, the OIRB staff ensures that adequate representation or consultation is present for discussions of research involving vulnerable human subjects (IRB Approval of Research Policy and Procedure).

F. Review Outcome(s)

1. For administrative modifications, the outcomes of review are approved by OIRB/OCR or forwarded for IRB review.

2. For review of exceptions and modifications, the outcomes of IRB review are the same as those outlined in the Initial Review of Research Policy and Procedure.

3. If the IRB approves the exception or modification, the end date of the approval period remains the same as that assigned at initial or continuation review unless the IRB specifically shortens the current approval period (requiring continuing review earlier) as part of the motion voted on by the members.

4. If the PI submits the modification request with a continuation review, it becomes a part of the CR approval. The OIRB staff incorporates the written notification of IRB approval or disapproval of the modification request into the IRB continuation review approval/disapproval letter.

5. Appeals. If the PI has concerns regarding the IRB decision, he/she may submit his/her concerns to the IRB including a justification for changing the IRB decision. This appeal will be reviewed by the convened IRB following the procedures outlined above.

6. After review, reporting is in accordance with the Reporting Policy and Procedure.

III. References

A. Definitions (see Glossary)

B. Regulatory (see Policy on Policies Policy and Procedure)