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AND MASSACHUSETTS GENERAL HOSPITAL

Title:	Informed Consent of Research Subjects
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Applies to:	Employees, Professional Staff or Other Agents of Brigham and Women's Hospital (BWH), Faulkner Hospital (FH), Massachusetts General Hospital (MGH), McLean Hospital (McLean), and North Shore Medical Center (NSMC)
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Contact Person:	Director, Human Research Review and Compliance

KEYWORDS:

IRB, Institutional Review Board

PURPOSE:

The purpose of this policy is to define the requirements for obtaining and documenting informed consent of research subjects.

DEFINITIONS:

See Definition of Human Subjects Research

POLICY STATEMENT:

When employees or agents of the applicable Partners-affiliated entities conduct human-subjects research at the entities or under the auspices of the applicable Partners-affiliated entities, informed consent will be obtained in compliance with all applicable federal and state regulations and the requirements of the Partners Human Research Committee.

Background

Informed consent is a vital part of the research process, and as such entails more than obtaining a signature on a form. Investigators must educate potential subjects to ensure that they can reach a truly informed decision about whether or not to participate in the research. Their informed consent must be given freely, without coercion, and must be based on a clear understanding of what participation involves.

The process of educating subjects about the study begins during initial contact and continues for the duration of their participation. Thus, information conveyed through advertisements, recruitment letters, pre-screening phone calls, study description sheets as well as written informed consent documents and discussions must be understandable to the subjects and should contribute to their understanding of the research. Technical and medical terminology should be avoided or explained in “lay” language, and materials should be written at an 8th grade reading level or lower. Non-English speaking subjects must have information presented in a language they understand (refer to [Obtaining and Documenting Informed Consent of Subjects Who Do Not Speak English](#) for guidance). The Partners Human Research Committee (PHRC) must approve written and oral information (including recruitment materials) provided to subjects before and during the informed consent process.

Consent Discussion

The consent discussion should begin sufficiently in advance of the initiation of study-related procedures to allow potential subjects time to reflect on the potential benefits and risks and possible discomforts of participation. The following method is preferred by the PHRC, though clearly it may need to be tailored to the circumstances of individual studies and may not be appropriate or feasible in all situations. First, potential subjects are given general information about the research (e.g., through advertisements, information sheets, letters or discussion with their treating physicians), and if they are interested in learning more about the study, they contact study staff. The investigator then meets with the potential subject to review and to discuss the details of the research study using the informed consent document as a guide. This discussion should include all of the required elements of informed consent, e.g., the purpose of the research, the procedures to be followed, the risks and discomforts as well as potential benefits associated with participation, and alternative procedures or treatments, if any, to the study procedures or treatments.

Preferably, potential subjects are then given a copy of the informed consent document to take home so they can carefully read the document and discuss the research with their family, friends and/or physician and develop questions to ask at their next meeting with the research staff. Please note that subjects must always be given the opportunity to ask questions and have them answered by the investigator and, whenever possible, to consult with friends/family and/or their physicians. Once they have read the consent document and their questions are answered, if they agree to participate in the research, they sign and date the informed consent document. (Note also that under the new federal Privacy Rule, subjects must be asked as well for written authorization for the use and disclosure of their identifiable information for research. For an explanation and forms, see [HIPAA and the Privacy Rule](#).)

Timing of Informed Consent

Special consideration must be given to the timing of the consent process when the subject population includes patients who will be same-day admissions for surgical procedures or who present for diagnostic or other tests, such as cardiac catheterizations or radiological

examinations. Clearly, the time frame for the consent process will be more limited in these situations. Generally, the investigator should allow potential subjects at least 12 hours to consider participation. Whenever possible, the patient's physician should be asked to provide potential subjects with information about the study well in advance, for example, when the surgery, test, or examination is scheduled.

With few exceptions, the informed consent of subjects, whether patients or healthy volunteers, must be obtained and documented in writing before the start of any study-related procedures, including screening tests and exams done solely to determine their eligibility for the study (refer to [Pre-screening of Research Subjects During Recruitment](#) for guidance). Informed consent is to be obtained directly from each subject, with the exception of children (see below) and adults who have impaired decision-making capacity. For guidance, refer to the [Obtaining Surrogate Consent to Research for Individuals with Impaired Decision-Making Capacity](#) memo (Partners Intranet link). Once the informed consent document has been signed, subjects are considered enrolled in the study.

