

9.5.1. CHS Approval

CHS approval must be documented with an ROA or letter of exemption (or a letter of participation; Appendix 44, if the student is receiving funding from the Faculty of Medicine and joining a study as research personnel) before any research activities may commence. Approval documentation will additionally be copied to: (a) OEP (if the student is receiving OEP funding); (b) the faculty mentor; (c) the on-site mentor, as appropriate; and (d) any other appropriate entity (such as additional IRB/ethics committee, facility manager, or advisor). Final approvals for research to be undertaken at external sites may be held until formal approval documentation from that site is forwarded to the CHS.

9.5.2. Research Site Approvals

As noted in Section 4.13 of this policy document, the CHS is required to have knowledge of the local research context (whether the research site is a domestic or international research site) in order to provide a thorough review, to understand particular risks and benefits of the study population, and the relevance, customs and cultural significance of study procedures and outcomes to the community in which the research is taking place. In addition, while the CHS provides institutional approval for the student (which is required), it cannot and does not cover the responsibility or replace the need of the student to receive approval from the local reviewing authority at the site where the research will be taking place. Site approvals are required in all circumstances.

9.5.3. Ceded Review of Student Research

Review and approval of independent student research projects ordinarily are not ceded to another institution. However if the research activities would require review by another Harvard IRB or the IRB of one of Harvard's affiliated institutions, a request to cede may be granted if approved by all involved/engaged IRBs. Affiliated and other institutions, however, may cede review of student projects (where appropriate) to the CHS.

10. Policies and Criteria for IRB Approval

10.1. Participation Review

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 CHS reviews the participation of humans in research, in accordance with applicable federal regulation (45 CFR § 46.111(a) and (b)), the Belmont Report, and University and CHS policy, as documented in the following section.

10.1.1. Equitable Selection of Participants

In assessing whether the selection of participants for a research study is equitable, in accordance with 45 CFR § 46.111(a), the CHS takes into account the purpose(s) of the research and the setting in which the research will be conducted. Equitable selection of participants is meant to ensure that a research study is: (a) as inclusive as possible of all gender, ethnicities, and racial groups, so that the risks and benefits are experienced equitably amongst the population and also are generalizable to the greater population; and (b) not overly inclusive of groups of participants that may be easy to enroll because of location or circumstance.

The CHS is particularly cognizant of the special challenges of research involving vulnerable populations (such as children, prisoners, pregnant women, and persons with cognitive impairments). When the participants of a study are likely to be vulnerable to coercion or undue influence, the CHS ensures that additional safeguards have been included in the study to protect the rights and welfare of these participants (see Section 11).

10.1.2. Risks vs. Benefits

According to the Belmont Report, risk refers to the “possibility that harm may occur,” and the *level* of risk (i.e. minimal, moderate, severe) also pertains to the likelihood of harm and the possible/likely magnitude of harm. Benefit refers to “positive value related to health or welfare.”

As set forth in 45 CFR § 46.111(a), the CHS must determine that:

- i. Risks to participants are minimized: (i) by using procedures which are consistent with sound research design and which do not unnecessarily expose participants to risk, and (ii) whenever appropriate, by using procedures already being performed for diagnostic or treatment purposes; and
- ii. Risks to participants are reasonable in relation to the anticipated benefits to participants from the research, if any, and the importance of the knowledge that may reasonably be expected to result.

The CHS evaluates all potential areas of risk including not only physical risk but also risk of psychological harm, and risk of social or economic harm, including legal risk. This aspect of risk evaluation is of particular importance as the majority of the research activities covered by the CHS are social and behavioral in nature. Thus, membership of the CHS over time has included sociologists, psychologists, ethnographers, lawyers and psychiatrists who are well versed in all aspects of risk assessment. Once risk in these categories have been identified, the CHS determines the level of risk, and whether the risk is outweighed by the benefit either in that particular area of research or with respect to society as a whole. Additionally the CHS may suggest ways to minimize identified risks, such as having a counselor on call for any emergent situations arising from sensitive issues, or eliminating questions from a survey instrument that are repetitive or redundant.

