

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](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

conditions, the CHS will consider in its review whether additional safeguards or protections are warranted to protect the rights and welfare of these participants, as outlined below. Similarly, the CHS will carefully review research projects which include as the primary participant population HMS or HSDM students, staff and fellows, as these populations may be subject to coercion, based on their status and accessibility to researchers at the University.

## **11.1. Pregnant Women, Neonates, and Fetuses**

### **11.1.1. Pregnant Women and Fetuses**

Pregnant woman can and are encouraged to participate in research studies. Research studies may recruit pregnant women for behavioral studies of minimal risk and which may offer no direct benefit to the pregnant women or fetus but may provide benefits to society. There are both Federal and Commonwealth requirements for research with pregnant women and fetuses.

#### **11.1.1.1. Federal Regulations Involving Pregnant Women and Fetuses**

Under 45 CFR § 46.204, research involving pregnant women or fetuses may be conducted if all of the following conditions are met:

- (a) Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
- (b) The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;
- (c) Any risk is the least possible for achieving the objectives of the research;
- (d) If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, the pregnant woman's consent is obtained in accord with the informed consent provisions of Subpart A of 45 CFR § 46;
- (e) If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions of Subpart A of 45 CFR § 46, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.
- (f) Each individual providing consent under paragraph (d) or (e) above is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
- (g) For children, as defined in 45 CFR § 46.402(a), who are pregnant, assent and permission are obtained in accord with the provisions of Subpart D of 45 CFR § 46;
- (h) No inducements, monetary or otherwise, will be offered to terminate a pregnancy;

- (i) Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
- (j) Individuals engaged in the research will have no part in determining the viability of a neonate.

#### **11.1.1.2. Massachusetts Law Involving Fetuses in Research**

Experimentation on human fetuses is also regulated under Massachusetts law, MGL Chapter 112C, § 12J(a), which states in part:

- I. No person shall use any live human fetus whether before or after expulsion from its mother's womb, for scientific, laboratory, research or other kind of experimentation. This section shall not prohibit procedures incident to the study of a human fetus while it is in its mother's womb, provided that in the best medical judgment of the physician, made at the time of the study, said procedures do not substantially jeopardize the life or health of the fetus, and provided said fetus is not the subject of a planned abortion. . . . This section shall not prohibit or regulate diagnostic or remedial procedures the purpose of which is to determine the life or health of the fetus involved or to preserve the life or health of the fetus involved or the mother involved. . . .
- II. No experimentation may knowingly be performed upon a dead fetus unless the consent of the mother has first been obtained, provided, however, that such consent shall not be required in the case of a routine pathological study. . . .
- III. No person shall perform or offer to perform an abortion where part or all of the consideration for said performance is that the fetal remains may be used for experimentation or other kind of research or study.
- IV. No person shall knowingly sell, transfer, distribute or give away any fetus for a use which is in violation of the provisions of this section.

For the purposes of this section, a fetus is a live fetus when, in the best medical judgment of a physician, it shows evidence of life as determined by the same medical standards as are used in determining evidence of life in a spontaneously aborted fetus at approximately the same stage of gestational development... [Also,] for the purposes of this section, "fetus" shall include a neonate and an embryo, but shall exclude a pre-implantation embryo or parthenote as defined in section 2 of chapter 111L and obtained in accordance with said chapter 111L.

The Massachusetts statute includes criminal penalties, but states that those who have performed a procedure that allegedly violates the statute's provisions will not be held liable if: (i) the procedure received the written approval of a duly appointed IRB; and (ii) at the time the procedure was performed, there was not an outstanding court judgment that the procedure violated the statute. The IRB's written approval must state specifically that the procedure does not violate the provisions of the statute and must set forth a reasonable basis for this conclusion. The written approval must contain a detailed description of the procedure and must be maintained as a "permanent record" of the IRB or the institution for which it acts. A copy of the written approval must be filed with the office of the District Attorney for the county in which the IRB's institution is located, and shall be available for public inspection at all times. MGL Chapter 112C, § 12J(a)(V-VII). IRB members are themselves immune from liability under the

statute if they acted in good faith in concluding that the procedure was lawful. MGL Chapter 112C, § 12J(a)(VI).

### **11.1.2. Neonates**

45 CFR § 46.205 provides as follows:

- (a) Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:
  - (1) Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates;
  - (2) Each individual providing consent under paragraph (b)(2) or (c)(5) of 45 CFR § 46.205 is fully informed regarding the reasonably foreseeable impact of the research on the neonate;
  - (3) Individuals engaged in the research will have no part in determining the viability of a neonate; and
  - (4) The requirements of paragraph (b) or (c) of 45 CFR § 46.205 have been met as applicable.
  
- (b) Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by 45 CFR § 46.205 unless the following additional conditions are met:
  - (1) The IRB determines that: (i) The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or (ii) The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and
  - (2) The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained in accord with subpart A of 45 CFR § 46, except that consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.
  
- (c) After delivery a nonviable neonate may not be involved in research covered by 45 CFR § 46.205 unless all of the following additional conditions are met:
  - (1) Vital functions of the neonate will not be artificially maintained;
  - (2) The research will not terminate the heartbeat or respiration of the neonate;
  - (3) There will be no added risk to the neonate resulting from the research;
  - (4) The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
  - (5) The legally effective informed consent of both parents of the neonate is obtained in accord with Subpart A of 45 CFR § 46, except that the waiver and alteration provisions of § 46.116(c) and (d) do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this

paragraph, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either of both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph.

- (d) A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of 45 CFR § 46 Subparts A and D.

### **11.1.3. Research Involving, After Delivery, the Placenta, the Dead Fetus or Fetal Material**

45 CFR § 46.206 provides as follows:

- (a) Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable federal, state or local laws and regulations regarding such activities.
- (b) If information associated with material described in paragraph 45 CFR § 46.205(a) is recorded for research purposes in a manner that could identify living individuals, either directly or through identifiers linked to those individuals, then those individuals are research subjects and all pertinent subparts of 45 CFR § 46 are applicable.