Individuals Who Can Obtain Informed Consent

For most studies involving more than minimal risk and all studies involving investigational drugs/devices, a licensed physician investigator listed on the protocol must obtain informed consent. Study nurses or other study staff may assist in the consent process, but physicians should be actively involved in the consent discussions and should not delegate this vital investigator function. It is the investigator's responsibility to ensure that proper informed consent is obtained from every subject according to the procedures approved by the PHRC.

For minimal risk studies and very carefully selected studies involving more than minimal risk (but not investigational drugs/devices), it may be appropriate for study nurses or other study staff to obtain consent, with "back up" provided by licensed physician investigators. The PHRC will allow a licensed nurse or non-licensed physician investigator to obtain informed consent if that nurse or non-licensed physician would be permitted, in a clinical setting, to perform the procedures for which consent is required. If the investigator proposes that other than licensed physician investigators obtain informed consent, the rationale and justification for this approach and the qualifications and training of the relevant study staff must be submitted to the PHRC for review and approval.

If subjects are to be enrolled from among the investigator's own patients, consent procedures must be put in place to ensure that subjects do not feel obligated to participate because the investigator is their treating physician. There is always concern about the possibility of patients feeling obligated to participate because it is their physician who is doing the asking. While the PHRC does not have an absolute prohibition about physicians obtaining consent from their own patients, researchers are asked to think about this issue and address it. There are many possible ways to do this. One can contact the patient in writing initially, and allow him/her to make the first contact if interested. One can ask a physician colleague to present the study to a patient to try to make it more impartial. One can have a nurse or colleague re-contact the patient after the investigator has had the consent discussion and offer them an opportunity to ask additional questions, raise concerns, or opt out, with someone who is not their physician.

Surrogate Consent for Adults

Federal regulations require informed consent for research to be obtained from the subject or the subject's legally authorized representative. In general, research that involves more than minimal risk and no anticipated direct medical benefit to subjects should be conducted in subjects who

personally give consent and who sign and date the written consent document. When investigators propose research that involves adults who are unable to give informed consent to participate in the research, they must follow PHRC guidance on Surrogate Consent to Research for Individuals with Impaired Decision-making Capacity (Partners intranet link).

Obtaining Parental/Legal Guardian Consent for Children

Federal regulations require that consent to participate in research on behalf of a child be provided by a parent or an individual authorized under applicable state or local law to provide consent on the child's behalf to general medical care. Under Massachusetts law, a parent is generally authorized to consent to general medical care on behalf of their child. However, in some circumstances (such as when both parents are deceased), it may be necessary to identify another individual with this authority (for example, a court-appointed guardian). Before an investigator allows an individual other than a parent to consent on behalf of a child, the investigator should document the basis for the individual's authority to consent on behalf of the child to general medical care and place any relevant documentation in the research file. In situations when it is unclear under state law who has the authority to provide consent to general medical care on behalf of a child, and thus who can consent to the child's participation in research, the PHRC will consult with the Office of General Counsel as needed.

Under the federal regulations, where consent to the research is to be provided by a child's parent and the research involves no greater than minimal risk or greater than minimal risk, but with the prospect of direct benefit to the subjects, the PHRC may decide that consent of one parent is sufficient. However, when the research involves greater than minimal risk and no prospect of direct benefit to the subjects, permission must be obtained from **both** parents, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when one parent has legal responsibility for the care and custody of the child.

In addition to permission of the parent(s) or guardian, assent to participate in the study must be obtained from each child age 7 years or older who, in the opinion of the investigator, is able to provide assent based on their age, maturity or psychological state. When the PHRC determines 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 involved in the research and the intervention or procedure is only available in the context of the research, the assent of the children is not a necessary condition for proceeding with the research. Even when the children are capable of assenting, the PHRC may waive the assent requirement as described elsewhere in this document [Alteration or Waiver of Elements of Informed Consent].

When obtained, assent must be documented in writing using the PHRC-approved consent/assent form. When assent is not obtained, the investigator must document his/her rationale in the research records.

