HUMAN RESEARCH PROTECTION PROGRAM DEPARTMENTAL POLICY AND PROCEDURE

2.3 MODIFICATIONS TO RESEARCH

RESPONSIBLE OFFICE: HUMAN RESEARCH PROTECTION PROGRAM DEPARTMENT (HRPPD) **EFFECTIVE DATE: JUNE 7, 2021**

I. POLICY STATEMENT

A. This procedure outlines the responsibilities of the investigator, IRB, HRPPD for the review of modifications to research previously approved by the IRB.

II. SCOPE

A. This policy and procedures applies to all IRB members, the HRPPD and investigators responsible for modifications to previously approved research.

B. Investigators may not initiate any minor or major changes in research protocol, procedures or consent form(s) without approval from the IRB of Record (and UTSW HRPP Acceptance for reliance studies), except where necessary to eliminate apparent immediate hazards to the subject. This includes single subject exceptions.

C. Investigators should promptly notify the IRB of any change in a protocol's status, such as discontinuation or premature/successful completion of a study. See 9.2 UPIRSO and UADE, 2.2. CONTINUING REVIEW OF RESEARCH, and the 1.4. STUDY CLOSURE AND INACTIVATION for additional procedures on reporting an activity status change to the IRB.

D. Emergency Deviations - If the investigator makes protocol changes without prior IRB approval to eliminate apparent immediate hazards or to protect the life or physical well-being of subjects or others, investigators must promptly report the changes to the reviewing IRB (and UTSW HRPP for reliance studies) via a Reportable Event submission, as outlined in the Reportable Event Guidance and 9.2 UPIRSO and UADE.

III. PROCEDURES FOR POLICY IMPLEMENTATION

A. Administrative Actions taken by HRPPD staff

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

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

3. The HRPPD staff may review and accept administrative changes to research previously approved by IRB.

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

B. Single subject exceptions

1. 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 These exceptions should be submitted as reportable events; see 9.5 REPORTABLE EVENTS GUIDANCE for additional information about submission of exceptions

2. An exception request is received by the HRPPD via from the PI including necessary documentation.
3. 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.
4. Approval for additional exceptions of the same type should be requested from the IRB with the submission of a modification by the PI.
5. All exception requests must include a confirmation from the PI that the request does not affect the rights, safety, or welfare of the subjects or the integrity of the study data.
6. The HRPPD staff will review and confirm whether the exception is considered a major or a minor change and will route to either expedited IRB Review or convened IRB review as described in this policy.

C. Minor and Major Changes
1. The PI makes a preliminary assessment of whether the changes are administrative, minor, or major on the Modification smart form.
2. The modification request is received by the HRPPD staff from the PI including the revised smart forms and documents reflecting the changes
3. The HRPPD staff will review and determine the appropriate IRB review (expedited or convened IRB) for the request. The HRPPD is responsible for opening all modification submissions promptly to conduct a preliminary assessment and to determine if convened IRB review is necessary.
4. Minor changes may be reviewed by the expedited IRB review procedure or by the convened IRB. See Table 1 below.
5. Major changes are reviewed by the convened IRB. See Table 2 below.
6. If the HRPPD staff determines the changes are minor, then the review follows the expedited IRB procedures listed below.
7. If the HRPPD staff determines the changes are not minor, modification request is scheduled for review at a convened IRB following procedures outlined in the 1.1 RECEIVING, ROUTING, AND ADMINISTRATIVE REVIEW OF SUBMISSIONS POLICY AND PROCEDURE.

D. Minor Changes: Expedited IRB Procedures
1. 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 or new recruitment methods/materials, new/modified safety monitoring procedures to decrease risks, etc.
2. The IRB may use the expedited IRB 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 Institutional Review Board Director

(IRBD), IRB Chair, Designated Reviewer or another experienced IRB member designated by the Chair (designee) (collectively referred to as the Designated Reviewer(s)).

