

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)**

IAAs are formed between institutions where there is no CA or RA, but where one institution will accept responsibility for the review of a specified study or studies. In contrast to CAs and RAs, which cover all human studies taking place at an institution for which that institution is all or partially responsible, IAAs are written between institutions generally for one specific study, though the institutions can agree that they will cover more than one study. IAAs usually are initiated by the IRB administrators of each institution, but must be approved and signed by the IOs. As is the case when there is a CA or RA, Designation Request Forms must be completed by the Investigator and submitted to the CHS, along with the Required Documentation (see Section 7.3). Once all documentation is in place and reviewed, the Investigator will receive formal notification of ceded review from the CHS office (see Section 7.4.1), and copied to the other IRB and the Faculty of Medicine's SPA representative, as appropriate.

Protection of participants in research projects under Cooperative, Reliance, and IRB Authorization Agreements remains the responsibility of all institutions involved in the research. Thus, designating a primary or reviewing IRB does not absolve another institution involved in the research of such responsibility.

## **7.2. Conditions for Ceded Review**

To avoid duplication of review, the CHS will consider accepting review responsibilities, or ceding review to another IRB, when the following conditions are met.

### **7.2.1. Accepting Review Responsibilities for another Institution**

The CHS will accept reviewing responsibilities on a case-by-case basis, including but not limited to the following situations:

- i. When the primary work involving participants takes place on Faculty of Medicine property under the jurisdiction of an Investigator from the Faculty of Medicine and the secondary institution's involvement is primarily financial or limited to minimal risk activities, or
- ii. When the study involves a secondary institution or institution's personnel but is initiated by an Investigator from the Faculty of Medicine. Such studies may include clinical rotation curriculum of students, program evaluations, surveys and questionnaires.

The acceptance of reviewing responsibilities will apply to all levels of risk and review categories and review level by the CHS. In all situations where a study is sponsored by a federal award, a CA, RA, or IAA must be in place with an institution holding a current FWA. When the CHS is accepting review for another institution, the CHS' review procedures and requirements are the same as those outlined in this policy document.

### **7.2.2. Ceding Review to other Institutions**

The CHS may cede reviewing authority to another IRB under one or more of the following conditions:

- i. The Faculty of Medicine acts solely as the funding recipient of an award and no research activities will be taking place at HMS or HSDM facilities;

- ii. The Faculty of Medicine is the recipient of a prime funding award and provides a subcontract for human studies work to be performed at another institution that either has or will have IRB approval for the human studies work;
- iii. The involvement of the Faculty of Medicine Investigator is limited to data analysis collected through the other institution or other minimal risk, engaged activities.
- iv. The other institution's reviewing IRB is more properly constituted to review a certain scope or topic of work, or may have knowledge of the local research context.

The CHS will ordinarily not cede review if any research activities conducted at HMS or HSDM require direct intervention or interactions with study participants.

Ceding of review to another institution's IRB will apply to all levels of risk and review categories. In all situations where a study is sponsored by a federal award, a CA, RA, or IAA must be in place with an institution holding a current FWA, and a designation confirmation letter (Appendix 40) must be issued before funds can be released and research activities can commence.

### **7.2.3. Harvard Clinical and Translational Science Center (CTSC)**

In 2008, the Harvard Faculty of Medicine received an award from the National Institutes of Health to establish a Clinical and Translational Science Center ("CTSC"). This award is intended to foster cooperative and collaborative research and the sharing of resources between the Faculty of Medicine and its affiliated institutions (e.g. Harvard University, Harvard School of Public Health, Brigham and Women's Hospital, Massachusetts General Hospital, Children's Hospital, Boston, Beth Israel Deaconess Medical Center, Joslin Diabetes Center, Dana Farber Cancer Institute). Research conducted at one or more of the CTSC sites and/or with CTSC funds will be reviewed by the appropriate institution's IRB, with ceded review as appropriate. Each institution's IRB may decide the appropriateness of ceding or accepting responsibility for the review of research involving human subjects, regardless of whether the project is related to the CTSC. Procedures for requesting ceded review are located in Section 7.3 and 7.4 of this policy document.

### **7.3. Required Documentation for Ceded Review**

The following documents must be submitted to the CHS for consideration of ceding review to another IRB:

- Designation Request form
- IRB approval letter from the reviewing IRB

### **7.4. Procedures for Ceded Review**

#### **7.4.1. Initial Approval**

The documentation listed in Section 7.3 must be submitted to the CHS for consideration of ceded review. As with all materials submitted to the CHS office, the information is logged into the HIRBERT database and a file is generated by CHS staff and submitted to the CHS

Administrator. Once the appropriateness of ceded review is determined by the Administrators of the affected IRBs, an IAA (if applicable) will be generated and signed by the appropriate IOs. Once all of the required documentation is in place, a letter will be generated by the CHS office, and, once approved by the ORSP Director, sent to the Investigator, with a copy to the reviewing IRB, and the Faculty of Medicine's SPA representative (as appropriate).