### **11.1.4. Research not otherwise approvable that present an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates**

Under 45 CFR § 46.207, where the CHS does not believe that the proposed research meets the requirements of 45 CFR § 46.204 or §46.205, but does believe that it presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates, it may refer the protocol to the DHHS for review. The research may proceed only if the Secretary of DHHS, after consulting with a panel of experts in pertinent disciplines (e.g., science, medicine, ethics, law) and following an opportunity for public review and comment (including a public meeting), determines either: (1) that the research in fact satisfies the conditions of 45 CFR § 46.204; or (2) the following:

- a) the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates;
- b) the research will be conducted in accordance with sound ethical principles; and
- c) informed consent will be obtained in accord with the informed consent provisions of 45 CFR § 46 Subpart A and any other applicable subparts.

## **11.2. Prisoners**

Under 45 CFR § 46, Subpart C, prisoners who participate in research are afforded additional safeguards because their incarceration might affect their ability to make truly voluntary and uncoerced decisions. These additional protections apply not just to individuals who are prisoners at

the time they are enrolled in a study, but also to *those who become incarcerated during the course of a study.*

A prisoner is defined as: “any individual involuntarily confined or detained in a penal institution.” The definition includes “individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial or sentencing.” 45 CFR § 46.303(c). The CHS interprets this definition to include individuals who are sent by court order to alcohol/drug rehabilitation facilities.

### **11.2.1. Additional CHS Composition Requirements**

45 CFR § 46.304 (a) and (b) requires that, in addition to meeting the composition requirements set forth in 45 CFR § 46.116 and 46.117, if the CHS reviews research involving prisoners as research participants then it must also meet the requirements set forth below. These requirements apply to all aspects of review, including initial review, continuing review, review of study amendments, and review of reports of unanticipated problems involving risks to the participants:

- (a) A majority of the CHS (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the CHS.
- (b) At least one member of the CHS must be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by more than one IRB, only one IRB need satisfy this requirement.

### **11.2.2. Additional Issues for Consideration by the CHS**

Under 45 CFR § 46.305(a), where prisoners are involved in potential research, the CHS may approve such research only if it finds that:

- (1) The research under review represents one of the categories of research permissible under 45 CFR § 46.306(a)(2) set forth below;
- (2) Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;
- (3) The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;
- (4) Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the Principal Investigator provides to the IRB justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;
- (5) The information is presented in language which is understandable to the subject population;

- (6) Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and
- (7) Where the IRB finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.

The Institution responsible for the conduct of the research shall certify to the DHHS Secretary that the CHS has made the required findings. The Institution must send to OHRP a certification letter to this effect, which should also include the name and address of the institution and specifically identify the research protocol in question and any relevant HHS grant application or protocol. Research involving prisoners as participants may not proceed until OHRP issues its approval in writing to the institution on behalf of the Secretary under 45 CFR § 46.306(a)(2).

### **11.2.3. DHHS-Funded Research Involving Prisoners**

Under 45 CFR § 46.306, biomedical or behavioral research conducted or supported by DHHS may involve prisoners as participants only if: the institution responsible for the conduct of the research has certified to the Secretary of DHHS that the CHS has approved the research under 45 CFR § 46.305; *and* in the judgment of the Secretary of DHHS, the proposed research involves solely the following:

- (1) Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;
- (2) Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;
- (3) Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Secretary of DHHS has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of the Secretary's intent to approve such research; or
- (4) Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary of DHHS has consulted with appropriate experts, including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of the Secretary's intent to approve such research.

Unless it meets the criteria set forth above, biomedical or behavioral research conducted or supported by DHHS shall not involve prisoners as research participants. In determining whether the proposed research meets these criteria, the CHS must apply the definition of “minimal risk” set forth in 45 CFR § 46.303(d), rather than the definition set forth in 45 CFR § 46.012(i). The applicable definition of “minimal risk” is: “the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.” 45 CFR § 46.303(d).

#### **11.2.4. Expedited Review Procedures**

Ordinarily, the CHS will not expedite its review of research involving prisoners, however expedited review procedures are permitted under 45 CFR § 46.110 and 21 CFR § 56.110 for minor changes in approved research and for certain kinds of research involving no more than minimal risk. As noted above, with respect to research involving prisoners, the CHS must apply the definition of “minimal risk” set forth in 45 CFR § 46.303(d).

#### **11.2.5. Exempt Research with Prisoners**

The exemptions set forth in 45 CFR § 46.101(b) **do not apply** to research involving prisoners. 45 CFR § 46.101(i), FN1.

### **11.3. Children**

45 CFR § 46 Subpart D affords special protections for children involved in research to prevent any unnecessary risk or harm. Under 45 CFR § 46.402(a), children are defined as “persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.” Massachusetts law contains a number of provisions which define minors and the limited number of circumstances under which children whom have not reached majority may consent to receive medical care, or to participate in research, and circumstances and conditions under which the child’s parents or legal guardians may consent on their behalf. These provisions are outlined below:

*Age of majority.* Eighteen is the age of majority both in Massachusetts (M.G.L. c. 231, § 85P) and under federal policy. When a person turns 18, s/he is considered to be an adult under the law. (Buying and consuming alcohol, however, are two activities that are not legal until a person turns 21 in Massachusetts.)

Massachusetts law recognizes two instances when teenagers under the age of 18 may have the legal capacity to consent to medical treatment. These are the **emancipated minor** and **mature minor** rules. Note that these rules concern individuals in their capacity as **patients**, not as participants in research, and also that they apply only to persons in Massachusetts. These rules would not apply, for example, to research participants living in a foreign country, although that country might have analogous rules.