In evaluating risks and benefits, the CHS considers those that may result from the research and not necessarily from the typical procedures participants would receive if not participating in the research.

10.1.3. Data Safety Monitoring

The CHS follows NIH policy regarding safety oversight and monitoring of clinical studies. It is the policy of the NIH for each institution to provide appropriate oversight and monitoring of the conduct of clinical trials (<http://grants.nih.gov/grants/guide/notice-files/not98-084.html>) to ensure the safety of participants and the validity and integrity of the data for all NIH-supported or conducted clinical trials. Data Safety Monitoring Boards (DSMBs) are required for all Phase III trials (for more information on trial phases, see Section 12.1). However, for Phase I and II trials, a DSMB or a Data Safety Monitoring Committee (DSMC) may be appropriate if a study has multiple sites, is blinded (masked), or if it involves particularly high-risk interventions or vulnerable populations.

Regardless of funding source/sponsorship of the study, and depending on the level of risk to participants (including non-clinical risks), the CHS may require that an Investigator form a DSMB/C before a study begins, or if risks are identified during the course of an ongoing study. These determinations or requested requirement for formation of a DSMB or DSMC are made on a case by case basis for studies involving more than minimal risk or when additional risks are identified during the course of study and presented as an amendment or are identified during the continuing review process.

While DSMB/Cs operate separately from IRBs, the CHS will review all research data safety monitoring plans and reports, which must be included with the research materials submitted for review and approval of the study. All monitoring plans must include a plan for reporting adverse and unanticipated events to the CHS, the FDA and the NIH, as applicable. Additionally, DSMB/C reports must be submitted to the CHS at the time the reports are available to the Investigator, regardless of the timing of the report to the continuation of the study.

10.1.3.1. Data Safety Monitoring Plans (DSMPs)

DSMPs outline how the DSMB/C will protect participants from any unnecessary harm. DSMPs are created by the Investigator and his/her DSMB/C and should include the following information:

- A list of the DSMB/C members, including the Chair, with a description of their expertise (such as drug or clinical trial or treatment expertise and biostatisticians).
- An outline of DSMB/C Chair, member and Investigator responsibilities (such as who is responsible for meeting scheduling, conduct of the meeting and generation reports for the CHS, the FDA and/or funding sponsor).
- The DSMB/C meeting schedule.
- A description of the potential risks and the factors that may influence them (i.e. how side effects may increase with drug escalation, or how drugs may affect a participant who may be entering a new phase of his/her medical condition)
- A description of any special information that the event reports should contain and timing of event reports to the DSMB/C Chair and members.
- The reporting schedule of events and DSMB/C reports to the CHS, the FDA and the study sponsor, as applicable.

- For multi-site trials, a description of a central reporting entity that will be responsible for preparing timely summary reports of unanticipated problems involving risks participants or others, including adverse events, for distribution among sites and the IRBs.

10.1.4. Privacy

Research protocols must include descriptions of how Investigators will protect participant privacy – whether related to recruitment, consent, or data collection and analysis. When designing and conducting their research, Investigators must consider how the release of certain information could damage a participant’s social or family structure, employability, insurance coverage, or even legal liability. Participants must be able to choose how and when their private information will be used, withheld, or disclosed. Potential risks of a breach of participants’ right to privacy must be reported to the CHS and evaluated under the organizations policy on unanticipated problems involving risks to participants or others (see Section 13).

For information on the Health Insurance Portability and Accountability Act (HIPAA) privacy rules, please see Section 10.4.

10.1.5. Confidentiality of Data

Investigators must include in their research applications and protocols a plan for maintaining confidentiality of participant data – including how data will be **collected** (such as whether identifiers will be maintained or coded on data collection forms, and where codes for identifiers will be maintained to prevent unauthorized access to this information), **stored** (for data stored in paper form, where the paper will be kept, how unauthorized access will be prevented, how paper will be disposed and when; for data stored electronically, how unauthorized access will be prevented and distributed (electronic protections such as firewalls, locking of laptops, and storage of memory disk); and for data stored on video or audio, how and by whom the information will be transcribed, and how the tapes will be disposed of), **analyzed** (aggregate or raw form) and **documented** (stripped of personal identifiers and other information that may identify someone by circumstance) in publications.