The designation confirmation letter (Appendix 40) specifies the Investigator, study title and number, funding source, reviewing institution, and the reviewing institution's study number, approval and expiration dates. Copies of designation letters are sent to the representative of the IRB accepting review responsibilities for the CHS.

If it is not appropriate to cede the study, the CHS Administrator will notify the Investigator of the reason for this decision and of the Investigator's need to complete the CHS Application for initial review of the research (see Section 4).

#### **7.4.2. Continuing Approval**

Studies that have been ceded to another institution's IRB must still receive continuing approval from the CHS each year, or as often as the reviewing institution's IRB deems it appropriate. The required documentation (as outlined above) must be submitted to the CHS office for continuing approval of ceded review each year.

If the CHS Administrator determines that it may no longer be appropriate to cede review of the study (if for instance, amendments have changed the study activities, engagement of Faculty of Medicine personnel, or location of activities), the Administrator will contact the Investigator with any questions or concerns. If these questions/concerns are not satisfactorily resolved, the Investigator will be informed of the reasons why the study is no longer appropriate to cede review and of the Investigators need to complete a Continuing Review application for CHS review (see Section 5).

#### **7.4.3. Amendments, Non-Compliance, and Unanticipated Problem Reporting**

If **amendments** to the protocol alter the engagement of the Faculty of Medicine or its investigators (e.g. relocation of activities to Faculty of Medicine property, changes in the Investigator's role, etc.), the Investigator should contact the CHS; these amendments may either trigger CHS review, or indicate that it is appropriate to close the study with the CHS office.

Incidents resulting in a determination of serious or continuing **non-compliance**, or **unanticipated problems** involving risks to participants or others, are reported to the CHS by the reviewing institution, as outlined in the IAA and RA. However, Investigators may also report these determinations to the CHS.

If the CHS Administrator has questions or concerns in the review of the paperwork and the Investigator's response to the questions are not satisfactory, the Administrator (in consultation with the IO and ORSP Director, and possibly the representative from the reviewing IRB) will determine the appropriateness of continuing ceded review. Depending on the seriousness of the

events and/or activities, the CHS may contact the reviewing IRB to coordinate actions to be taken, or review minutes of meetings when the events were discussed. If ceding review is no longer appropriate, the Administrator will notify the Investigator (with a copy to the reviewing IRB) of the reasons for this determination and the need to complete a Continuing Renewal application, inclusive of the amendment request (see Sections 5 and 6, respectively).

The Leadership Team may be asked to evaluate the effectiveness of ceding review to a particular institution. Additionally the management of procedures for ceding review will be evaluated regularly to assess best practices for the HRPP to insure protection of participants while decreasing unnecessary redundancies in oversight.

#### **7.4.4. File Closure**

Studies that have been ceded to another institution's IRB may be closed with the CHS office (even if there is continuing IRB approval at the reviewing institution), assuming one or more of the following conditions:

- i. When there is no more funding for the research activities awarded through the Faculty of Medicine;
- ii. When the funding is transferred to another institution and there is continuing review at that institution; or
- iii. When the study is closed by the Institution providing review responsibilities and research activities are no longer taking place. Note: if the study is closed at the reviewing institution, but there is data analysis being performed by a Faculty of Medicine Investigator, then the CHS will review the study.

To request file closure, the Investigator must complete the CHS File Closure form (Appendix 34) and submit it with the closure confirmation of the reviewing IRB and other documentation noted on the form, as appropriate. CHS file closure is confirmed with a letter to the Investigator (Appendix 41) that is copied to the reviewing IRB and the Faculty of Medicine's SPA representative, as appropriate.

## **8. Multi-Site Studies**

Faculty of Medicine Investigators often participate in collaborative research projects that involve multiple research sites.

### **8.1. Where the Faculty of Medicine is the recipient of the primary funding award (regardless of the source), and the research is conducted at HMS or HSDM (with additional sites coordinated by the HMS/HSDM Investigator)**

- i. The CHS is responsible for the initial and continuing reviews of the main study, the grant, all research materials and activities, and participant safety.
- ii. The CHS is responsible for receiving copies of IRB approvals, approved consent documents and research materials (including language translations) from all sites and, for