Minors Who Can Give Legally Effective Informed Consent

Under Massachusetts State law and applicable Partners-affiliated entities' clinical policies, some minors (less than 18 years of age) can provide legally effective consent for their own medical care, in certain circumstances, without parental consent or knowledge and therefore may not meet the DHHS and FDA definition of "children" and the requirements of Subpart D may not apply. "Emancipated" minors, i.e., those who are married, widowed or divorced, or have a child or are pregnant (or believe themselves to be), are in the armed forces, or living apart from their parents and managing their own affairs, can provide informed consent for their own medical care. Minors in Massachusetts may also give consent to research procedures that involve:

- psychiatric treatment, if the minor is 16 or over;

- treatment of drug dependency, if the minor is 12 or over; and
- treatment of certain diseases dangerous to public health (VD and others).

Because these minors nonetheless may represent a vulnerable population, the IRB will review all consent issues involving these minors on a case-by-case basis to ensure that any required additional protections are met. For example, although these minors may be allowed to consent to the research, the IRB may decide that permission of a parent or other individual is appropriate either instead of or in addition to the minor's consent.

If the PHRC approves the obtaining of informed consent from specified minors, informed consent follows generally the same procedures that are being followed for adults. The investigator must also document the specific circumstances that justify designating a particular subject less than 18 years of age as capable of providing consent to the treatments and procedures involved in the particular research.

Use of a Subject Advocate

In certain situations, the PHRC will require the use of a subject advocate in the consent process. The subject advocate is an individual who has no vested interest in the research and who agrees to act as an impartial third party in the consent process. When a subject advocate is appointed, the subject advocate is expected to act in the best interests of the subject by sharing in discussions with the investigator and with those responsible for giving consent. Individuals who might fulfill this role include the subject's primary care physician or other health care professional not involved in the research. The subject advocate is responsible for ensuring that the subject understands the research procedures and the risks and potential benefits of participation and that his/her consent is free and voluntary. When a subject advocate is used, the subject advocate must sign and date the consent form.

Situations in which the use of a subject advocate may be required include:

- when the risks to subjects are significant and the subject is the patient of the investigator and, as such, may feel obligated to participate; or
- when consent is to be obtained in the emergency room or in an emergency situation when the time frame to obtain consent prior to start of study-related procedures is limited; or
- when surrogate consent is to be obtained for research involving more than minimal risk with the potential for direct benefit to the subject.

Documentation of Informed Consent

In almost all cases, investigators must document the informed consent process by use of a written consent document (research consent form) signed and dated by the subject or his/her legally authorized representative (or surrogate) and the investigator (or study staff if approved by the PHRC) who obtained the subject's consent. When the research will begin on the same day that informed consent is obtained, the PHRC recommends recording time of consent in addition to date of consent to document that informed consent was obtained prior to any study-related procedures. In certain situations, the PHRC may approve a waiver or alteration in the consent process (see below).

The research consent form must include the following information about the study:

1. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;
2. A description of any reasonably foreseeable risks or discomforts to the subject;
3. A description of any benefits to the subject or to others which may reasonably be expected from the research;
4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
5. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained, and when applicable, that notes the possibility that the Food and Drug Administration may inspect the records;
6. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;
7. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and
8. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

When appropriate, the following information must be provided to each subject:

1. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;
2. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
3. Any additional costs to the subject that may result from participation in the research;
4. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;
5. A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; and
6. The approximate number of subjects involved in the study.

NOTE: Any informed consent, whether written or oral, must not include exculpatory language such that the subject is made to waive, or appear to waive, any of his or her legal rights or to release the institutions or its agents, the investigators, from liability or negligence.

Examples of exculpatory language:

- By agreeing to this use, you will give up all claim to personal benefit from commercial or other use of these substances.
- I voluntarily and freely donate any and all blood, urine, and tissue samples to the U.S. Government and hereby relinquish all right, title, and interest to said items.
- By consent to participate in this research, I give up any property rights I may have in bodily fluids or tissue samples obtained in the course of the research.

- I waive any possibility of compensation for injuries that I may receive as a result of participation in this research.