*Emancipated minor.* A patient under 18 years of age may consent to treatment of any kind, except abortion, and may authorize the release of his or her medical records if s/he is: (a)

married/widowed/divorced, a parent, (b) a member of the armed forces, (c) living apart from parents and managing his or her own finances, or, in the case of a female, (d) pregnant or believes herself to be pregnant. M.G.L. c. 112 § 12F. A female under the age of 18 may consent to an abortion if she is or has been married. Otherwise, consent must be obtained from her parent(s) or the procedure must be authorized by court order. M.G.L. c. 112 § 12S. Further, patients under 18 years of age may consent to treatment and may authorize the release of their medical records relating to: diseases dangerous to the public health, drug dependency (but not alcohol dependency), and pregnancy (but not abortion, except in the case of those who had married).

Mature minor. Under Massachusetts case law, students under the age of 18 who are not emancipated under M.G.L. c. 112, § 12F, can, in certain circumstances, nevertheless consent to treatment and control access to their medical records. In such cases, the clinician proposing to provide the treatment may determine that the patient is a mature minor capable of consenting to treatment. To reach this determination, the clinician must conclude that the minor is capable of giving informed consent to the treatment; and that it is in the best interest of the minor not to notify his or her parents of the intended medical treatment. In general, where a minor has the capacity to consent to medical treatment, that minor also has the capacity to control his or her medical records, including releasing them to others, such as researchers. In addition, there is an argument that a minor who has the capacity to consent to medical treatment also should have the capacity to consent to research that may accompany that treatment. However, this argument has not been tested in a Massachusetts court.

Parents or Guardians of minor children. In general, and as more fully explained below, parents and guardians may provide consent to participation in research for their minor children or wards. The definition of who is a parent or guardian differs in some respects under federal and Massachusetts laws. The Massachusetts Uniform Statutory Will Act (the “Will Act”) indirectly defines “parent” in its definition of “child.” See M.G.L. c. 191B, § 1(1). Under this law, the “parent” is the biological or adoptive mother or father of a child. However, a father of a child who is not married to the child’s mother may not always be considered a parent; his status would depend on whether he openly treats the child as his offspring or on whether a court has made a paternity determination. Under the Will Act, the term “parent” does not include step-parents who have not formally adopted the child, foster parents, grandparents or other relatives. *Id.* In general, the term “guardian” is widely understood to mean a person lawfully invested with the power, and charged with the duty, of taking care of and managing the property and rights of someone who is considered incapable of administering his or her own affairs. This definition includes a person who legally has responsibility for the care and management of the person or estate or both of a child during his or her minority. Parents are usually considered the guardians of their minor children under Massachusetts law. For example, with respect to children, the Department of Mental Retardation defines “guardian” in its regulations concerning research as “a natural or adoptive parent, or the individual or agency with legal guardianship of the person.” 115 CMR 10.02.

Legal guardianship in Massachusetts usually is created through a court process, most often through the Probate Court, M.G.L. c. 201 § 2, although parents may designate another adult to be a guardian without having to invoke a court proceeding. This kind of guardian, once appointed,

is also referred to as a “standby proxy,” whose authority becomes enforceable when the parent dies, becomes incapacitated or is unavailable to care for the child. M.G.L. c. 201 §§ 2B – 2D. The Department of Social Services (DSS) or other state agencies may become the legal guardian of children it takes into custody. The CHS will make a determination based on the risk/benefits to determine whether to accept DSS, or other agency consent for children in their custody.

In general, a parent or legal guardian is considered under federal policy to be the legally authorized representative of a child, and thus may consent to the child’s participation in a research project. Thus, for a child participant in research, a parent or guardian acting as a legally authorized representative can give permission (consent) on behalf of the child to participate in research. As discussed above, an exception to this general rule is where the research involves medical treatment and the child has the capacity to consent under the emancipated minor or mature minor rules.

### **11.3.1. Research Not Involving Greater than Minimal Risk**

Under 45 CFR § 46.404, where the CHS has found that the proposed research presents no greater than minimal risk to the children, it may approve the research only if it also finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in 45 CFR § 46.408. (Note that 45 CFR § 46.408(b) the permission of both parents is required unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child. The CHS may find that the permission of one parent is sufficient for research to be conducted under 45 CFR § 405 even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child.)

### **11.3.2. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual child participants**

Under 45 CFR § 46.405, where the CHS has found that the proposed research presents more than minimal risk to the children but involves either an intervention or procedure that holds out the prospect of direct benefit for the individual participant, or a monitoring procedure that is likely to contribute to the participant’s well being, it may approve the research only if it also finds that:

- a) the risk is justified by the anticipated benefits to the subjects;
- b) the relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and
- c) adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in HHS regulations at 45 CFR § 46.408.

(Note that 45 CFR § 46.408(b) the permission of both parents is required unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child. The CHS may find that the permission of one parent is sufficient for research to be conducted under 45 CFR § 405 even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for care and custody of the child.)

**11.3.3. Research involving greater than minimal risk and no prospect of direct benefit to the individual child participants, but likely to yield generalizable knowledge about the participant’s disorder or condition**

Under 45 CFR § 46.406, where the CHS has found that the proposed research presents more than minimal risk to the children and involves either an intervention or procedure that does not hold out the prospect of direct benefit for the individual participant, or a monitoring procedure that is not likely to contribute to the participant’s well being, it may approve the research only if it also finds that:

- a) the risk of the research represents a minor increase over minimal risk;
- b) the intervention or procedure presents experiences to the child subjects that are reasonably commensurate with those inherent in their actual, or expected medical, dental, psychological, social, or educational situations;
- c) the intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition which is of vital importance for the understanding or amelioration of the disorder or condition; and
- d) adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in 45 CFR § 46.408.