Under 45 CFR § 46.111(a)(6), before approving a study, the CHS must confirm that each research protocol contains adequate provisions for the confidentiality and maintenance of data to ensure the safety of participants. The CHS may request additional protections, if it believes the research plan is not sufficient to protect participants. In addition, depending on the type of research being conducted, the CHS may request that the Investigator secure a Certificate of Confidentiality (see Section 10.1.6).

10.1.6. Certificates of Confidentiality

In some circumstances, the CHS may require an Investigator to obtain a Certificate of Confidentiality from the NIH (or other Health and Human Services department) in order to protect research participants should they disclose activity that would likely result in legal action against them or damage to other aspects of their lives. Circumstances for such a requirement generally include research that specifically targets (or is likely to include information pertaining to) illegal activities, such as drug use or distribution, illegal sexual practices, stealing, or fraud.

The OHRP Guidance States:

Certificates of Confidentiality are issued to protect identifiable research information from forced or compelled disclosure. They allow the investigator and others who have access to research records to refuse to disclose identifying information on research participants in civil, criminal, administrative, legislative, or other proceedings, whether federal, state, or local. Certificates of Confidentiality may be granted for studies collecting information that, if disclosed, could have adverse consequences for participants, such as damage to their financial standing, employability, insurability, or reputation. By protecting researchers and institutions from being compelled to disclose information that would identify research participants, Certificates of Confidentiality help to minimize risks to participants by adding an additional level of protection for maintaining confidentiality of private information. (<http://www.hhs.gov/ohrp/humansubjects/guidance/certconf.htm>)

Certificates of Confidentiality protect participants from compelled disclosure of identifying information but do not prevent the voluntary disclosure of identifying characteristics of research participants. Researchers, therefore, are not prevented from voluntarily disclosing certain information about research participants, such as evidence of child abuse or a risk of harm to themselves or others. If a researcher intends to make such voluntary disclosures, the consent form must clearly indicate this intent.

For more information on certificates of confidentiality, visit: <http://grants.nih.gov/grants/policy/coc/index.htm>.

10.1.7. Remuneration Guidelines

Payment, compensation or remuneration to individuals who participate in research projects is an acceptable practice. The CHS reviews and must find that the amount, schedule and type of any proposed remuneration is fair, and whether the payments could be considered coercive (due to an excessive enticement of money, goods or services). Thus, remuneration:

- Should be comparable to other projects involving similar time, effort, and inconvenience.
- Should be pro-rated on the number of procedures and study visits and should not be a condition of completing the entire study, although a bonus for completing the study may be acceptable. However, any amount paid as a bonus for completion must be reasonable and not so large as to unduly induce participants to stay in the study when they would otherwise have withdrawn.
- Should ensure that confidentiality of participants is protected and participants are paid in a manner that allows them to retain privacy. Thus, cash or a money order might be acceptable, but a check that participants would have to negotiate and that might link them to the research might not.
- Must include the specifics (including the amount per visit and payment schedule) documented in the consent form under the “Compensation” section of the consent form—but not under the “Benefits” section.
- Must not include “finder fees” (referrals of prospective participants).

- Must not include a coupon from a trial sponsor for a discount on the purchase price of the product once it has been approved for marketing.

Investigators should note that payments to participants of \$600 or more per year require IRS reporting on Form 1099-MISC as non-employee compensation. For more information, consult the Harvard Tax Office http://vpf-web.harvard.edu/ofs/tax_services/index.shtml, or the IRS <http://www.irs.gov/>. The Harvard University policy on processing payments to research participants can be found at: <http://vpf-web.harvard.edu/ofs/home/policies.shtml> (Appendix 45).

10.2. Recruitment

The CHS must review and approve the procedures for recruitment and consent of research participants to ensure compliance with 45 CFR § 46.111 and 116. All materials to be used with research participants must be reviewed and approved by the CHS, including materials such as recruitment advertisements, telephone scripts, direct mailings, consent forms, assessments of understanding of consent forms, questionnaires, surveys, and payment slips for remuneration of study procedures, to be sure that accuracy, non-coercive language and confidentiality is maintained at all times.

