

and responsibilities are well defined and understood by the CHS (Chair, members and staff) and the HMS/HSDM community.

- The Leadership Team will review appropriate reports of the QA Coordinator (described in the preceding section) and evaluate the necessity of policy changes or CHS actions as a result of the reports.
- The Leadership Team will present planned improvements to the institution's HRPP to the University wide Committees to evaluate where changes would be best implemented across the University.
- The Leadership Team will assist in the further development of the CHS's outreach activities to the community and evaluate its effectiveness.

2.8.1.3. Institutional Official

The HMS Dean for Faculty and Research Integrity, who serves as the IO of the CHS is responsible for the implementation and maintenance of the HRPP and the CHS.

2.8.1.4. University Level

Provost Office: Harvard's three IRBs operate independently, but all participate in a University-wide Human Subjects Research Committee, established and supported by the Office of the Provost.

2.8.1.5. Federal Level

OHRP is the federal agency overseeing the compliance of the IRB's in relation to the federal regulations and also provides assistance to the IRBs in the interpretation and enforcement of the federal regulations. OHRP occasionally performs site visits of IRBs.

2.8.2. Researcher Grievances, Comments, or Suggestions

Filing grievances, concerns and suggestions may be sent to the CHS Administrator (Pamela Richmond, PJG7@med.harvard.edu, 617-432-2597), the ORSP Director (Carolyn Connelly, carolyn_connelly@hms.harvard.edu, 617-432-0651), the IO of the CHS (Gretchen Brodnicki, Gretchen_brodnicki@hms.harvard.edu 617-432-2496) or to the Office of Research Compliance Hotline (617-432-5555). More contact information is listed on the CHS website: <http://www.hms.harvard.edu/orsp/human/human.html> (Appendix 12).

All grievances will be reported to the IO, who will determine the appropriate level of investigation (and by whom the investigation will be conducted). The person reporting the grievance will be contacted regarding resolution.

3. CHS Member and Staff Policies

3.1. CHS Chair

The Chair is selected by the Dean for Academic and Clinical Programs with the recommendation of the IO. The Chair's official appointment comes from the Dean for Academic and Clinical Programs and begins on July 1, the start of Harvard's fiscal year. There is no term limitation on length of service; however, Chairs are asked to serve for a minimum of three years. Each year the CHS Chair's service is reviewed by the IO and the ORSP Director.

3.1.1. CHS Chair Qualifications

The CHS Chair should be a senior member of the Faculty of Medicine with significant human studies research experience. Selection is based on the person's experience and knowledge of human studies research along with an in-depth understanding not only of the federal regulations governing such research, but also of the ethical concerns related to such research. Historically, Chairs have been long term members on an IRB and have achieved an Associate or Full Professor rank.

3.1.2. CHS Chair Training

The CHS Chair must have undergone training in human subjects research within the past three years, must have a certificate from either the HETHR program or equivalent training from a certified source (not more than three years old), and must complete the OHRP Assurance training. Attendance at a Public Responsibility in Medicine and Research (PRIM&R) conference or other relevant conference is recommended yearly if possible, but at least every three years.

3.1.3. Expectations for the CHS Chair

For each year of his or her appointment, the Chair presides over the majority of CHS convened meetings. The Chair presents the meeting agenda, conducts the meeting, allowing sufficient time and opportunity for members present to discuss and vote on the studies under review, and provides clarification and leadership for CHS members. The Chair also performs expedited and exempt reviews, when necessary. The CHS Chair recommends, reviews and participates in the development and approval of CHS policies and procedures.

3.2. CHS Members

CHS members are selected by the IO upon the recommendation of Director of the ORSP. The official appointment comes through the Dean for Academic and Clinical Programs. CHS members are asked to serve for a minimum of three years, however there is no term limitation.

The CHS membership roster is filed with the Office of Faculty Affairs (OFA), the CHS office, the OGC and OHRP. Each office is informed of changes to membership in a timely manner. In preparation for each new fiscal year, the CHS membership is reviewed by the IO and the ORSP Director to determine whether any change needs to be made to the CHS. The CHS members are evaluated on their attendance, performance and participation on the committee and any subcommittee and as reviewers of research qualifying for expedited review processes.