(Note that, under 45 CFR § 46.408(b), where research to be conducted under 45 CFR § 406, and permission is to be obtained from parents, both parents must give their permission unless either: one parent is deceased, unknown, incompetent, or not reasonably available, deceased; or only one parent has legal responsibility for the care and custody of the child.)

**11.3.4. Research not otherwise approvable that presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children**

Under 45 CFR § 46.407, where the CHS does not believe that the proposed research meets the requirements of 45 CFR §§ 46.404, 46.405, or 46.406, but does believe that it presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children, it may refer the protocol to DHHS for review. The research may proceed only if the Secretary of DHHS, after consulting with a panel of experts in pertinent disciplines (e.g., science, medicine, education, ethics, law) and following an opportunity for public review and comment, determines either: (1) that the research in fact satisfies the conditions of 45 CFR § 46.404, § 46.405, or § 46.406, or (2) the following:

- a) the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
- b) the research will be conducted in accordance with sound ethical principles; and
- c) adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth at 45 CFR 46.408.

(Note that, under 45 CFR § 46.408(b), where research to be conducted under 45 CFR § 407, and permission is to be obtained from parents, both parents must give their permission unless either: one parent is deceased, unknown, incompetent, or not reasonably available, deceased; or only one parent has legal responsibility for the care and custody of the child.)

### **11.3.5. Requirements for Permission by Parents or Guardians**

Under 45 CFR § 46.408(b), for research involving children, the CHS must determine, in accordance with and to the extent required by 45 CFR § 46.116, that adequate provisions are made for soliciting the permission of each child's parents or guardian. As noted above, for research conducted under 45 CFR §§ 46.404-405 (minimal risk), the CHS may find that the permission of one parent is sufficient. Where research is to be conducted under 45 CFR §§ 46.406-407 (greater than minimal risk), and permission is to be obtained from parents, both parents must give their permission unless either: one parent is deceased, unknown, incompetent or not reasonably available; or only one parent has legal responsibility for the care and custody of the child.

Under 45 CFR § 46.408(c), in addition to the provisions for waiver set forth in 45 CFR § 46.116, if the CHS finds that a study is designed for conditions or for a participant population for which parental or guardian permission is not a reasonable requirement to protect the participants (for example, neglected or abused children), then it may waive consent, provided an appropriate mechanism for protecting the children is substituted, and provided further that the research is not FDA-regulated and the waiver is not inconsistent with federal, state or local law. The choice of an appropriate mechanism depends on the nature and purpose of the proposed activities, the risk and anticipated benefit to the research participants, and their age, maturity, status and condition.

Under 45 CFR § 46.408(d), permission of parents or guardians for their children to participate in research must be documented by a signature on the consent/permission form, unless a waiver of consent/permission or documentation is approved by the CHS. The CHS will determine whether parental permission is required of both parents, of one parent, or if a waiver of parental permission or permission documentation, is warranted.

### **11.3.6. Requirements for Assent by Children**

“Assent” means agreement – specifically, in this context, a child's agreement to participate in research. Assent, like consent, is a process that should be documented.

Under 45 CFR § 46.408(a), when, in the CHS's judgment, children are capable of providing assent, the CHS must determine that adequate provisions are made for soliciting their assent. The CHS will additionally determine how assent will be solicited, obtained and documented. In determining whether children are capable of assenting, the CHS takes into account their ages, maturity, and psychological state. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the CHS deems appropriate. If the CHS determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, then the assent of the children is not a necessary condition for proceeding with the research. Even where the CHS determines that the participants are capable of assenting, the CHS still may waive the assent requirement in accord with 45 CFR § 46.116.

Under 45 CFR § 46.408(e), when the CHS determines that assent is required it shall also determine whether and how assent must be documented. Assent forms are designed similarly to consent forms and should include the purpose, procedures, risks and benefits of participating in a particular research study. The assent should be written at the age level of the children, with jargon and technical terms explained or removed.

For children ages seven and under, the CHS recommends that the Investigators verbally explain the study to the child, including its purpose, procedures, and potential risks and benefits (if appropriate, depending on the child's age, maturity and development). For children ages seven through 17 years, the CHS typically requires written assent from the child, although this may be waived by the CHS. Depending on the study, its procedures, risk and benefits, the CHS may also approve verbal assent. Assent (written and verbal) should be obtained in the presence of a parent or legal guardian, unless the study procedures are taking place in a setting (such as a school) where parents are not usually present. However, in nearly all cases, a child's assent must be accompanied by the permission or consent of the child's parent or guardian.

#### **11.3.7. Additional Requirements for Wards and Foster Children**

Under 45 CFR § 46.409(a), children who are wards of the state or any other agency, institution, or entity can be included in research approved under § 46.406 or § 46.407 only if such research is: (1) related to their status as wards; or (2) conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as participants are not wards.

Even if such research is approved under 45 CFR § 46.409(a), 45 CFR § 46.409(b) requires the appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the CHS) with the research, the Investigator(s), or the guardian organization.

Massachusetts law (MGL Chapter 119, et. seq.) allows the Department of Social Services (DSS) to remove children from their parents' custody in certain circumstances, but the placement of a child in foster care does not automatically terminate all parental rights. Because these situations are complicated, investigators who wish to use foster children as participants in their research are urged to consult in advance with the CHS.

#### **11.3.8. Child Abuse Reporting**

Research proposals involving children ordinarily must include a plan for reporting suspected abuse of children to DSS. Additionally, consent and assent forms for children and parents ordinarily must include a statement that suspected child abuse or neglect may be reported to DSS.