3. The HRPPD Designated Reviewers performs most of the expedited IRB 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 Designated Reviewers are not available or have a conflict of interest, the HRPPD staff contacts a secondary reviewer to conduct the review.
4. The Designated Reviewers conduct the review, using standard expedited IRB review procedures and is provided all information that would be reviewed by the convened IRB. The Designated Reviewers exercise all of the authority of the IRB except that the reviewer may not disapprove the modification. The IRB is notified of the expedited IRB approvals by providing a report of expedited IRB actions to the members of IRB 1, 2, 3, and 4 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 IRB approvals.
5. The Designated Reviewer also considers if the proposed changes to the study may impact:
    a. Currently enrolled subject's willingness to continue participation in the research. If applicable, the IRB will consider whether the information should be provided to the subject through an updated consent process (also referred to as re-consent).
    b. Subjects who have completed research involvement. If applicable, the IRB will consider whether the PI should re-contact these subjects and provide them with additional information.
6. If the Designated 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 Designated Reviewer's documentation to support the determination.
7. When the modification involves the addition of categories of subjects vulnerable to coercion or undue influence, the Designated Reviewer considers whether consultation is necessary for review of the research involving vulnerable human subjects (6.2 IRB APPROVAL OF RESEARCH POLICY AND PROCEDURE)
8. The Designated Reviewer documents the determination regarding whether the convened IRB or expedited IRB review procedures are appropriate in the electronic IRB system.
9. The Designated Reviewer documents the applicable approval determinations regarding expedited IRB 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 in the electronic IRB system.

E. Major Changes: Convened IRB Review Procedures
1. 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.
2. The HRPPD 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 2.1 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).

c. The UT Southwestern Medical Center has designated all IRBs operated by the UT Southwestern Medical Center to review non-exempt human research conducted under its Federalwide Assurance (FWA).

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

3. The HRPPD staff sends the meeting agenda, including all documents associated with the MOD to IRB members scheduled to attend per 2.1 INITIAL REVIEW OF RESEARCH POLICY AND PROCEDURE. 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.

4. 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 their 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 they determine 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 IRB Chair or Regulatory Specialist provides the Primary Reviewer's written comments or recommendations to the IRB at the convened meeting.

5. The IRB also considers if the proposed changes to the study may impact:

   a. Currently enrolled subject's willingness to continue participation in the research. If applicable, the IRB will consider whether the information should be provided to the subject through an updated consent process (also referred to as re-consent).

   b. Subjects who have completed research involvement. If applicable, the IRB will consider whether the PI should re-contact these subjects and provide them with additional information.

6. When the IRB reviews research that involves categories of subjects vulnerable to coercion or undue influence, the HRPPD staff ensures that adequate representation or consultation is present for discussions of research involving vulnerable human subjects (6.2 IRB APPROVAL OF RESEARCH POLICY AND PROCEDURE).

7. Changes related to PRMC, Radiation Safety and/or Biosafety oversight – Approval to implement the changes will not be granted by the IRB until prior PRMC, RSO, and/or IBC approval is obtained.

F. Review Outcome(s)

1. For administrative modifications, the outcomes of review are approved by HRPPD and forwarded for IRB review.

2. For review of modifications, the outcomes of IRB review are the same as those outlined in the 2.1 INITIAL REVIEW OF RESEARCH POLICY AND PROCEDURE.

3. If the IRB approves the 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. 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.
5. After review, reporting is in accordance with the Reporting Policy and Procedure.

IV. DEFINITIONS

SEE GLOSSARY OF HUMAN RESEARCH TERMS

Designated Reviewer:

- For Expedited IRB Review - refers to the Expedited Reviewer designated to conduct Expedited IRB Reviews on behalf of the IRB Chair. This individual must be formally designated by the Chair.
- For Administrative Review – refers to HRPPD staff member who may make administrative review decisions for items not requiring review by the IRB

IRB: Refers to both Expedited and Convened (full board) IRB review

V. REFERENCES

Resource
21 CFR 50 – PROTECTION OF HUMAN SUBJECTS
45 CFR 46 – PROTECTION OF HUMAN SUBJECTS
45 CFR 164 – SECURITY AND PRIVACY (HIPAA PRIVACY RULE)
21 CFR 56 – INSTITUTIONAL REVIEW BOARDS