The CHS is made up of members in the scientific disciplines of research typically reviewed. When there are changes to the trends in scientific topics of research received by the CHS then an

additional member with expertise in such disciplines will be considered. Also, if a particular vulnerable population (i.e. children or persons with cognitive impairments) is recruited for research projects, an ad hoc member of the Committee will be considered to represent the interests of that population. The CHS Administrator is responsible for reporting all membership changes to OHRP.

3.2.1. CHS Composition

The Faculty of Medicine is committed to diversity among its CHS members – whether it is diversity of ethnicity, culture, gender, faculty or non-affiliated persons of Harvard University, as well as professional disciplines within the Medical and Dental Schools. In accordance with 45 CFR § 46.107, the CHS is comprised of at least five members, with at least one member who is *not* affiliated with Harvard University (either directly or through an immediate family member); at least one member whose “primary concern” is in a scientific area, and at least one member whose “primary concerns” are in a non-scientific area and who must be present at each meeting. HMS research is primarily socio-behavioral research while HSDM is primarily clinical with some socio-behavioral components. The composition of the CHS thus reflects this research base; however it also meets Massachusetts Department of Public Health requirements for review of clinical studies involving investigational new drugs and schedule II narcotics.

Designated alternate members are appointed to the CHS and have similar qualifications and human studies training to the primary CHS member with whom they alternate. Alternate members are selected by the IO upon the recommendation of ORSP Director. The official appointment of alternate members comes through the Dean for Academic and Clinical Programs. Alternate members are asked to serve for a minimum of three years, co-terminus with the terms of the primary CHS member with whom they alternate, however there is no term limitation. The alternate members are called upon to attend CHS meetings when their designated member cannot attend. Additionally these alternate members are asked to review studies qualifying for expedited review in their specific discipline or, in the case of the non-scientific alternate members, when community representation and/or opinion are needed. Alternate members are provided with and review the same material which the primary members are provided.

In the event that the CHS reviews research that involves prisoners, the IO, upon the recommendation of the ORSP Director, is responsible for ensuring that a qualified prisoner representative is appointed as a member of the CHS and serves in the capacity for all aspects of the study (see Section 11.2.2).

3.2.2. CHS Member Training

CHS members must receive training in human studies protection (through HETHR or other training programs as required by their primary institutions), and they must have a certificate not more than three years old.

Each new CHS member receives a packet containing the following documents: 45 CFR § 46 and its subparts B, C and D; list of exempt and expedited categories; informed consent guidelines and the OHRP informed consent checklist; the Belmont Report; the Declaration of Helsinki; the

Nuremburg Code; the International Conference on Harmonization, Guidelines to Good Clinical Practice; FDA regulations 21 CFR §§ 50 and 56; DHHS policies on the Inclusion of Women and Minorities, Children, and common compliance findings and guidance; FDA policies on Investigational Device Exemptions, Investigational New Drugs, Acute Care Waiver of Informed Consent, and the Bioresearch Monitoring Program; and the CHS Policies and Procedures. In addition to the above materials, any updated regulations, education and policy materials are circulated with the monthly meeting packets and reviewed at convened CHS meetings.

New CHS members attend several meetings before they are put on the agenda as Secondary Reviewers, or until they, and the Chair, believe they are ready act as Secondary Reviewers. This determination is generally made from the new member's comfort in speaking-up at the meeting, and demonstrating through their comments that they understand their responsibility as an IRB member, the federal regulations and University policies, and the processes of the Committee. Secondary Reviewers review in conjunction with Primary Reviewers (see Section 3.6) for several months, thus the responsibility is not solely theirs until they have demonstrated as a Secondary Reviewer that they are ready to act as a Primary Reviewer. The Chair makes the final determination of when a Secondary Reviewer is appropriately trained and ready to be a Primary Reviewer, for both convened CHS meetings, and to conduct expedited reviews.

