

5.6. CHS Study and File Closure

Upon completion of a research project, meaning that all research activities are complete and data have been analyzed, the investigator must notify the CHS office that the study has ended and should be closed. A study may be closed using the File Closure Form (Appendix 34) and submitting all appropriate information and documentation listed on the form, including the Investigator's signature.

File closure may also be appropriate if the jurisdiction of IRB review has been transferred to another institution. Transfer of jurisdiction occurs when an Investigator leaves the Faculty of Medicine for another institution and will be conducting his or her research at that institution, or when his or her grant is administered through or transferred to another institution and no research activities are (or are no longer) taking place at HMS or HSDM facilities and Faculty of Medicine students are not the prime participants in the research study.

6. Amendments to Research Activity

6.1. Amendment Requests

If, after the initial approval of a research project, the Investigator wishes to amend or modify the study in any way (such as: changes to the study population, research personnel roster, recruitment, consent, inclusion/exclusion criteria, medications, devices or study procedures) the requested change(s) must be submitted on an Amendment Request form (Appendix 35) or a revised Personnel Roster form (Appendix 21), and preferably accompanied by a cover letter outlining the changes and the reasons for the them.

The most frequent example of non-compliance reviewed by the CHS is the implementation of study changes without prior CHS approval. *Any changes*, no matter how minor (minor changes include: a change that does not alter the risk:benefit analysis of the study, affect the safety of participants, include the addition of study procedures, interactions or interventions, alter in any way the scientific integrity of the study, or include a procedure or vulnerable population for which expedited review is not permissible), must be submitted to and approved by the CHS, documented by a ROA (Appendices 36 and 37), *prior to implementation* of the change(s).

The federal regulations specifically require the CHS to review proposed changes in research activity and to ensure that such changes are not initiated without CHS review and approval, except when necessary to eliminate apparent immediate hazards to the participant [45 CFR § 46.103(b)(4)(iii) and 21 CFR § 56.108(a)(4) (see Sections 10.3.3. and 12.6.1). As noted in Section 5.3, in some circumstances, the CHS may request verification from others (such as a Department Chair, the study or site Coordinator, or the CHS QA Coordinator) that requested changes by the CHS have occurred, or that *no* material changes have occurred without appropriate and prior CHS review and approval.

6.2. Required Materials for Amendment Requests

Significant changes to the study, such as changes to the study population and study procedures, must be incorporated into the CHS Initial Application (and protocol, when appropriate), as all current study activities must be documented in one place. In addition, if changes are sought to the consent form, or if the change to the study will affect the risk:benefit analysis for participants or should otherwise be communicated to potential participants, then two consent documents (one with highlighted changes and one unmarked copy incorporating the proposed change) must be submitted to the CHS for review and approval. Incomplete submissions (lacking requisite forms, signatures, or documentation) will not be placed on the CHS monthly agenda or sent for expedited review.

6.3. CHS Procedures for Processing Amendment Requests

After an amendment request (including all relevant materials) has been received, CHS staff will date-stamp the materials, enter the appropriate information into the HIRBERT database, add the newly submitted materials to the existing study folder, and provide the appropriate CHS staff member with the folder for pre-review. As with study continuations, the CHS staff member who has been working with the Investigator and the study will be responsible for seeing the amendment(s) through the approval process.

The CHS staff will communicate with the Investigator (or personnel designated by the Investigator) any requests for changes or additional documentation needed for a thorough review by the CHS (see Section 6.5), or CHS member (see Section 6.6).

6.4. Document Distribution to CHS Members

The following documents are submitted for distribution to all CHS members to review at a full meeting (or to a CHS member for expedited review) for amendments to previously approved research:

- Amendment Request form and cover letter
- Supporting documentation (such as the revised CHS application, current findings, DSMB/adverse/unanticipated event reports, present and revised or new materials for review/approval, and other documentation as applicable and/or requested by CHS staff or members)
- Citations of current findings that might affect the risk:benefit balance of the study
- Continuing Review materials from current review period

6.5. Amendment Review by the Convened CHS

In accordance with 45 CFR § 46.108 (b), review of proposed (more than minor) study changes must be conducted at a full CHS meeting. The Investigator will be reminded that if the amendment is the result of new findings that may affect participants' willingness to continue, then those new findings must be communicated to participants.

For amendments reviewed at full CHS meetings, the same criteria and procedures for initial review apply see: Research involving more than minimal risk, Proposals not involving more than minimal risk, but that require full committee review, Document distribution, Committee review

procedures, Committee determinations, Committee actions and notifications, Voting validity, Participation by phone, Research requiring review more often than annually, and Research monitoring (see Section 4.10).

