

Harvard Faculty of Medicine Committee on Human Studies Policies and Procedures

1. Introduction

The preamble to Harvard University's "Statement of Policies And Procedures Governing the Use of Human Subjects in Research," voted by President and Fellows of Harvard College on September 22, 2003 (Appendix 1), informs the oversight of all research covered by these policies and procedures:

Harvard University is guided by the ethical principles regarding research involving human subjects set forth in the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (*Ethical Principles and Guidelines for the Protection of Human Subjects of Research* [the "Belmont Report"]). The minimum standard is set by the Department of Health and Human Services [DHHS] regulations at 45 CFR 46 (the "Common Rule"). Harvard University has additional provisions beyond that standard, which help to establish the highest expectations for performance and oversight by investigators, Institutional Review Boards (IRBs), and the University.

The actions of Harvard University regarding research involving human participants also must conform to all other applicable federal, state, and local laws and regulations.

To oversee and regulate research involving human participants most effectively, the University maintains three Institutional Review Boards, with three separate Federal Wide Assurances (FWAs): one for the Harvard Faculty of Medicine (comprised of Harvard Medical School (HMS) and the Harvard School of Dental Medicine (HSDM)), one for the "University Area" (which includes the Faculty of Arts and Sciences; Harvard Graduate School of Education; John F. Kennedy School of Government; Harvard Divinity School; Harvard Business School; Harvard Law School; Harvard Graduate School of Design; and the Radcliffe Institute for Advanced Study); and one for the Harvard School of Public Health. Each of these three IRBs reviews research protocols involving human participants and evaluates risk to participants, protection against risks, and potential benefits likely to result from proposed research. It is the function of each IRB to 1) determine and certify that all projects reviewed by the IRB conform to policies and procedures set forth by the University's "Statement of Policies And Procedures Governing the Use of Human Subjects in Research," and, as appropriate, applicable regulations of the Department of Health and Human Services (DHHS) and other federal agencies regulating (e.g. the Food and Drug Administration) the health, welfare, safety, rights, and privileges of human participants; and 2) assist the investigator in complying with relevant federal, state, and local laws and regulations, and University policy.

While the three Harvard IRBs operate independently, the Directors, Administrators, Institutional Officials, and Chairs of each IRB participate in a University-wide Human Subjects Research Committee, established and run by the Office of the Provost. Representatives are also present from the Office of the General Counsel. This meeting serves as a forum to discuss issues affecting the University, and the University's IRBs.

In fulfillment of its FWA, the Harvard Faculty of Medicine has established the Committee on Human Studies (the “CHS,” also referred to as the Committee, the IRB, or the Research Review Unit), which reviews research projects and activities that involve human participants and oversees the implementation of all policies and procedures for human studies research. The Faculty of Medicine Office for Research Subject Protection (ORSP) has been established as the appropriate administrative oversight office for the CHS. The ORSP is supervised by the Dean for Faculty and Research Integrity, an official with sufficient standing, authority, and independence to ensure implementation and maintenance of the HMS and HSDM Human Research Protection Program (HRPP).

The CHS is authorized to function independently as the entity authorized to review human research proposals for the Faculty of Medicine. In accordance with federal requirements, the decision of the CHS disapproving or restricting research proposals cannot be overruled elsewhere at Harvard; nor can another individual or entity at the Faculty of Medicine approve human research under the purview of the CHS that the CHS has not reviewed and approved. Research reviews are conducted in a manner ensuring the independent judgment of Committee members, who will be excluded from voting on projects or activities in which they have a role, or a personal, professional, or financial conflict of interest.

The Faculty of Medicine holds a FWA with DHHS. This FWA is the Institution’s assurance of compliance with human studies regulations at 45 CFR § 46 and the ethical principles of the Belmont Report. The Faculty of Medicine FWA registration number is: FWA00007071 (Appendix 2). The IRB registration number for the CHS is: IRB00000298.