Certain people, as a function of their professions or provisions, are deemed to be mandated reporters. Under Massachusetts law, (MGL Chapter 119, § 51A), mandated reporters include any: “physician, medical intern, hospital personnel engaged in the examination, care or treatment of persons, medical examiner, psychologist, emergency medical technician, dentist, nurse, chiropractor, podiatrist, optometrist, osteopath, public or private school teacher, educational administrator, guidance or family counselor, day care worker or any person paid to care for or work with a child in any public or private facility, or home or program funded by the commonwealth or licensed pursuant to the provisions of chapter twenty-eight A, which provides day care or residential services to children or which provides the services of child care resource and referral agencies, voucher management agencies, family day care systems and child care food programs, probation officer, clerk/magistrate of the district courts, parole officer, social worker, foster parent, firefighter or policeman, licenser of the office of child care services or any successor agency, school attendance officer, allied mental health and human services professional as licensed pursuant to the provisions of section one hundred and sixty-five of chapter one hundred and twelve, drug and alcoholism counselor, psychiatrist, and clinical social worker, priest, rabbi, clergy member, ordained or licensed minister, leader of any church or religious body, accredited Christian Science practitioner, person performing official duties on behalf of a church or religious body that are recognized as the duties of a priest, rabbi, clergy, ordained or licensed minister, leader of any church or religious body, or accredited Christian Science practitioner, or person employed by a church or religious body to supervise, educate, coach, train or counsel a child on a regular basis.”

Reports must be made where the mandated reporter, in his or her professional capacity, has reasonable cause to believe that a child under the age of 18 is suffering physical or emotional injury resulting from abuse inflicted upon him or her which causes harm or substantial risk of harm to the child's health or welfare, including sexual abuse, or from neglect, including malnutrition, or who is determined to be physically dependent upon an addictive drug at birth. A mandated reporter must immediately make a verbal report to DSS and must make a written report within 48 hours.

#### **11.3.9. Confidential Birth Information**

MGL Chapter 117, § 67E requires physicians to report diagnoses of congenital anomalies and birth defects to the Department of Public Health (DPH). 105 CMR § 305.070 provides a mechanism by which researchers may access and use this confidential birth information. Researchers must submit an application that includes: the purpose and design of the study, its public health benefits, its relationship to the DPH’s goal of reducing morbidity and mortality, the data requested, a justification for the data request, a description of the extent to which the study involves “contact with the data subjects,” a description of the extent to which informed consent will be obtained from the participants, information regarding CHS review and approval of the project, proposed measures to preserve the confidentiality of the data, and the names and titles of all persons who will access the data requested. Investigators also must also submit to DPH copies of consent forms, questionnaires or telephone interview scripts, their filings with an IRB, the IRB’s written determinations, and their CVs. 105 CMR § 305.070(B) and (C). Investigators’ use of confidential birth information released by the DPH is subject to the terms and restrictions set forth in 105 CMR § 305.080. Thus, in addition to following CHS policies, investigators also must comply with DPH IRB requirements.

#### **11.4. Embryonic Stem Cell Research**

Chapter 27 of the Acts of 2005, referred to hereinafter as the “MA Stem Cell Law” which, among other things, authorized with some restrictions the use of human Embryonic Stem Cells (hESCs) in research, also imposed certain IRB approval requirements on institutions conducting such research. Activities that the law specifically authorizes include “research and clinical applications involving the derivation and use of [hESCs], including somatic cell nuclear transfer, human adult stem cells from any source, umbilical cord cells, parthenotes and placental cells”. The MA Stem Cell Law also specifically prohibits certain research activities, including those involving “human reproductive cloning,” and those involving the creation of an embryo by the means of fertilization “solely for the purpose of donating the embryo for research”. The law also requires that all research “involving the derivation of human embryonic stem cells” must be reviewed and approved by a duly constituted IRB, regardless of whether IRB approval may or may not also be required under federal law, and to report such projects to the Massachusetts Department of Public Health (DPH) on an annual basis. The statute describes the IRB’s required role as follows:

*Research involving the derivation of human embryonic stem cells through the use of human genetic material, including somatic cell nuclear transfer, parthenogenesis and other asexual means . . . shall only be conducted upon the written approval of a duly authorized institutional review board. The written approval of the institutional review board shall include a detailed description of the research, experimentation or study to be conducted and a detailed description of the research or a copy of the protocol, all of which shall be maintained as a permanent record by the board or by the hospital or institution for which the board acts.*

All research with embryonic stem cells must first be reviewed by the Embryonic Stem Cell Research Oversight (ESCRO) Committee. Once approved by ESCRO, such studies must be submitted to the CHS for review and approval or exemption.

#### **11.5. Participants with Cognitive Impairments**

The CHS respects the autonomy of each individual and his or her decision-making. Those with cognitive impairments or less of a capacity of understanding (as a result of, for example, age, illness or genetic impairment) deserve respect when participating in research activities. The difficulty lies in establishing when, and to what degree, a person has the capacity to understand and to make an informed decision about participation in research.

##### **11.5.1. Research outside the jurisdiction of the Massachusetts Department of Mental Health (DMH)**

Research involving potential participants who are under the jurisdiction of the Massachusetts Department of Mental Health (DMH) is governed by state regulation as described below. Even where the DMH regulations do not apply, however, the CHS review process incorporates special protections when people who have a limited capacity to understand research or research concepts are potential research participants.

### 11.5.2. Research within the Jurisdiction of the DMH

Under 104 C.M.R. § 31.00, et. seq., DMH has the jurisdiction to review and approve any human research “related to” the Department, its facilities or programs in which its “clients” are proposed participants. HMS or HSDM Investigators whose research proposals fall within the DMH’s jurisdiction must submit them to the DMH IRB, the Central Office Research Review Committee (CORRC), for approval.

DMH regulations (104 CMR § 31.01 et seq.) describe information Investigators must submit to the agency concerning such studies, and the standards governing review and approval of studies by the agency, which are very similar to the standards of review utilized by IRBs operating under the 45 CFR § 46. However, the regulations impose a few additional content requirements for informed consent forms for these studies, beyond those included in the 45 CFR § 46, such as: statements describing “the basis for selection of the subject”, and a statement indicating that participation in the study is not required of participants in order to obtain continued access to DMH services. Please see DMH regulations (available through <http://www.mass.gov/dmh>) for specific information.