VI. REVISION AND REVIEW HISTORY

Revision Date	Author	Description
June 2021	HRPP	Separated policy from P&P manual. Updated references to AVPHRA and IRB Director. Minor administrative edits.
November 2019	HRPP	Clarified emergency deviations
July 2018	HRPP	Revision to RSO (dissolved SHUR)
August 2017	HRPP	New Policy Development
March 2012	IRB Office	IRB Written Procedures

TABLE 1

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

Research initially approved by expedited review (expedited study)	
Examples of minor change	Example of major changes
-- Modifications that are minimal risk and fit within the expedited review categories 1 – 7 -- a modification that does not change the study's eligibility for expedited review	-- Modifications that are greater than minimal risk (e.g., addition of anesthesia ionizing radiation, or IV contrast for MRI imaging) -- Modifications that do not fit within the expedited review categories
Note: Changes, which, in the opinion of the Designated Reviewer do not meet the criteria or intent of a minor modification, will be forwarded to the convened IRB for review.	

TABLE 2

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:

Research initially approved by the convened IRB		
Area of study affected by modification	**Examples of minor change to the risk/benefit ratio**	**Example of major changes to the risk/benefit ratio**
Elements of consent	-- Changes to improve the clarity of statements or to correct typographical errors, provided that such a change does not alter the content or intent of the statement; -- Alter or waive informed consent;	-- Use of surrogate consent for incapacitated or incompetent adult subjects; -- Addition of new safety information that will directly affect the subjects willingness to participate (e.g., new unanticipated problems involving risks)
IRB Approval 46.111 – Risks minimized	-- Clarification of risks without changing the expected nature, severity or frequency of risks; -- Add a new risk to existing procedures that is considered not serious; -- Addition of research activities that would be considered exempt or expedited if considered independent from the main research protocol or that will not change, or will reduce, the likelihood or magnitude of harm while still addressing the purpose -- Modification of the study design or research activities that will not change, or will reduce, the likelihood or magnitude of harm while still addressing the purpose (e.g., increase hospital stay to improve safety monitoring); -- Modification of the study population that will not change or will reduce the likelihood or magnitude of harm while still addressing the purpose (e.g., broaden exclusion criteria or narrow inclusion criteria); -- Modification of a study procedure that will not change or will reduce the likelihood or magnitude of harm while still addressing the purpose (e.g., reduce the number procedures or reduce amount collected or administered);	The following are examples of new or modified risk information that would not be eligible for Expedited review if the change adversely impacts the overall risk/benefit relationship— ---Add a new procedure with an expected serious harm; -- Add a new risk to existing procedures that is considered serious; -- Change in severity of an expected risk from not serious to serious; -- An increase in the incidence of an expected serious risk (either from rare to likely or less likely or less likely to likely); -- Modification of the study design that will increase the likelihood or magnitude of harm; -- Modification of the study population that will increase the likelihood or magnitude of harm; -- Modification of a study procedure that will increase the likelihood or magnitude of harm;

TABLE 2 CONTINUED

Area of study affected by modification	Examples of minor change to the risk/benefit ratio	Example of major changes to the risk/benefit ratio
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;	-- Modifications that decrease the acceptability of the risks in relation to the benefits; -- Removal of a direct benefit to the subjects enrolled if the overall risk/benefit ratio is adversely impacted due to the change
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;	-- Addition of children under 46.405 - 408; -- Addition of a pregnancy women/fetus population; -- Addition of a prisoner population;
IRB Approval 46.111 – adequate safety monitoring	-- Addition/modification of safety monitoring plan that will likely improve the safety of subjects;	-- Modifications to the safety monitoring plan that will reduce the current protections;
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;	-- Modifications to the privacy or confidentiality safeguards that will reduce the current protections;
Qualification of the research team	-- Changes in study staff requiring training for specialized procedures	-- Suspension/lapse of investigator privileges that directly reflect research procedures; -- New disclosures of significant related conflict of interest
Facilities available to support safe conduct of the study	-- Changes in study sites	-- Withdraw of institution/staff support for research that directly affects safe conduct of research;
Note: Changes, which in the opinion of the Designated Reviewer do not meet the criteria or intent of a minor modification, will be forwarded to the convened IRB for review.		