The CHS has been assigned the responsibility to determine that each study planned and conducted meets the following criteria: 1) Risks to participants are minimized by using procedures consistent with sound research design and which do not unnecessarily expose participants to risk, and whenever appropriate, by using procedures already being performed on the participants for diagnostic or treatment purposes; 2) Risks to participants are reasonable relative to anticipated benefits to participants, if any, and importance of the expected knowledge to be gained; 3) Selection of participants is equitable taking into account the purpose and setting; 4) Informed consent will be sought from each prospective participant or the participant’s legally authorized representative, in accordance with, and to the extent required by the regulations; 5) Informed consent will be appropriately documented , in accordance with, and to the extent required by the regulations; 6) The research plan, as defined in the CHS application and protocol, provides for ensuring the privacy of participants and confidentiality of the data; 7) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of participants; and 8) When some or all of the participants are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, persons with cognitive disabilities, or those with educational or economic disadvantages, additional safeguards have been included in the study to protect the rights and welfare of these participants.

All research involving human participants (also referred to as subjects) will be reviewed, administered and overseen in accordance with all applicable federal and state regulatory requirements and institutional policies when any of the following are true:

- The research is funded by or through HMS or HSDM;
- The research is conducted by HMS-based and HSDM-based faculty, acting in their capacities as such;
- The research is conducted by students of HMS or HSDM acting in their capacity as such;
- The research is conducted by non-faculty employees of HMS or HSDM acting in their capacities as such;
- The population from which participants will be drawn is exclusively or substantially composed of individuals who are patients, students or employees of HMS or HSDM;
- The research makes substantial use of the property or facilities of HMS or HSDM;
- The research involves the use of HMS or HSDM non-public information for the purposes of the research, or to identify or contact prospective participants.
- No funds (federal, foundation, private, corporate, departmental, or other) may be expended for research involving human participants unless the requirements of the FWA have been satisfied and a CHS approval or exemption has been documented.
- Any studies subject to regulations of the Food and Drug Administration (FDA) will be conducted in accordance with those regulations.

The CHS reviews mostly social and behavioral research studies with a wide array of participant populations, including, for example, persons with mental illnesses or addictions to substances. Other studies involve medication adherence, program evaluations, and Medical and Dental School curriculum. The CHS does review a number of clinical studies that take place at the Harvard Dental Clinic, the Veterans Administration Boston Healthcare System and at international sites. However, the majority of the clinical studies performed by Harvard faculty are reviewed by the IRBs at the hospitals or clinics where the research is taking place.

1.1. Mission

The mission of the CHS is to ensure that all participants are protected from any unnecessary risk when enrolled in a research study; to ensure participants make an informed decision to participate, and when possible, ensure that participant and/or society at large benefits from the knowledge gained from the research study. The goal of the CHS is to assist Investigators in developing appropriate research protocols in accordance with federal, and University policies, and within accepted ethical guidelines.

1.2. Ethical Principles

The CHS is guided by the ethical principles set forth in the Belmont Report. The Belmont Principles apply regardless of whether the research is subject to Federal regulation, with whom the research is conducted, or source of support or sponsorship.

In addition to the Belmont Report, HMS/HSDM faculty, staff and students are expected to comply with all applicable provisions of the HMS *Faculty Policies on Integrity in Science*, as well as Harvard University's *Statement of Policies and Procedures Governing the Use of Human Subjects in Research*, its *Information Security and Privacy* policies, and its *Statement of Values* (Appendix 3).

As Harvard Medical and Dental Schools are educational institutions, the CHS also reviews student projects that do not fall under the federal definition of “human subjects research” (such as program evaluations or community service projects that are not designed to contribute to generalizable knowledge). The CHS reviews such projects to ensure that appropriate institutional and ethical standards have been incorporated into the project design and materials to be used with project participants.

All institutional and non-institutional performance sites, domestic or foreign, will be obligated to conform to ethical principles which are at least equivalent to those of HMS and HSDM. In the case of federally funded studies, all sites (including international sites) will be asked to apply for an FWA and to obtain protocol review by an IRB or equivalent ethical review board.