The entire text of all research consent forms must be approved by the PHRC as part of the review process. The effective date of the PHRC-approved consent form and expiration date of PHRC approval (one year or less) are noted in the footer added to the research consent form by the Human Research Office staff. Subjects must be given and sign the most recently approved version of the research consent form. Out-dated and/or expired research consent forms must not be used in the consenting process and to document informed consent.

Usually, three copies of the signed and dated research consent form are needed. The original signed and dated research consent form should be retained in the research records. A copy of the signed and dated research consent form must be given to the subject and a copy placed in the subject's medical record, if relevant to his/her ongoing medical care. If the study involves sensitive research, (e.g., alcohol or drug use, some genetic studies) a copy of the research consent form ordinarily should not be placed in the subject's medical record. (If the sensitive study involves a drug or otherwise might implicate care decisions, the investigator should discuss with the IRB how best to make this information available to a caregiver with a need to know.)

To further document and facilitate clarification of any future questions regarding the consenting process, the investigator should consider including the following information in a clinic chart/progress note/other source document: that XX study was explained, questions were answered (if any), subject agreed to participate and signed the consent form, and a copy of the signed consent form was given to subject. This note should be signed and dated by the person obtaining consent.

Waiver of Written Informed Consent

The PHRC may waive the requirement to document informed consent with a signed written informed consent document (consent form) for some OR all subjects if it finds either: (1) that the research is not subject to FDA regulations and the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether s/he wants documentation linking him/her with the research, and his/her wishes will govern;

If the PHRC approves waiver of signed consent based on consideration **(1)**, the full consenting process for these subjects including being given a written informed consent document embodying all the elements of informed consent remains the same except that the subject will have the option to not sign the consent document or have information linking them to the study placed in their medical file.

OR

(2) that the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

If the PHRC approves a waiver of the requirement to obtain a signed written consent form based upon consideration **(2)**, investigators must fully inform prospective subjects about the study, answer their questions and obtain their verbal informed consent. In lieu of a written consent form, the PHRC may require the investigator to provide subjects with a written statement regarding the research. (To obtain oral authorization for use/disclosure of identifiable

information under the Privacy Rule, see Obtaining Oral Authorization For Use and Disclosure of Identifiable Information.)

When the PHRC approves a waiver of the requirement to obtain a signed written consent form based upon consideration **(2)**, the investigator should consider including the following information in a clinic chart/progress note/other source document: who was approached, for what study, who explained the study, brief summary of what was explained, subject (or surrogate) expressed an understanding of the research study and willingness to participate, questions (if any) were answered to the subject's satisfaction, subject agreed to participate, and written information about the study was given to the subject, if appropriate. This note should be signed and dated by the person obtaining consent.

Alteration or Waiver of Elements of Informed Consent

The PHRC can approve a consent process that does not include, or that alters, some or all of the elements of informed consent or even waive the requirement to obtain informed consent provided the PHRC finds that the research is not subject to FDA regulations and documents that all of the following requirements are met:

1. the research involves no more than minimal risk to the subjects;
2. the waiver or alteration will not adversely affect the rights and welfare of the subjects;
3. the research could not practicably be carried out without the waiver or alteration; and
4. whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Requests for alterations in or a waiver of informed consent requirements should be made in writing and justified by addressing each of the 4 points above. (For waiver or alteration of authorization under the Privacy Rule, see Waiver and Alteration of Informed Consent and Authorization for Research.)

Obtaining New Consent and/or Notifying Subjects of Major Changes to any Component of the Informed Consent Document

Subjects should be asked for new consent -- i.e., through the investigator's explanation and request to sign a revised, PHRC-approved consent form -- when they are actively engaged in the research and there have been major changes to any component of the consent form, e.g., drug dose(s), device, study procedures, risks and discomforts, benefits, and alternatives. This is paramount if knowledge of the new information might affect subjects' willingness to continue participation. Subjects should also be notified of a change of the principal investigator or contact information; however, in most cases this type of change can be adequately communicated in a letter. Please note that a change in co-investigators and/or study staff is not considered a major change requiring new consent or notification.

It is important to note that as part of the review of amendments to the protocol and/or informed consent document, the PHRC will determine whether the change(s) require obtaining new consent from subjects enrolled in the study.