10.2.1. Recruitment Guidelines

The CHS must ensure that recruitment methods are not coercive, do not promise what they cannot deliver, and maintain confidentiality and privacy of potential participants. Research applications submitted to the CHS office should include the following information:

- How potential participants will be identified
- How, by whom and where potential participants will be approached
- How long after recruitment consent procedures will take place
- Whether parties other than the Investigator and study personnel will recruit participants (i.e. treating clinicians or calling centers).

Recruitment of participants can take many forms, including identification through medical record review, patient databases or registries, treating clinicians, family members or friends, faculty, students, and advertisements through media, such as print, radio, television and the Internet.

10.2.2. Recruitment Materials

Any materials to be sent to, seen or heard by research participants must be approved by the CHS. Recruitment materials should include the following information for the potential participants:

General advertisements should include:

- Name of the research project
- Purpose of the project
- Special inclusion or exclusion criteria (i.e. smoker/non-smoker, age range, medical or social condition)
- Duration of participation

- Name and contact information of study personnel for questions, or to participate

Direct mailing to potential participants should include the above information, in addition to the following:

- How the Investigator received his/her name and contact information
- Opt in or opt out information
 - Opt in** – participants receive a letter about the study which includes a phone number to call or a post card to return if they *are* interested in participating or learning more about the study. The Investigator does not call potential participants if they do not indicate by letter or phone that they wish to participate or receive more information.
 - Opt-out** - participants receive a letter about the study, which includes a phone number to call or post card to return if they *are not* interested in participating or learning more about the study. Not opting-out indicates to the Investigator that they can proceed with contacting the individuals.
- Letters should be signed by the Investigator and/or the treating clinician.

10.2.3. CHS Review of Recruitment Materials

When reviewing recruitment materials, the CHS must have the following:

- The mode of communication from the Investigator to the potential participant (eg. public flyers, direct email, direct mail, phone calls)
- The final copy of all printed materials/study advertisements;
- The final audio/video taped advertisements.

When reviewing advertising materials, the CHS must insure that advertisements do not:

- State or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol.
- Make claims, either explicitly or implicitly, that the drug, biologic or device is safe or effective for purposes under investigation.
- Make claims, either explicitly or implicitly, that the test article is known to be equivalent or superior to any other drug, biologic or device.
- Use terms, such as “new treatment”, “new medication”, or “new drug” without explaining that the test article is investigational.
- Promise “free medical treatment”, when the intent is only to say participants will not be charged to take part in the study.
- Include exculpatory language.
- Emphasize the payment or the amount paid, by such means as larger or bold type.

10.3. Informed Consent Guidelines

Informed consent is a process, not a form. Thus, the CHS pays particular attention to all information given to potential participants from recruitment through enrollment. The CHS will sometimes require re-consent of participants when, for example, a study is to be carried out over long periods of time; involves participants who may need to be reminded of study activities (such as the elderly, or those with cognitive disabilities); includes numerous procedures; or has

been modified in a way that could affect participants or their decision to continue to participate in the study.

Once a participant has been recruited, he or she must provide informed consent to participate in the research. Consent form content must:

- Be provided in a format understandable to the participant. Reading levels should generally be at an 8th grade level or under;
- Be provided in the primary language of the individual;
- Define medical terminology and jargon; and
- Be written in a context that is easy to follow (i.e. subject headings, short and concise sentences).

Pursuant to 45 CFR § 46.116, participants (or their legally authorized representatives) should be presented with study information in ample time to consider whether to participate, and to reduce the likelihood of their being or feeling coerced or unduly influenced. No informed consent (verbal or written) should include exculpatory language, whereby participants or their representatives are made to waive or appear to waive any of the participants' legal rights, or release or appear to release the Investigator, the sponsor, the Institution or its agents from liability for negligence.