1.2.1. IRB Independence from Undue Influence

The Faculty of Medicine takes seriously allegations that the CHS, its staff or any of its members have been subjected to any form of coercion or undue influence by Investigators, Harvard officials, study sponsors or other individuals. These incidents should be reported so that appropriate investigation may be made to assure that the independence of the CHS is not compromised. Allegations may be made to a number of officials, including the Dean of the Faculty of Medicine, the Dean for Faculty and Research Integrity, the Faculty of Medicine and HSPH Ombudsman, the CHS Chair, the ORSP Director, the CHS Administrator, and the Director of Research Compliance. In cases involving allegations of undue influence or coercion by faculty members, the processes set forth in the *HMS Principles and Procedures for Dealing with Allegations of Faculty Misconduct* (Appendix 4) will ordinarily be followed.

1.2.2. Institutional Conflict of Interest

Harvard University is in the process of developing an institutional conflict of interest policy and procedures to ensure that research involving human participants at the University is conducted free from any influence stemming from the University's financial investments. After review by appropriate offices and officials, the draft policy and procedures will then go before the Risk Management Committee and Provost, prior to going before the Corporation for approval.

1.2.3. Conflicts of Interest Policies for Faculty, Senior Officers and Others

The Faculty of Medicine has developed individual conflict of interest policies for its faculty (Appendix 5) and in addition the University has conflict of interest policies for its senior officials (Appendix 6) and members of its governing boards, as well as policies relating to conflicts of interest in procurement, in the granting of technology licenses (Appendix 7), and the creation of start-up companies (Appendix 8). These policies specify various limitations on Harvard and its trustees, officers, and employees in making a range of business and academic related decisions, some of which might involve or have an affect (real or perceived) on human research studies or the protection of research participants.

1.3. Applicable Laws

All requirements of 45 CFR § 46 and subparts A (Protection of Human Subjects), B (Additional Protections for Pregnant Women, Human Fetuses and Neonates involved in Research), C (Additional Protections Pertaining to Biomedical and Behavioral Research involving Prisoners as Subjects), and D (Additional Protections for Children Involved as Subjects in Research) will be met for all research, regardless of sponsorship, except if otherwise noted in the CHS FWA.

Any studies that fall under the jurisdiction of the FDA will be conducted in accordance with applicable FDA administered statutes and regulations, including the Code of Federal Regulations 21 CFR § 50 (Protection of Human Subjects), 21 CFR § 56 (Guidance for IRBs and Clinical Investigators), 21 CFR § 312 (Investigational New Drug/IND), and 21 CFR § 812 (Investigational Device Exemptions/IDE), as applicable.

In addition to federal regulations, the CHS follows certain Commonwealth of Massachusetts requirements relating to the ethical conduct of research. Where state regulations differ from federal regulations, the more stringent regulations shall be followed. This is noted in the appropriate policy sections.

2. Roles and Responsibilities

2.1. Responsibilities of the Institution

The Faculty of Medicine bears responsibility for the performance of research involving human research participants covered by its FWA, including compliance with previously noted federal and state laws as they may relate to such research.

The Faculty of Medicine, including all its named components (Appendix 9), acknowledges and accepts its responsibilities for protecting the rights and welfare of research participants covered by its FWA, including:

- Ensuring that CHS and University policies are in compliance with evolving laws and regulations.
- Publicizing policies and requirements regarding research with human participants for the research community.
- Establishing and maintaining an appropriately qualified CHS.
- Providing both meeting space and sufficient staff and resources to support the CHS, its review and record-keeping responsibilities.

2.1.1. Resources for the CHS

The Faculty of Medicine provides appropriate staff, office space, computer equipment, finances, materials and other resources for the CHS. The budgets supporting the CHS are reviewed annually as part of the budget review cycle. The budget reviews include annual assessments of staffing and salary levels, and of non-salary resources, including equipment, materials and training needs. The Dean for Faculty and Research Integrity (the CHS Institutional Official, or IO) and the ORSP Director undertake the budget review with the HMS Budget Director from Financial Operations and Analysis (FOA).