Continuing Review of Approved Research

FDA-regulated research and studies which are greater than minimal risk where activities are not limited to long-term follow-up and data analysis must be reviewed at least annually. The purpose of continuing review is to review the entire proposal and informed consent form(s) using the same criteria as those used for initial review, not merely the modifications to the protocol and/or informed consent form(s). The Institutional Review Board (IRB) will determine that the frequency and extent of continuing review for each study is adequate to ensure the continued protection of the rights and welfare of the human subjects. If any new findings arise during the continuing review process that might affect subjects' willingness to take part or continue in the study, the new findings must be provided to all enrolled participants. Based on its review, the IRB may require that the research be restricted, modified, or halted altogether. Alternatively, special precautions or IRB-imposed restrictions may be relaxed. The investigators will be informed of the study's continuing review deadline in the initial approval letter from the IRB Chair.

Continuing review of approved research not meeting exempt or expedited criteria must occur at an interval appropriate to the degree of risk as determined by the IRB, but not less than once per year. The IRB may decide that some protocols will require review more often than annually. Some studies may require review every six months or every three months. This determination may be based on:

- Multi-center clinical trials that have a high incidence of adverse events
- Studies with a proposed high risk / benefit ratio and the nature of the risks of the study, and studies with uncertainty regarding the possible risks
- The vulnerability of the subject population
- The experience of the investigators conducting the study
- Any previous noncompliance from investigators or previous problems conducting research studies found in IRB audits
- The projected rate of enrollment of subjects
- If the study involves novel therapies

Studies Subject to Continuing Review

The Final Rule at 45CFR46 revised the requirements for Continuing Review, eliminating it for some studies. Based on the regulatory changes, the following types of studies still require continuing review:

- FDA regulated research;
- Greater than minimal risk research (including research reviewed under Expedited category 8(b));
- Studies categorized under expedited categories 8b (where no subjects have been enrolled and no additional risks have been identified) or 9 (continuing review of research, not conducted under an investigational new drug application or investigational device exemption, where categories 2-

8 do not apply) require expedited continuing review. The IRB has elected to follow guidance issued by the Office of Human Research Protections, and under this guidance continuing review via expedited review is required for these two categories.

- Research reviewed under the pre-2018 Common Rule; or
- Research for which the IRB has determined that Continuing Review is required

The following types of studies do NOT require continuing review:

- Exempt studies and exempt studies approved with limited IRB review
- Expedited studies approved after January 21, 2019, under categories 1-8(a and c only), unless the reviewer(s) explicitly justify why continuing review is necessary to protect human subjects. These categories include:
    - Studies initially approved via full board review whose activities are now limited to data analysis, including analysis of identifiable private information or identifiable biospecimens
    - Studies initially approved via full board review whose activities are now limited to accessing follow-up clinical data from procedures subjects would undergo as part of clinical care

If the IRB requires continuing review of any study when it is not otherwise required, the rationale for the review will be documented. The research office will contact investigators of studies not undergoing continuing review for information on the studies' status to maintain oversight.

Administrative Review of Studies not Otherwise Subject to Continuing Review

For studies not subject to continuing review, an annual administrative review will still be conducted to assess the study's status, including data collection and progress of analysis, ascertaining if any changes have been implemented to the study protocol, and if there have been any adverse events or unanticipated problems. The research staff in the Woman's Health Research Center will contact the principal investigator for completion of the Expedited/Exempt Study Follow-Up Information form and, once completed, will forward the form to R&D and file with the IRB study information. Studies will be asked for annual follow-up information until such time as indicated on the form that all analysis and subject participation is completed.

If any revisions have been implemented to the study without prior IRB approval, if there have been serious adverse events or unanticipated problems, or if there is any new information that may cause the study to no longer qualify for exempt or expedited review categories that do not require continuing review, the investigator will be contacted to submit the study to the IRB for continuing review.

Continuing review by the full board

Periodic review of research activity by the IRB is necessary to determine if the risk/benefit ratio has changed, if there are unanticipated findings involving risks to subjects, and if any new information regarding the risks and benefits should be provided to subjects. All research involving human subjects that has been approved via full board review must be periodically reviewed.

Before a convened meeting, for each continuing review (excluding those projects that either meet one or more of the exemption categories as authorized by 45CFR46.101(b) or one or more of the expedited categories as authorized in 45CFR46.110), the HPA shall assign primary and secondary reviewers. The reviewers will document their findings using an IRB Reviewer form, present their recommendations to the full board, and lead the discussion at the convened meeting. Packets containing review materials and reviewer forms will be distributed to all IRB members via mail at least one week prior to the IRB meeting. All members will also receive a list of continuing review approval criteria distributed at the meeting.