### 11.5.3. Research Protocol Considerations

For any research protocol that may involve persons with decisional or cognitive impairments:

- 1) Where applicable, the Investigator must describe the reasons why recruiting this vulnerable population is necessary.
- 2) The Investigator must consider whether and which of the following safeguards would be appropriate for the research and must document the decision process in his or her application to the CHS. The CHS may, at its discretion require additional safeguards. Where appropriate, for example, the CHS may require the Investigator to assess participants’ comprehension at various stages in the protocol.
  - a) Use of a party independent of the research team with appropriate expertise to assess the capacity of a potential participant. Investigators may conduct a preliminary **competency assessment** whenever there is a possibility of either impaired cognitive status or decision-making capacity in prospective participants, however, a final determination that the prospective research participant is incompetent or has an impaired decision-making capacity must be made and documented by a physician after appropriate medical evaluation. Consultation with a psychiatrist or licensed psychologist must be obtained when the physician’s determination that the prospective research participant lacks decision-making capacity is based on a diagnosis of mental illness.
  - b) Use of a standardized assessment of cognition and/or decisional capacity.
  - c) Use of methods that could enhance participants’ ability to decide for themselves whether to participate in the proposed research, such as, for example, reading the

- consent form aloud to the participant, showing a video recording to the participant, or communicating with the participant by some other method that is aimed at the participant's level of understanding.
- d) Use of other informational or educational techniques for the potential participants and/or their legal representatives. Tools to aid in this effort may include single sheet summaries of important information about key elements of the studies, regular opportunities for participants and their legal representatives to ask questions, and other educational tools to enhance understanding, including use of videos demonstrating study interventions or use of post-test assessments documenting comprehension.
  - e) Use of a party independent of the Investigators to monitor the consent process and verify what information was conveyed.
  - f) Use of waiting periods to allow potential participants additional time to consider information about the research protocol. Planning waiting periods into the informed consent process may be useful to increase comprehension in decisionally impaired populations and to allow involvement, where appropriate, of participants' legal representatives.
  - g) Obtaining informed consent by proxy from a participant's legally authorized representative. If feasible, the Investigator must explain the proposed research to the prospective participant even when his or her legal representative gives consent.
  - h) Where informed consent is obtained by proxy, also obtaining assent from participants. Under no circumstances may a person be forced or coerced to participate in a research study.

#### **11.5.4. Assent, Consent, and Legally Authorized Representatives and Proxy Consent**

Respect for the autonomy of individuals requires that, regardless of diagnosis or condition, all adults generally should be presumed competent to consent to participate in research unless there is evidence of a serious disability that would impair the individual's ability to comprehend either the voluntary nature of research participation, the nature of the research procedures, the potential risks and benefits of the study, and/or his or her ability to make a personal judgment about the value of participation.

Thus, ordinarily, an Investigator must obtain informed consent directly from prospective research participants. However, when the prospective participant is an adult whose own consent would not be legally effective because s/he lacks the capacity to comprehend or communicate informed consent, then research may be conducted only with the consent of the potential participant's **legally authorized representative** (the "LAR"), also known as "surrogate consent." This policy is designed to protect persons from exploitation and harm and, at the same time, make it possible to conduct essential research on issues that are unique to persons who are not competent, or who have an impaired decision-making capacity. The federal regulations

define “*legally authorized representative*” as “an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the participant's participation in the procedure(s) involved in the research.” 45 CFR 46.102(c). Under Massachusetts law, this means the consent must come either from the legal guardian of the participant, or, in the case of research that is part of medical treatment, from the participant’s health care agent (either as appointed under the Massachusetts health care proxy law, or as designated by a health care provider under the common law for obtaining consent to the provision of medical care and associated procedures). If the participant is able to give assent (affirmative agreement) this is required, but the CHS may waive the requirement if the participant is not competent to assent.

The Massachusetts Department of Mental Retardation (DMR) regulations concerning research are useful in understanding how Massachusetts defines “**guardian**.” Those regulations state that “with respect to persons 18 years of age and older,” a guardian is the “individual, organization or agency, if any, that has been appointed legal guardian of the person found to be incompetent by a court of competent jurisdiction.” 115 CMR 10.02. Massachusetts law allows for guardianships to be created for persons who are judged to be mentally ill or mentally retarded, or for persons judged unable to communicate informed decisions. M.G.L. c. 201 §§ 6, 6A, 6B. The guardianship law does not enumerate all of the guardian’s authority, except to say that the guardian “shall have the care and custody of his ward . . . and the management of all his estate.” As this authority is generally accepted to mean that the guardian may take all actions for the ward that the ward might have taken if competent, there is no reason to believe that the ability to consent to research is not within the guardian’s authority. Indeed, this view is consistent with the manner in which the DMR conducts its research using consent from guardians. See 115 CMR 10.00.

Massachusetts law provides for **proxy consent** for medical decisions to be given on behalf of a patient who does not have the capacity to consent. The law allows a competent adult to appoint a designated person as his or her “**health care agent**.” M.G.L. c. 201D. If the person then becomes incapacitated, and is in need of medical care, the health care proxy becomes empowered to make medical decisions on his or her behalf. If no health care agent has been appointed in advance, then medical care providers are authorized by the law to accept consent from “responsible parties,” under common law principles, usually meaning the patient’s next-of-kin. M.G.L. c. 201D, §16. It is generally accepted in Massachusetts that if research involves the provision of medical care, a health care agent, whether appointed or holding that status by virtue of being a “responsible party,” may consent to that treatment and to the accompanying research.