10.3.1. Informed Consent Form

The Investigator is responsible for using a current, validated consent form with participants. A copy of the informed consent form must be given to the participant (or his/her legal representative) to read and sign; the original should be placed in the participant's record (hospital/clinic, or other, as appropriate); and a copy must be maintained in the Investigator's study file. Investigators' study files are subject to CHS review, as well as federal audits (i.e. FDA, NIH, or OHRP).

10.3.1.1. Basic Elements of Informed Consent

Consent forms must contain the following, as required by 45 CFR § 46.116(a)(1-8):

- (1) A statement that the study involves research
- (2) The purpose of the research
- (3) The expected duration of participant involvement in the study
- (4) A description of the procedures to be followed
- (5) Identification of the procedures which are experimental
- (6) Description of any reasonably foreseeable risks or discomforts to the participant
- (7) Description of any benefits to the participant or to others that may reasonably be expected from the research
- (8) Disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the participant
- (9) A statement describing the extent, if any, to which confidentiality of records identifying the participant will be maintained. For FDA-regulated research, a statement that notes the possibility that the FDA might inspect the records.

- (10) For research involving *more than minimal risk*, an explanation as to whether any compensation or any medical treatments are available if injury occurs, and if so, what they consist of, or where further information may be obtained.

To address Element 10, the following statement must be in the Informed Consent:

HARVARD'S WORDING FOR DISCLOSURE OF COMPENSATION FOR INJURY –

“If physical injury resulting from participation in this research should occur, although Harvard’s policy is not to provide compensation, medical treatment will be available including first aid, emergency treatment and follow-up care as needed, and your insurance carrier may be billed for the cost of such treatment. In making such medical treatment available, or providing it, the persons conducting this research project are not admitting that your injury was their fault.”

- (11) The Consent form includes the contact information of the research team for the participant to obtain answers to questions about the research and voice concern or complaints or about, or problems with the research. The consent form should also include the contact information for a person independent of the research for participants to voice complaints about the research, obtain answers to questions in the event the research staff could not be reached or if they wished to talk with someone other than the research staff, and to obtain information about their rights as a research participant.
- (12) A statement that participation is voluntary and refusal to participate will involve no penalty or loss of benefits to which the participant is otherwise entitled; and that the participant may discontinue participation at any time without penalty or loss of benefits to which they would otherwise be entitled.

Additional Elements of Informed Consent to be used when appropriate as defined below and, as required by 45 CFR 46.116 (b)(1-6):

- (1) A statement that the particular treatment or procedure may involve risks to the participant which are currently unforeseeable such as when the research involves investigational test articles or drugs or other procedures in which the risks to the participants are not well known.
- (2) A statement that if the participant is or becomes pregnant, the particular treatment or procedure may involve risks to the embryo or fetus, which are currently unforeseeable. This statement must be included when the research involves pregnant women or women of child-bearing potential *and* the risk to the fetuses of the drugs, devices or other procedures in the research is not well known. In the majority of cases this statement would apply to clinical studies, but any social and behavioral studies involving stress may also be considered and as such this statement may be required according to the judgment of the CHS.
- (3) Anticipated circumstances under which the participation may be terminated by the investigator with out regard to the participant’s consent. This statement should be considered for inclusion in the consent when there are anticipated circumstances under which the investigator may terminate participation of a participant.

- (4) Any additional costs to the participant that may result from participation in the research. This statement would be appropriate when it is anticipated that participants may have additional costs.
- (5) The consequences of a participant's decision to withdraw from the research and procedures for orderly termination of participation. This statement must be included when withdrawal from the research is associated with adverse consequences.
- (6) A statement that significant new findings developed during the course of the research which may relate to the willingness of a participant to continue in the study will be provided to the participant. This statement is appropriate when the research is long term and interim information is likely to be developed during the conduct of the research.
- (7) The approximate number of participants involved in the study should be stated in the consent when the research involves more than minimal risk.