Examples of when a subject should be asked for new consent in writing:

- the Procedures section of the consent form has been revised to include a new procedure that the subject will be asked to undergo, e.g., genetic testing, cardiac catheterization, biopsy, colonoscopy, mammogram, ultrasound, etc. An investigator

may not perform a procedure on a subject without new consent if the procedure was not mentioned in the original consent process and form.

Subjects should be given the following information in a timely manner so that they can make a fully informed decision about whether they wish to continue their participation. The greater the import of the new information, the more quickly subjects should be made aware of it.

- the Risks and Discomforts section of the consent form has been revised to include a newly identified serious adverse event
- the Risks and Discomforts section of the consent form has been revised to include a change in the severity or frequency of a serious expected event
- the Alternatives section has been revised to include newly identified alternative therapies or diagnostic tests
- the Procedures and Alternatives section have been revised to include a change in FDA approval status of the drug or device being studied

Examples of when the PHRC may approve a letter being sent to notify the subject of the change include:

- the principal investigator has been changed
- the study contacts have been changed and/or the contact telephone numbers have been changed
- the subject has completed the study interventions and is in the follow-up phase of the study or in some cases has completed the study, and the information is such that learning it would not materially affect the subject's decision to continue participation in follow-up

Withdrawal of Subjects: Record Retention and Requirements for Informed Consent for Continued Limited Participation

When a subject withdraws from the study before completion, there may be concerns about how to handle the incomplete set of data. Investigators may contact the IRB Office to discuss these situations. Note that when the study is regulated by FDA, the FDA takes the position that the data that has already been collected cannot be removed from study databases and that the consent document cannot give the subject the option of having this data removed.

An investigator may ask a subject who is withdrawing whether s/he wishes to provide continued follow-up and further data collection subsequent to his/her withdrawal from the interventional portion of the study. The discussion with the subject about his/her limited continuation in the study should distinguish between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through noninvasive chart review, and address the maintenance of privacy and confidentiality of the subject's information. If the subject agrees, the investigator must obtain the subject's informed consent for this limited participation using a separate PHRC-approved consent form, unless this limited participation after subject withdrawal was described in the original PHRC-approved consent form. If the subject does not agree, the investigator must not access for purposes related to the study the subject's medical record or other confidential records requiring the subject's consent. However, an investigator may review study data related to the subject collected prior to the subject's withdrawal from the study, and may consult public records, such as those establishing survival status.

REFERENCE:

45 CFR 46

21 CFR 50

Guidance for Sponsors, Clinical Investigators, and IRBs: Data Retention When Subjects Withdraw from FDA-Regulated Clinical Trials, October 2008

ATTACHMENTS:

Federal Requirements for Informed Consent

DEVELOPMENT AND CONSULTATION

Human Research Office

Office of the General Counsel

Reviewed by:	Original Review Date:	Revision Approval Dates:

FEDERAL REQUIREMENTS FOR INFORMED CONSENT
(45 CFR 46.116 and 21 CFR 50.25)

The Department of Health and Human Services (DHHS) regulations [45 CFR 46.116(1)(1-8)] and the Food and Drug Administration (FDA) regulations [21 CFR 50.25(a)(1-8)] require that the following basic elements of informed consent be provided to each subject:

- (1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;
- (2) A description of any reasonably foreseeable risks or discomforts to the subject;
- (3) A description of any benefits to the subject or to others which may reasonably be expected from the research;
- (4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
- (5) A statement describing the extent, if any, to which confidentiality of records identifying the subjects will be maintained, and when applicable, that notes the possibility that the Food and Drug Administration may inspect the records;
- (6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;
- (7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject;
- (8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

When appropriate, one or more of the following elements of information shall also be provided to each subject [45 CFR 46.116(b)(1-6) and 21 CFR 50.25(b)(1-6)]:

- (1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject may become pregnant) that are currently unforeseeable;
- (2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
- (3) Any additional costs to the subject that may result from participation in the research;
- (4) The consequences of a subject's decision to withdraw from the research, and procedures for orderly termination of participation by the subject;
- (5) A statement that significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to the subject; and
- (6) The approximate number of subjects involved in the study.