3.2.3. Expectations for CHS Members

CHS members attend monthly CHS meetings and prepare for these meetings by reading the materials sent to them a week in advance and by completing Reviewer Sheets (Appendices 13, 14, 15, and 16). CHS members must be knowledgeable about federal human research regulations and familiar with standards of professional conduct and practice. CHS members are expected to perform full committee, expedited and exempt reviews, as necessary. CHS members participate in study discussions, voicing any concerns they may have with the study under review, vote on protocols, and recuse themselves in the event that they have a conflict of interest (either financial, personal or professional) with the research under review.

CHS members who recuse themselves must leave the room for the discussion of the study and the vote. In the event that questions arise during the discussion for which the member is not present, the Chair may request that the CHS member come back into the room to answer any pointed questions pertaining to the study, but that member must leave again for any further discussion.

The performance of CHS members, both primary and alternate, is evaluated on a three year basis, coincident with their appointed terms, by the IO and the ORSP Director, who meet to review the participation, contributions, and attendance of the members before making a reappointment decision. Additionally, the performance of CHS members, both primary and alternate, may be reviewed by the IO and the ORSP Director more frequently if there are issues concerning participation, contributions and attendance.

3.3. CHS Consultants

When the CHS determines that a study involves a population or subject matter not within its expertise (such as technical, cultural or scientific [See also Section 4.4.1 *Additional Consultant for Scientific Review*]), the CHS will seek a consultant with such expertise. CHS members, faculty and other local IRBs are asked to suggest individuals with knowledge and competence in the topic area. When the CHS reviews research that involves categories of participants vulnerable to coercion or undue influence, the ORSP Director is responsible for ensuring that one or more individuals who are knowledgeable about or experienced in working with such participants are present at the meeting (see Section 11).

3.3.1. CHS Consultant Qualifications

Consultants must have significant experience, background and expertise in the topic of the research study or knowledge of the particular population being recruited for the study. For consultants associated with Harvard, their faculty position and standing are considered when evaluating their expertise. For non-Harvard consultants, a CV or copies of publications will be required to assure proper qualification in the field to consult for the CHS.

3.3.2. CHS Consultant Training

Consultants are not required to have human subjects training. Consultants are expected to provide technical or cultural expertise pertaining to a particular topic. The CHS will assimilate the information received from the consultant into its review and use its judgment to evaluate the information in accordance with the ethics of the study and the protection of research participants.

3.3.3. Expectations for CHS Consultants

Consultants will be asked to submit written comment about the study and/or attend the CHS meeting and participate in the discussions (per 45 CFR § 46.107 and FDA regulations at 21 CFR § 56.107). Consultants will be asked, prior to research materials being sent to them whether they have a conflict of interest (financial, personal or professional) with the particular research study under review, and if so, another consultant will be sought. Consultants cannot vote but can participate in the discussion of the review of the particular research project at the meeting

The consultant may be given a list of questions by the CHS, and the CHS should receive enough information from the consultant to adequately review, evaluate and vote on the study. Documentation from the consultant will be filed with the CHS study file as well as with the meeting packet, if reviewed at a CHS meeting.

3.4. CHS Member Conflict of Interest

Separate sections on Conflict of Interest exist for Investigators (see Section 4.7.1) and the Institution (see Section 1.2.2).

At the beginning of each CHS meeting, the Chair, or the Chair's designee asks the CHS if any members have a conflict of interest (professional, financial, or personal) with the particular research study under review that might influence his/her evaluation and thus might jeopardize

the rights and welfare of the research participants or the credibility of the CHS. CHS members and consultants also have a conflicting interest when their spouse, partner, or relative has a professional or financial conflict of interest. All CHS members with a potential conflict identify themselves and the nature of the conflict. CHS members with conflicts may provide additional information about the project if so requested by the Chair; however they may not be present for the vote. Consultants and ad hoc members must disclose any potential conflicts. CHS members conducting expedited reviews are required to sign the Reviewer Sheet indicating that they have no conflict with the study he/she has reviewed.

Any conflict revealed at the meeting is documented in the minutes and the CHS members who recuse themselves are not counted towards the quorum for that particular vote.

3.4.1. Professional/Personal Conflict of Interest

Professional conflicts of interest arise where, for example, a CHS member or ad hoc member (or consultant to the CHS): has a supervisory/mentoring role with respect to someone on the research team for the study being considered; is supervised/mentored by someone on the research team; has a role in the study (such as a co-investigator or collaborator); is a member of a board supporting the study; or may suffer a professional loss, such as standing in the professional community, if the study is or is not approved.