If the study involves the collection of DNA for genetic analysis, a statement must be included indicating that information is being obtained for this purpose and specific options and information for the participant (such as whether participant's biological samples may be used for other purposes, and whether any incidental finding may be determined about the participant's condition) should be given to the participant, as well as other elements as determined by the CHS, depending on the nature of the study. On the consent form, the statements should appear as "Yes or No" options and read: (1) *I wish to receive a letter with information about the study once some relevant results have been obtained. I understand that this letter cannot discuss my personal case or data related directly to my family;* (2) *I agree to donate genetic material for the approved study;* and (3) *I agree that my genetic material may be stored and used for future studies.*

10.3.1.2. Documentation of Consent

According to federal regulations 45 CFR § 46.117(b) documentation of signed consent is required in the following manner (unless a waiver of consent/element of consent is granted; see waiver criteria, below):

- (1) A written consent document must contain the required elements of informed consent, as outlined above. The consent form may be read to the participant or the participant's legally authorized representative, and ample time should be given to the participant / legal representative to read it before it is signed (and dated for FDA-regulated research);
or
- (2) A short form written consent document, stating that the elements of informed consent required by § 46.116 (or 21 CFR§ 50.27 for FDA-regulated research) have been presented orally to the subject or the subject's legally authorized representative, may be used. However, when this method is used, there must be a witness to the oral presentation. The IRB must approve the written summary of what is to be said to the participant or their representative (and dated for FDA-regulated research). Only the short form itself is to be signed by the participant or their representative. However, the witness shall sign (and date for FDA-regulated research) both the short form and a copy of the summary, and the person actually obtaining consent shall sign (and dated for FDA-

regulated research) a copy of the summary. A copy of the summary shall be given to the participant or their representative, in addition to a copy of the short form.

10.3.2. Guidelines for Waiver or Alteration of Consent Requirements

Under 45 CFR § 46.116(c), the CHS may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent, or waive the requirement to obtain consent, provided the CHS finds and documents that:

- (1) The research or demonstration project is to be conducted by, or subject to, the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs;
- (2) The research could not practically be carried out without the waiver or alteration, and
- (3) The research is not FDA-regulated.

Additionally, under 45 CFR § 46.116(d), the CHS “may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent” or waive the requirement to obtain consent all together, provided the CHS finds and documents that:

- (1) The research involves no more than minimal risk to the participants;
- (2) The waiver or alteration will not adversely affect the rights and welfare of the participants;
- (3) The research could not practicably be carried out without the waiver or alteration;
- (4) Whenever appropriate, the participants will be provided with additional pertinent information after participation, and;
- (5) The research is not FDA-regulated.

According to 45 CFR § 46.117(c) the CHS may waive the requirement for the Investigator to obtain a signed consent form for some or all participants if it finds either:

- (1) That the only record linking the participant and the research would be the consent document, the principal risk would be potential harm resulting from a breach of confidentiality, and the research is not FDA-regulated. In each circumstance, the participant should be asked whether they want documentation linking them with the research, and their wishes will govern; or
- (2) That the research presents no more than minimal risk of harm to participants and involves no procedures for which written consent is normally required outside of the research context.

10.3.2.1. Waiver Requests to the CHS

Investigators must outline their requests for waivers in the CHS application and the requests must contain the above criteria (as appropriate) in order for the CHS to approve the waiver of a

specific element(s). Investigators who wish to obtain a waiver (either for informed consent or for documentation of informed consent) must include a request in their CHS application with an explanation of why their study meets the criteria set forth in this section. Waivers requested for written documentation of the consent process must be accompanied by a written description of the information that will be provided to participants. CHS must determine for each waiver of written consent whether the Investigator must provide participants with a written statement regarding the research. Waivers that have been granted by the CHS are noted on the ROA. In cases in which the documentation requirement is waived, the CHS may require that the Investigator provide participants with a written statement or short form explaining the research. The CHS will validate such documents with the CHS stamp and this validated document (or version of the document, if translated into another language) must be used with study participants.

Please note that consent requirements are different in research involving children (see Section 11.3).

10.4. Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule

In 1996, DHHS was obligated under federal law to create privacy regulations governing the protection of personal health information held by health care providers, insurers and others (“covered entities”). The HIPAA Privacy Rule, effective April 14, 2003, protects the privacy and confidentiality of all individually identifiable health information, such as medical history, diagnosis, treatment or payment information. This Protected Health Information (PHI) also includes demographic information that is maintained with health information (e.g., an individual's date of birth and social security number). HIPAA protection applies to all forms of PHI, both electronic and paper.