In light of Massachusetts law, federal policy, and existing judicial opinions on the interrelationships of the two, it is unclear whether an IRB may approve a study that involves consent by an LAR for a cognitively-impaired adult to participate in non-medical research in the Commonwealth with more than minimal risk to that participant. In such situations, the CHS will not approve research in which cognitively impaired adults participates in non-medical research in the Commonwealth with more than minimal risk to that participant until legal counsel determines that the individual proposed to serve as legally authorized representatives meet the federal definition of “legally authorized representative”.

#### **11.5.4.1. Additional Policies Relating to Proxy Consent**

In cases where a protocol approved by the CHS contemplates proxy consent, all of the following conditions apply:

- 1) Consent by proxy is not acceptable for research that presents an increase over minimal risk and does not have the potential for direct individual benefit.
- 2) Consent by proxy may be given only by the potential participants legally authorized representative (as discussed above).
- 3) Where informed consent is sought by proxy, the Investigator must fully inform the LAR about the risks, benefits and alternatives to the research. The LAR also must be informed that his or her decision should be made (i) in accordance with his or her assessment of the potential subject's wishes, including the potential subject's religious and moral beliefs, or (ii) if the potential participant's wishes are unknown, in accordance with the LAR's assessment of the potential participant's best interests. See M.G.L. Chapter 201D, § 5.
- 4) If a potential participant with decisional impairment is capable of exercising some judgment concerning the nature of the research and his or her participation in it, then the investigator should obtain the participant's assent in addition to the consent of his/her health care agent.
- 5) A potential participant's objection to participation in research, in whatever form, shall be binding. If the participant, at any time, objects to continuing in the research study, such objection must be respected and his or her participation shall cease.
- 6) Where the condition causing a participant's decisional impairment is of an intermittent or temporary nature, then the informed consent process should include a mechanism for obtaining the participant's subsequent direct informed consent to participate in the research. If the participant, upon regaining decisional capacity, declines to continue participation in the research, his or her decision must be respected and his or her participation shall cease.

#### **11.6. Participants with Limited Capacity to Speak English**

The CHS requires that research information and materials be presented to potential research participants in language understandable to them, which means that, where the potential participant has limited capacity to speak or understand English, all informed consent information, written and oral, must be translated into the language of the potential participant. Written consent documents, regardless of the language in which they are written, must contain all of the elements of consent, as noted in Section 10.3.1.1.

45 CFR § 46.117(b)(2) permits an Investigator to verbally present the information required to allow a participant to make an informed judgment about participation in research, provided that there is a witness to the oral presentation and the participant is given a written summary of the presentation (approved by the CHS), as well as a copy of the short form written consent

document (stating that the elements of consent have been presented orally). When this procedure is used with potential participants who do not speak English:

- (i) the oral presentation and the short form written document should be in a language understandable to the potential participants;
- (ii) the CHS-approved English language informed consent document may serve as the summary; and
- (iii) the witness should be fluent in both English and the language of the participant.

At the time of consent,

- (i) the short form document should be signed by the participant (or the participant's legally authorized representative);
- (ii) the summary (i.e., the English language informed consent document) should be signed by the person obtaining consent as authorized under the protocol; and
- (iii) the short form document and the summary should be signed by the witness. When the person obtaining consent is assisted by a translator, the translator may serve as the witness.

The CHS “must receive all foreign language versions of the short form document as a condition of approval” under the provisions of § 46.117(b)(2). Expedited review of these versions is acceptable if the CHS application/protocol, the full English language informed consent document, and the English version of the short form document have already been approved by the CHS.

If research is taking place in settings where the primary language spoken is not English, and the Investigator and study staff are fluent in that language, then the witness need only be fluent in the language of the potential participant (for example, if the research is taking place in Mexico and the Investigator, study staff, potential subjects and witnesses all are fluent in Spanish, then there is no need for the witness to speak English).

When study materials are translated into languages other than English, the English and other language (e.g. Spanish, French, Mandarin, Creole) versions of all materials to be used with potential participants (such as recruitment notices, consent forms and survey instruments) must be submitted to the CHS for review and approval accompanied by the Translation Attestation Form signed by the Investigator.

### **11.7. Participants with Economic Disadvantages**

HMS/HSDM faculty and students at times perform research, both in the US and abroad, with people who have limited resources in terms of finances, health, goods, and/or access to services. The CHS pays particular attention to remuneration and other inducements that might encourage people with limited resources to participate in research projects in which they might not otherwise participate. Money, goods and/or services should not be the sole grounds for participation in a research project and these inducements should not cause participants to assume risks that they would not ordinarily find acceptable.

The CHS considers persons with limited resources to be vulnerable to the extent that inducements to participate in research may result in their acting against their own best interests. Where the population from which participants will be recruited primarily consists of people with limited resources, the CHS will look carefully at recruitment procedures, the potential risks in relation to the compensation being offered and the potential benefits irrespective of compensation. The Investigator will be asked to justify the compensation being offered. If the CHS finds it to be coercive, the CHS will ask the Investigator to provide alternative compensation so as not to impede the participants' decision about whether they should participate in the research project.

### **11.8. Participants with Educational Disadvantages**

Research may involve participants who have limited education and either cannot read or write, or may do so at a lower level than the general population of a given community. Of course, the ability to read or write may not be an indication of a person's ability to understand the research, the procedures involved, the risks and benefits associated with the research, or the ability to make an informed decision about whether to participate in the research. When research is likely to involve persons who cannot read or write or who do so at a low level, the CHS is likely to require the use of materials (pictures, demonstrations, videos, etc.) that aid in understanding the risks, benefits and procedures involved in the research. In addition, the CHS may require an assessment of the participant's understanding (i.e. a short quiz) after the consent is read and explained, as well as a witness to the consent process who will also be required to sign the consent form. Consent requirements are the same as required by 45 CFR § 46.116 and 117.