The approval criteria are:

- The risks to the subjects continue to be minimized and reasonable in relation to anticipated benefits
- The selection of subjects continues to be reasonable in relation to the anticipated benefits
- Informed consent continues to be appropriately documented, and
- There are:
    - Provisions for safety monitoring of the data
    - Protections to ensure the privacy of subjects and confidentiality of data
    - Appropriate safeguards for vulnerable populations

If substantive changes are required that will require full board review prior to implementation, these revisions should be submitted for review at the next convened IRB meeting. If the study expires before the revisions or conditions are approved, all research activities must stop, all interventions and interactions with current participants must stop (unless the IRB determines they must continue for participant safety or their best interests), and no new participants may be enrolled until the study has been reviewed by the IRB for re-activation and approval of the requested revisions.

If there are any new significant findings, either as reported on the Continuing Review / Revision form or discussed at the convened meeting through the review process, that may affect participants' willingness to continue taking part in the study, these findings will be provided to participants.

Any research studies not listed in the categories below that are still enrolling subjects, or which continue to intervene or interact with subjects (e.g., telephone follow-up, chart review, interview, etc.) must undergo continuing review.

Submission of a Study for Continuing Review

It is the investigator's responsibility to ensure that the research is reviewed on or before expiration date of IRB approval, even if the research activity did not begin until some time after the IRB gave its initial approval. Investigators will be notified via letter after the study is initially approved that their study is approved as written or will require revisions.

It is the investigators' responsibility to submit the materials listed below to the research office for submission to the IRB for continuing review before the deadline. As a courtesy, however, the Human Protections Administrator (HPA) will send a reminder to the principal investigator approximately three months prior to the expiration date. It is recommended that continuing reviews be submitted to the IRB two months in advance in order to avoid delays in enrollment and data collection in the case of unforeseen circumstances. Continuing review of a research study may require full board review or it may be expedited if it meets certain criteria. There is no grace period extending the conduct of the research beyond the expiration date of IRB approval. Extensions beyond the expiration date will not be granted.

Submission Materials for Continuing Review

The following materials should be submitted to Woman's Hospital Research Center for continuing review:

- Continuing Review Application
- The most current version of the study protocol. If revisions are requested with this submission, submit the document with the changes tracked.
- Copies of any surveys, questionnaires, advertisements, demographic forms, and case report forms
- Two copies of the Investigational Brochure (for studies involving investigational drugs or devices), if revised since last review
- An updated, signed Financial Interests Disclosure form for each investigator, if the
- study is funded
- Updated certificates of completion of CITI training for each investigator, if not previously submitted. All investigators and research coordinators must be current on CITI training requirements in order to submit a study for continuing review.
- Current informed consent form or subject information sheet, if applicable, including the cover sheet
- A summary of any adverse events, serious adverse events, unanticipated problems, and minor/major protocol deviations that occurred since the previous IRB review
- Patient scripts for recruiting/enrollment, if applicable
- Authorization form (HIPAA form), if applicable
- Any statistical reports or sponsor reports, if applicable
- Any publications or abstracts in progress

Continuing reviews of studies temporarily or permanently closed to enrollment

Studies requiring continuing review that are temporarily or permanently closed to participant enrollment are subject to continuing review until they are terminated. Studies that are temporarily or permanently closed to participant enrollment and will undergo *expedited* continuing review do not require inclusion of the informed consent form or authorization form with the submission materials.

Expiration of a study from IRB approval

If the IRB does not approve continuation of the research by the expiration date, enrollment of new subjects, data collection, and data analysis must be suspended pending re-approval of the research by the IRB unless the IRB finds that it is in the best interests of enrolled subjects to continue in the study for safety concerns. In addition, all currently enrolled subjects must be notified that the study has been closed.

If the investigator is actively pursuing renewal with the IRB and the IRB, or the IRB Chair on behalf of the full board, finds through review of the protocol or assessment of the enrolled participants that it may be in the best interests of currently enrolled subjects' safety to continue with study treatment and procedures, the IRB may allow continuation of treatment for currently enrolled subjects during the time required to complete the review process. It may be in the best interest of individual participants to continue in the research during the period of approval lapse.

The IRB (or IRB Chair on behalf of the board) will review the study procedures and current status of enrolled participants to make this determination and may allow participants to continue their participation while the study is under review. If continuation of study treatment and procedures for safety or other reasons is permitted by the IRB, the subjects must be informed and any adverse events should be reported to the IRB and, when applicable, to the sponsor.

If the investigator wishes to reinstate the study after the approval period lapses due to expiration, the protocol and all associated materials (case report forms, informed consent forms, etc.) must be submitted to the IRB as a reactivation. All research activity for the expired study must cease, including patient enrollment and recruiting, data analysis, and data collection, until the study has been approved for reactivation, unless the IRB determines that certain activities must continue for subject safety.

Questions Regarding Continuing Review

A calendar of IRB meeting dates and submission deadlines dates is available by calling the Woman's Hospital Research Center at 225-231-5275 or by emailing research@womans.org.

For questions regarding study expiration dates, please consult the Notification of IRB Decisions and Determinations policy, or call Woman's Hospital Research Center at 225-231-5275.