AAH RSPP GUIDANCE
Changes to Already Approved Research

PURPOSE
The purpose of this document is to describe the types and processing of changes to already approved non-exempt research (‘Changes’) overseen by the Advocate/Aurora IRB. It is a supplement to RSPP SOPs 3 & 4, 9 & 10.

Information about Changes to exempt research can found in RSPP Guidance: Exemptions.

Changes in research that is ceded to an external IRB are processed by the IRB of Record. Certain types of Changes in ceded research must be brought to the attention of the AAH RSPP prior to implantation. At a minimum these include changes in research sites/location and changes in key personnel. See RSPP Guidance: Deferral/Ceding of IRB Oversight to an External IRB for more information.

Definitions of Italicized words can be found in the AAH RSPP Glossary.

GUIDANCE
What constitutes a Change?
Changes in approved research includes modifications, additions or deletions to study documents or study plans/processes that were reviewed and approved by the IRB or require IRB review and approval. See RSPP SOP 9 for examples of what constitutes a Change in approved research.

Changes to already approved research fall into two categories: minor and major.

Changes that are minor are minimal risk in nature, and may be approved under an expedited review process. See RSPP Guidance: Expedited Review for information on what constitutes a minor change.

Major changes are those that are not minor in nature. These changes are those that are greater than minimal risk, affect the regulatory criteria for approval or affect the rights and welfare of subjects. Major changes must be reviewed by the convened IRB.

• Examples of a major Change include: revision to the drugs used in the research study or the addition of a research arm to the study.

When are Changes to be submitted to the IRB?
Changes in approved research may not be initiated/implemented without prior IRB review and approval, except where necessary to eliminate apparent immediate hazard to subjects (see below). NOTE that Changes to eliminate apparent immediate hazard to subjects are expected to be rare.
Principal investigators must not unreasonably delay IRB submission of Changes that are proposed by sponsors or lead principal investigators of multi-center studies, or otherwise deemed important to the safe and effective conduct of the research.

- Any proposed Change that may have an impact upon subject safety or the risk-benefit analysis of the study should be submitted within thirty (30) days after notification of the proposed Change from the sponsor or lead PI of a multi-center study or after a local PI determines that a Change is necessary. All other Changes should be submitted within ninety (90) days after notification/determination that a Change is necessary.

**How are Changes submitted to the IRB?**
Changes in nonexempt research are submitted to the RSPP using the *Changes to Previously Approved Human Subject Research* form.

**How are Changes reviewed?**
Change forms are reviewed by a Research Compliance Analyst in the RSPP office, a qualified IRB member, to check for completeness and to determine the manner of IRB review – that is, expedited review (minor change) or convened board meeting (major change).

If the review of the proposed Change qualifies as an expedited IRB action, the change will be reviewed by an expedited reviewer (See RSPP Guidance: Expedited Review).

If the review of the proposed Change does not qualify as an expedited IRB action, the Change will be scheduled for review by the convened IRB at the next available IRB meeting (See RSPP Guidance: Convened IRB Meeting).

**How are outcomes of review communicated to PI?**
Only after the IRB approves the change may it be implemented – unless the Change was to eliminate an apparent immediate hazard.

The RSPP Office will notify the PI and study contact in writing of expedited or convened IRB review outcome.

The PI must ensure Changes approved by the IRB are implemented within the parameters communicated to/by the RSPP Office.

Changes are considered effective on the date of IRB approval and should be implemented as soon as possible but no later than 30 days after receipt of communication from the RSPP Office.

**What if the Change cannot be implemented within 30 days of IRB approval?**
If the Change cannot be implemented within 30 days of receipt of IRB approval, it must be reported to the RSPP office prior to the end of the 30 day period.

The PI must report the delay in implementation via email to the RSPP Office. The email report must include:

- the reason(s) for the delay,
• a summary of why the delay will not negatively impact currently enrolled or yet to be enrolled subjects, OR if there is a negative impact, what is being done to mitigate that impact, AND
• a proposed implementation date.

The IRB Chair or designee will review the report and determine whether additional action (e.g., placing a hold on study recruitment) or convened IRB review of the delay is needed.

The Principal Investigator will be notified of the outcome of the review.

**How are Changes to eliminate apparent immediate hazards to human subjects reviewed?**

Changes to eliminate apparent immediate hazards to human subjects are reviewed as Unanticipated Problems (see RSPP SOPs #7 and 8).

The PI must inform the IRB of the implementation of the Change within the timeframe noted in SOP #7 (UP Submission Requirements).

Review of the unanticipated problem will occur per RSPP SOP #8 (Review of UPs).

**What if the IRB determines that change did not address apparent immediate hazard to subjects?**

If a change of protocol is implemented prior to IRB approval, and the IRB determines that the change was not necessary to eliminate apparent immediate hazards to a subject, such an occurrence is considered to represent noncompliance with the regulations governing human subjects research.

Additional action by the IRB as indicated in RSPP SOP #6 (Review of Noncompliance) will be considered.

**What is an administrative hold on research?**

An administrative hold is a voluntary action by the Principal Investigator to temporarily or permanently stop some or all research activities as a Change to Approved Research (RSPP SOP #4: Review of Post-Approval Submissions).

A Principal Investigator may voluntarily suspend research activities of an approved protocol. Examples of when such a hold would be appropriate include: investigation into an allegation of noncompliance or unanticipated problem; unexpected or planned leave on the part of the Principal Investigator or other key personnel.

Although the Principal Investigator may discuss this action beforehand with an IRB chair, RSPP Director or the Institutional Official, the hold must be initiated voluntarily by the Principal Investigator and must not be used to avoid IRB mandated suspension or termination or reporting requirements.

During administrative hold, the research remains subject to continuing review and requirements for reporting non-compliance and unanticipated problems involving risks to subjects or others.
Administrative holds must not be used to avoid reporting deficiencies or circumstances that otherwise require reporting by federal agencies. An administrative hold of the research does not need to be reported to OHRP, FDA or other federal agency.

Administrative holds on research should not be confused with IRB suspensions or terminations of research (RSPP SOP #4; RSPP Guidance: Suspensions and Terminations).

**REQUIREMENTS**

- Common Rule Regulations: 45 CFR 46.103(b)(4)
- FDA Regulations: 21 CFR 56.108(a)
- OHRP Guidance on Written IRB Procedures (July 1, 2011)
- AAH RSPP SOPs: 4, 5, 7, 8, 9 &10
- RSPP Guidance: Suspensions and Terminations, Expedited Review, Deferral/Ceding of IRB Oversight to an External IRB, Exemptions