The OHRP and FDA human subject protection regulations (21 CFR § 46 and 21 CFR § 50, respectively) contain some provisions concerning protection of research participants’ confidential information that are similar to but separate from the HIPAA Privacy Rule research provisions. The HIPAA Privacy Rule built upon those pre-existing federal protections, creating a second, partly overlapping but also complementary tier of privacy protection for research participants whose PHI will be accessed or used in research.

Harvard is not a covered entity under HIPAA. It is a "hybrid entity", consisting of both covered and non-covered components. The University's covered components include the University Health Service (UHS), the Harvard Dental Center, and the Harvard University Group Health Plan (HUGHP). All other parts of the University, including Investigators whose research involves health care information, are not covered components.

An Investigator seeking data must first find out if the data exists as PHI at a HIPAA covered entity. If the entity holding the data is not a covered entity, then the Investigator does not need to be concerned with the HIPAA Privacy Rule to obtain the data, unless the entity passes along secondary restrictions in disclosing the data. However, the entity may still be bound by other laws, contractual agreements or institutional policies which restrict or condition its ability to

provide the data. The Faculty of Medicine SPA office is available to help Investigators obtain these data, under appropriate restrictions and conditions.

If the data source is a HIPAA covered entity, Investigators should work with the covered entity's Privacy Officer to establish the permissible ways of accessing the PHI. Examples include: obtaining written authorizations from individuals; the Privacy Board may grant a waiver of the individual authorization requirement; or the Investigator and the HIPAA covered entity may enter into strict data use agreements (DUA) permitting the sharing of PHI with the least number of identifiers necessary for the research to proceed.

HIPAA waivers are approved by an institution's Privacy Board. For the Faculty of Medicine, the CHS serves as the Privacy Board.

For more information on HIPAA and Harvard, patient authorizations, data use agreements, and the use of limited data sets, please see the CHS website; the Harvard University Research Administration website: http://vpf-web.harvard.edu/osr/support/sup_tra_regs_hipaa.shtml (Appendix 46); or the HSDM website: <http://www.hsdm.harvard.edu/asp-html/research-links.html> (Appendix 47).

10.5. CHS Review of HIPAA Waivers of Patient Authorization

Requests by Investigators for waivers of the individual authorization requirement under HIPAA are reviewed at full CHS meetings (generally at the end of the meeting when CHS business is concluded and then performs its function as the so designated Privacy Board). However, if a study/protocol or HIPAA waiver request meets a federal category of an expedited study under 45 CFR § 46.110 and 21 CFR § 56.110, then the request may be reviewed by expedited procedures noted elsewhere in these policies (see Section 4.9). Requests for waivers of patient authorization (Appendix 48) under HIPAA, along with appropriate study documents (such as the CHS application, protocol, etc.) will be sent to the CHS Chair or designee for expedited approval. The Chair will review and approve such waiver requests, if appropriate. However, the Chair may request that the full CHS review the waiver request at its next regularly scheduled meeting. Any HIPAA waivers approved by expedited means will be reported at the Privacy Board/CHS meetings with the other expedited actions of the CHS.

11. Vulnerable Populations and Special Protections

The CHS is guided by 45 CFR § 46 and 21 CFR § 50 when reviewing research involving the following categories of vulnerable participants: pregnant women, neonates and fetuses (45 CFR §§ 46.201-207 (Subpart B)); prisoners (45 CFR §§ 46.301-306 (Subpart C)); and children (45 CFR §§ 46.401-409 (Subpart D); 21 CFR §§ 50.50-50.56 (Subpart D)). Where a potential research population falls into more than one protected category, such as, for example, adolescents in a juvenile detention facility, then the CHS will apply all relevant review criteria.

Additionally, while there are no specific review criteria in the federal regulations for participants with cognitive impairments, economic or educational disadvantages, or stigmatizing health