Personal conflicts of interest arise where, for example, a CHS member or ad hoc member (or consultant to the CHS) is the spouse, partner or relative of an Investigator on the study being considered, or of the investigator's Department Head.

Note that CHS members who are members of a Principal Investigator's Department are not necessarily considered to have a professional conflict and may in fact be called upon to review a study from their department.

3.4.2. Financial Conflict of Interest

Financial conflicts of interest arise where, for example, a CHS member or ad hoc member (or consultant to the CHS) has *any* financial interest in the study under review, including financial gains or losses through payments or consulting fees, equity interest or intellectual property rights from the research study or its sponsor. While it is possible for financial conflicts to be managed under the Faculty of Medicine's specific policy on financial conflicts of interest for faculty members, CHS members must recuse themselves from all studies in which they have any financial conflict as defined above.

3.5. CHS Member Indemnification

CHS staff and members are agents of the University. Thus, they ordinarily will be indemnified by the University in the event of lawsuits against them based on their involvement with the CHS actions as CHS members, provided of course that they were acting within the scope of their duties and in good faith. Indemnification means that the University will defend a lawsuit (incurring all legal fees and other expenses) and pay any judgment or settlement.

3.6. CHS Primary Reviewer System

The Primary Reviewer system is a system whereby a designated CHS member is responsible for the review and presentation of a study at a CHS meeting (or for review and approval via expedited review procedures). Primary reviewers are used for initial and continuing reviews, as well as review of modifications to previously approved research. The CHS Chair serves as the Primary Reviewer for all reviews of unanticipated problems involving risks to participants or others and serious or continuing non-compliance (see Sections 13 and 14, respectively)

The CHS Administrator will select a Primary Reviewer (herein referred to as the “Reviewer”) from the CHS membership (from which the Chair has designated as appropriately trained for such responsibility), for each study to be reviewed at a convened meeting, or review via expedited procedures. Whenever possible, the Reviewer shall have a field of expertise appropriate to the review of the study s/he is assigned. If this is not possible, the CHS Administrator will arrange for a consultation.

Occasionally, a Secondary Reviewer will be asked to provide additional review. The Secondary Reviewer is chosen to present the study if the Primary Reviewer is unable to be present at the CHS meeting or if the issues presented in the study are unusually complex. The Secondary Reviewer may have additional expertise relevant to the study. For example, for a HSDM study involving radiographs, the Primary Reviewer may be a dentist and the Secondary Reviewer may be a radiologist. The Secondary Reviewer may also be a new CHS member, added as a Reviewer to gain experience.

The Reviewer (Primary or Secondary) has the responsibility to conduct a thorough review of all protocol materials submitted by the Investigator (see required materials, Section 4), and to ensure that the Investigator’s submission provides sufficient information to permit the CHS to make an informed judgment about whether to approve the study. Where the submission requires more information, the Reviewer may either ask the CHS staff to request this information from the Investigator, or contact the Investigator directly. Direct communications between the Reviewer and Investigator are at the discretion of the Reviewer.

The Reviewer is responsible for presenting the research proposal at the CHS meeting, together with a clear recitation of any issues raised, and his/her recommendation for action (i.e., approval, contingent approval, deferral or disapproval of a research proposal).

If the Reviewer is unable to be present at the meeting, then s/he is responsible for providing the Secondary Reviewer and Chair with a written summary of any issues and his/her recommendations for CHS action. The Secondary Reviewer will present these concerns to the CHS at the meeting along with his/her own recommendation for action. In the event that a Secondary Reviewer is a new member, the Chair will determine who will act as Primary Reviewer; the Chair, or the Secondary Reviewer.

Following the CHS meeting, the Reviewer(s) are responsible for reviewing the portion of the minutes which pertain to the protocol(s) s/he presented, and for requesting any changes to the minutes to ensure accuracy (see Section 17.3).