### **11.9. Participants with Stigmatizing Conditions**

The CHS is particularly mindful of the privacy and confidentiality needs of person who has a stigmatized condition, such as HIV or AIDS, sexually transmitted diseases or mental health issues. Investigators working with people with such conditions must incorporate special protections into the recruitment, consent, study and follow-up procedures, form of remuneration, data storage, data analysis, data destruction and study publications. While the CHS understands that there may be public health reporting requirements for some conditions, the privacy of research participants must always be maintained.

Suggested practices:

*Recruitment* - Direct mailings should not indicate that a person has a certain condition; if the potential participant is required to call to inquire about the study, a person knowledgeable about the study should answer the phone, and only study personnel should have access to the phone messages. When the Investigator or study personnel return a potential participant's call, s/he should only leave their name and contact information – not information about the study or condition being studied.

*Consent* – Consent should take place in a private setting where the discussion is unlikely to be overheard by others. Consent materials should contain a tear-off sheet with the name and contact information of the Investigator, in case the participant does not wish to carry a copy of the entire consent form. Participants should always be advised that while the Investigator and study personnel will do his/her best to maintain their privacy and confidentiality, it is always possible

that a breach in confidentiality could happen, or that others close to them may guess their condition or participation in a study.

*Study/follow-up Procedures* – study and follow-up procedures should take place in a private setting, whenever possible. While some research may take place in a participant’s home, the Investigator should take measures not to obviously identify themselves to family and neighbors. Investigators working in international settings may have more difficulty not being obvious, therefore alternative settings for research procedures should be considered.

*Form of Remuneration* – Remuneration pay slips or checks should not contain the name of the study, nor should they include the social security number of the participant.

*Data Storage* – Data should be stored in secure and private settings. Hard copies of study documents (such as medical histories and questionnaires) should not contain the name of participants and codes/keys to any participant IDs should **never** be kept with study documents. Data stored on laptop or desktop computers should be password protected at the very least, and whenever possible, data should be maintained on a separate disk or accessed on a secure server.

*Data Destruction* – Investigators must have a plan for when and how they will strip data of participant’s personal identifiers and should notify participants of this practice.

*Publications* – No publications should contain a participant’s personal identifiers or scenarios that could identify a participant by someone close to them. In certain situations, however, the participant may want to be identified – if this case arises, it should be discussed with the CHS and a special permission for the use of the participant’s name and or image may be used.

#### **11.10. Participants who are Students, Fellows, or Employees of Harvard University**

University employees, fellows and students may participate in any study for which they are eligible. However, in order to prevent any coercion (or perception of coercion) or undue pressure to participate, Investigators should not specifically recruit individuals who work directly or indirectly for them, nor should they recruit fellows or students who work with or for them, or for whom they have any educational oversight.

Participation in a research study may never be a condition of employment, insurance, grades, promotion, or any other benefits or bonuses. The CHS is particularly mindful of situations that may put undue pressure on employees, fellows or students to participate in research projects, and thus recommends that Investigators refrain from directly soliciting participants from these populations. Instead, all recruitment should take place via public forums, such as bulletin boards and school notices where those interested in participating may contact the Investigator.

The Faculty Council of the Harvard Faculty of Medicine in 1986 set forth the *Rules Governing the Participation of Medical Students as Experimental Subjects in Research Studies* (Appendix 49) which apply to research projects specifically recruiting (or conducted with) Faculty of Medicine students in biomedical research.

### **11.10.1. Curriculum Studies and Studies Specifically Recruiting Students**

#### **11.10.1.1. Harvard Medical School**

Research involving HMS curriculum or specifically recruiting/targeting HMS students must be reviewed and approved by the HMS Center for Evaluation (CfE) Research Review Committee (RRC). The CfE will perform its own review of the research to make sure it is in keeping with the values and direction of the University and the curriculum, where appropriate. When CfE has approved the study, the CHS application, study materials and CfE approval letter will be forwarded to the Dean for Medical Education (or the Dean of Students, if the project does not involve curriculum) for further approval and signature on the CHS application. The Dean for Medical Education's (or Dean of Students) office will forward the CHS application and all related materials (including the CfE RRC approval letter) to the CHS office for its review. No curriculum study or study specifically recruiting or targeting students at HMS can take place without all three (CfE, Dean for Medical Education/Dean of Students, and CHS) approvals.

Amendments to these studies must first be submitted to the CHS Office. If the CHS determines that the change is minor, the CHS will review the amendment and copy the CfE on the approval notice. If the CHS determines that the change is major, it will send the amendment materials to the CfE for review and approval first, and once CfE has approved the changes, it will send the materials to the CHS office for final review and approval.

#### **11.10.1.2. Harvard School of Dental Medicine**

Research involving HSDM curriculum or specifically recruiting/targeting HSDM students must be reviewed and approved by the HSDM Office of Dental Education (ODE) and HSDM Office of Research. The ODE will perform its own review of the research to make sure it is in keeping with the values and direction of the University and the curriculum, where appropriate. When the ODE has approved the study, the CHS application and all study materials will be forwarded to the HSDM Dean for Research for further approval and signature on the CHS application. The HSDM Dean for Research will forward the CHS application and all related materials back to the Investigator, who will then be required to submit all materials and approvals to the CHS for its review and approval. No curriculum study or study specifically involving students at HSDM can take place without all three (ODE, Dean for Research, and CHS) approvals.

### **11.11. Investigator Self-Experimentation**

The Faculty of Medicine does not prohibit Investigator self-experimentation. However, as it would with any proposed research, the CHS will review each protocol and determine the appropriateness of the research. The CHS will consider as part of its review the level of self-experimentation and the potential risks and benefits to the Investigator as a research participant.

One of the main concerns of the CHS is that the enthusiasm for a novel concept may outweigh the Investigator's concern for his/her own welfare. For this reason, the CHS may require that a Department Chair or even a CHS member obtain informed consent from the Investigator. The CHS also may institute additional safeguards for the research project, such as shorter review periods and monthly progress reports.