6.6. Amendment Review Meeting Expedited Categories

Expedited review of amendments to research that was previously approved at a full CHS meeting is permissible, providing the research meets the appropriate categories at 45 CFR § 46.110 f 8 (a-c) or 9.

For applicable procedures and criteria for amendments via expedited review, see: Research meeting expedited review categories, Reviewer determination, When there are contingencies for approval, Notification to Investigators (SPA and to the CHS), Categories of Research that may be reviewed through an expedited review procedure, Research Categories, and Expedited review criteria for CHS members (see Section 4.9).

6.7. Modifications to Research Resulting from Emergency Procedure/Process

If an Investigator has changed a study procedure or process to eliminate an immediate hazard to participants, the Investigator must notify the CHS office as soon as possible by phone or email within 48 hours. Emergency modifications will be reviewed as unanticipated problems involving risks to participants or others and will be treated according to that policy (see Section 13). According to the policy, the Investigator should follow the immediate notification to the CHS with a formal letter describing the problem. The letter should include the following:

- A description of the reason for initiating the change without prior CHS approval;
- The provisions made to maintain the safety and privacy of participants;
- An indication of whether the hazard was (and is anticipated to be) a one time occurrence;
- A statement as to whether modifications need to be made to the study itself as well as relevant study materials (such as the consent form). If study modifications are indicated, the amendment will be reviewed according to the policies and procedures outlined above (see Section 6).

The letter is sent to the CHS Chair for immediate review and followed by a review at the next convened CHS meeting unless an emergency meeting is called to review the changes (see Section 3.7). Depending on the facts and circumstances, the Investigator may be required to halt the research (or a portion of the research) until necessary changes have been reviewed and approved, and if appropriate, notification of the study sponsor.

6.8. Amendment Review of Studies Meeting Exemption Criteria

Investigators should submit modifications to studies that have met the criteria for exempt research (see Section 4.8.3) when there is a possibility that the modification could result in a change to the risk:benefit analysis and have an impact on study participants. If the modification does not alter the risk:benefit analysis and exemption criteria, an acknowledgement letter (Appendix 38) will be sent to the Investigator. If the modification does alter the risk:benefit

analysis and the study requires expedited or full CHS review, the appropriate CHS staff will notify the Investigator via email and the Investigator will be asked to complete or modify the CHS application and submit appropriate study materials for review and approval according to the policies and procedures outlined previously in this section.

7. Ceding Review

Under 45 CFR § 46.114, institutions engaged in research projects involving more than one institution may enter into joint reviewing arrangements or rely on the review of one of the institutions' IRBs. Three vehicles are available to cede review to another IRB – Cooperative Agreements, Reliance Agreements, and IRB Authorization Agreements, as defined below.

7.1. Definitions

7.1.1. Cooperative Agreements and Reliance Agreements

Cooperative Agreements (CAs) and Reliance Agreements (RAs) are written between the institutions and agreed upon by the IRB Chairs and Institutional Officials, with advice from legal counsel. CAs and RAs apply to all human research studies where both institutions are involved either financially as the awardees for grants/contracts or as the study site of the research activity. Each site must hold an active FWA. The CHS currently has one CA in place –with The Forsyth Dental Center. It has a Reliance Agreement in place with Harvard University, Harvard School of Public Health, Brigham and Women's Hospital, The General Hospital Corporation d/b/a Massachusetts General Hospital, Children's Hospital Boston, Beth Israel Deaconess Medical Center, Joslin Diabetes Center, and Dana Farber Cancer Institute.

Each IRB may decide the appropriateness of ceding or accepting responsibility for the review of human studies, regardless of the presence of a CA or RA. The CHS will not cede review to another institution if students from the Faculty of Medicine are to be recruited specifically for a study, and thus reserves the right to review and approve all such studies.

Investigators never should assume that a study is automatically approved by one or the other institution even if a CA or RA is in place. For this reason, the CHS requires Investigators to complete a Designation Request Form (Appendix 39). The Designation Request form outlines the materials required (see Required Documentation, below) for the CHS to make a determination of the appropriateness of ceding or accepting review. Once this determination is made by the CHS Administrator and conferred by the ORSP Director, the Administrator contacts the appropriate IRB administrative personnel at the other institution to confirm acceptance of review for a given study. The Investigator will receive formal notification of ceded review from the CHS office (see Notifications, below), which is copied to the other IRB as well as the Faculty of Medicine's SPA representative, as appropriate.

7.1.2. IRB Authorization Agreements (IAA)