3.7. CHS Meeting Schedule

CHS meetings ordinarily are held on the last Tuesday of the month from 4:00 pm to 7:00 pm. The December meeting is held earlier in the month due to the University winter break and holidays. On occasion, meetings during other times of the year are held on different days and times, depending on holiday or quorum issues, or emergency situations. Emergency meetings are not ordinarily called unless safety issues or significant regulatory issues with a study or Investigator have arisen. Subcommittee meetings are held on an ad hoc basis depending on necessity.

Research proposals are sent to meetings based on readiness for approval (i.e. methodologies are within the framework of 45 CFR § 46), as determined by CHS staff assigned to pre-review the study, and not based on the date the study materials were received by the CHS Office.

3.8. CHS Quorum

Quorum requirements are half of the CHS membership plus one and at least one non-scientific member (i.e. if the membership is 14, then the quorum is 8, and if the membership is 15, then the quorum is 9). Committee members are encouraged to attend all CHS meetings (for reasons such as last minute quorum issues, scientific expertise, experience with previous reviews of a study, and familiarity of studies conducted by an Investigator).

3.9. CHS Staff

CHS staff are selected by the ORSP Director in accordance with the University's personnel policies and procedures (see <http://www.employment.harvard.edu/careers/>). The requirements for the CHS staff positions are found in the University's job descriptions or those position descriptions (Appendix 17). CHS staff are evaluated annually in accordance with the Harvard Medical School Performance Planning and Review Program (Appendix 17a).

Each new CHS staff member receives a packet containing the following documents: 45 CFR § 46 and its subparts B, C and D; list of exempt and expedited categories; informed consent guidelines and the OHRP informed consent checklist; the Belmont Report; the Declaration of Helsinki; the Nuremberg Code; the International Conference on Harmonization, Guidelines to Good Clinical Practice; FDA regulations 21 CFR §§ 50 and 56; DHHS policies on the Inclusion of Women and Minorities, Children, and common compliance findings and guidance; FDA policies on Investigational Device Exemptions, Investigational New Drugs, Acute Care Waiver of Informed Consent, and the Bioresearch Monitoring Program; and the CHS Policies and Procedures.

CHS staff members must complete training in human studies protection through HETHR upon employment and they must have a certificate not more than three years old. CHS staff members also receive initial and on-going training from the ORSP Director and the CHS Administrator. In

addition to the above materials, any updated regulations, education and policy materials are provided to CHS staff. CHS staff are afforded opportunities to attend training sessions and conferences addressing human research protections offered through Harvard and/or outside organizations.

4. Initial Review of Research

Each Investigator whose proposed research is subject to the jurisdiction of the CHS must submit a CHS Application, which can be found on the CHS website: <http://www.hms.harvard.edu/orsp/human/human.html>. In addition to the application, all materials related to the research study must be submitted to the CHS office. These materials include:

- CVs/Biosketches for the Investigator and research personnel with human studies responsibilities (including members of the team who interact with participants or handle data/specimens containing participant identifiers);
- HETHR or equivalent human subjects protection certification (such as CITI or NIH) for all research personnel with human studies responsibilities (including members of the team who interact with participants or handle data/specimens containing participant identifiers);
- IRB approvals from appropriate institutions, or letter of support if the institution does not require IRB review, as applicable;
- All funding application/s (including grants, subcontracts and clinical trial agreements) supporting the research;
- The full protocol;
- The sponsor protocol (when one exists);
- The complete DHHS-approved protocol (when one exists);
- Recruitment materials (cover letters, fliers, brochures, email notices);
- Study materials (telephone scripts, question guides, written questionnaires and surveys);
- Educational materials (information sheets, study guides);
- Consent materials, including any requests for waivers;
- HIPAA materials (including any waiver requests and proposed authorizations);
- Investigator's Brochure (or package insert or pages from the *Physicians Desk Reference*, if a marketed drug).

4.1. Office Procedures for Processing New Applications

Applications received by the CHS office are date-stamped and screened for completeness (meaning that all questions on the application have been answered, including a "N/A" when a question is not applicable, and that appropriate signatures appear on the signature page); the relevant study information is entered into the HIRBERT database by CHS staff, and a study number and file is generated. The CHS Administrator will designate a CHS staff member to be responsible for the study, including pre-reviewing the materials and seeing the proposal through the approval process.