PARTNERS HEALTHCARE | FOUNDED BY BRIGHAM AND WOMEN'S HOSPITAL AND MASSACHUSETTS GENERAL HOSPITAL

Title:	Informed Consent of Research Subjects
Issuing Entity:	PHS (Partners HealthCare System)
Business Unit:	PHS (Partners HealthCare System)
Department:	Human Research Affairs
Policy Type:	Partners System-wide
Applies to:	Employees, Professional Staff or Other Agents of Brigham and Women's Hospital (BWH), Faulkner Hospital (FH) and Massachusetts General Hospital (MGH). McLean Hospital (McLean), North Shore Medical Center (NSMC), Spaulding Rehabilitation Hospital (SRH), and MGH Institute of Health Professions (MGH IHP)
Approved by:	Chief Academic Officer
Original Approval Date:	08/01/2008
Original Effective Date:	08/01/2008
Current Revision Effective Date:	04/10/2017
Next Review Date:	04/10/2020
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

Scope and Applicability:

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 or agree to be contacted by 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 HIPAA and the Privacy Rule, subjects must be asked as well for written authorization for the use and disclosure of their identifiable information for research. The HIPAA authorization is included in the privacy section of the consent form. For more information, see HIPAA and the Privacy Rule.

Individuals Who Cannot Read the Consent Form

When a person cannot read the consent form, the entire consent form may be provided as an audio recording that the person can listen to, in an electronic format that the computer can read to the person or, for persons who are visually impaired and able to read Braille, in Braille. These formats afford people who cannot read the consent form with equivalent consent procedures and an accessible version of the consent document for their records. When the consent form is provided in these formats, the investigator or person obtaining informed consent should confirm that the subject listened to the audio version or electronic consent form, or read the Braille consent form when they begin the consent discussion and provide an opportunity to review the information and ask questions. When enrollment of subjects who cannot read the consent form is anticipated, the protocol submission should include a description of the process for obtaining and documenting informed consent of subjects who cannot read the consent form.

Remote (Phone) Consent

Remote consent by phone may be considered on a case-by-case basis, and should be appropriate for the study. Consent discussions may take place by phone in situations where it is not possible for the participant/legally authorized representative (surrogate) to meet with the investigator in person. When investigators anticipate the need to obtain informed consent by phone, they should justify in the protocol submission why this is necessary, and describe how the phone consent process will be operationalized and documented. The remote (phone) consent process must be approved by the IRB.

An example of a study for which remote consent by phone may be considered is a time sensitive therapeutic intervention in acute stroke patients where the patient is not able to give consent and an appropriate surrogate is not physically available. In this situation,

the investigator would call the surrogate and send them the consent form electronically. The surrogate would review the consent form, discuss participation in the study with the physician investigator, sign and date (including time) the consent form agreeing to the patient's participation in the research and return the signed (handwritten or digital) and dated consent form electronically. We recommend that consent discussions that take place by phone include a healthcare worker not associated with the study as a witness to the consent process. The investigator and, if applicable, the witness should sign and date (including time) the consent form signed and dated by the surrogate.

Remote (Mail) Consent

Remote consent may also be considered for certain minimal or low risk studies where some or all of the potential subjects are unable to meet with the investigator in person due to logistical or other reasons. When investigators anticipate the need to obtain informed consent by mail, they should justify in the protocol submission why this is necessary, and describe how the mail consent process will be operationalized and documented. The remote (mail) consent process must be approved by the IRB.

When documentation of informed consent is required in writing, the consent form is sent to the prospective subject by USPS or other mail carrier, or electronically. If the consent form is sent and returned by mail, include two copies - one for the subject to keep for their records. The person reads the consent form and contacts the investigator if s/he wishes to discuss participation in the study or has any questions about the study. If the person agrees to be in the study, they sign and date the consent form and return it by mail, or electronically to the investigator. When there is a line for signature of the person obtaining informed consent in the consent form, the person verifying informed consent would sign and date the consent form upon receipt.

An example of a study for which remote consent by mail may be considered is a genetic study where only medical and family history and a mailed blood sample are needed. Another example is a study of a vitamin supplement provided by mail, where subjects take the vitamin, answer medical questionnaires and request their physicians send their medical records to researchers. The opportunity to discuss the study and ask questions must be offered, but some subjects may find no discussion is necessary. Consent discussions should be documented in the research records. The person verifying informed consent should sign and date the consent form when they receive the signed consent form and confirm eligibility and enrollment of the subject in the study.

Timing of Informed Consent

Special consideration must be given to the timing of the consent process when the subject population includes patients who will, for example, 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). For example, subjects might be asked to fast before a morning blood draw or to bring in a stool sample to a screening visit. The subject's agreement can be documented in the research records.

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 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 informed 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 asking. While the PHRC does not absolutely prohibit 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 pursue it further, 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.

Individuals Who Can Give Informed Consent/Permission
Informed consent is to be obtained directly from subjects, with the exception of adults with impaired decision-making capacity and children. Once the informed consent document has been signed, subjects are considered enrolled in the study.

Surrogate Consent for Adults
Federal regulations require informed consent for research to be obtained from the subject or the subject's legally authorized representative (surrogate). 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 research, they must follow PHRC guidance on
Surrogate Consent to Research for Adult Individuals with Impaired Decision-making Capacity..

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 record. 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 generally should 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 assent is not obtained, the investigator must document his/her rationale in the research records.

Assent of Children
When assent is obtained, it is generally advised that it be documented in writing using the PHRC-approved consent/assent form. Written assent is not always mandated and investigators may request verbal assent. When assent of children is planned, the protocol submission should include a description of and justification for the method chosen for obtaining and documenting assent of children.

Children Who Turn 18 During Study Participation
Children who turn 18 years of age while they are participating in a study are now adults and must give consent to continue their participation if any of the study procedures that remain require informed consent for participation, including consent to future uses of individually identifiable speciments or data.

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 relevant regulatory requirements 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:

- psychiatry 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 (e.g., sexually transmitted infections and others).

Because minors who can consent to the treatments specified above nonetheless may represent a vulnerable population, the IRB will review all consent issues involving these minors on a case-by-case basis. For example, although minors may be legally allowed to consent to the research procedures independently, the IRB may decide that permission of a parent or other individual is feasible and appropriate either instead of, or in addition to, the minor's consent.

When the PHRC approves the obtaining of informed consent from "emancipated" minors or minors for the treatments specified above, 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. This documentation would usually be in a note to clinical and/or research records

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 a health care professional knowledgeable about, but not involved in, the research. Psychiatrists, social workers, or nurses, all typically with specialized expertise in a given field of medicine, have been chosen as advocates in studies supervised by the PHRC. Advocates should be formally identified, and may be paid for their time. 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;
- 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;
- when surrogate consent is to be obtained for research involving more than minimal risk with little or no potential for direct benefit to the subject;
- when exceptionally challenging or risk research is performed; or
- when many potential participants are expected to overestimate the likelihood of health benefits.

Documentation of Written 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. The basic and additional elements of informed consent, i.e., the information required by regulation to be provided to subjects, are provided in Appendix 1.

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 substance.
- 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.
- I agree to indemnify the sponsor, should there be any misuses of the mobile health application provided to me as part of 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 post approval. Subjects must be given and sign the most recently approved version of the research consent form with the PHRC approval information in the footer, also referred to as the 'stamped' version. Outdated and/or expired research consent forms must not be used.

Digital Signatures
"Digital signatures" may be acceptable forms of documentation of written informed consent. Electronic, computer or tablet-based consent documents may facilitate record keeping even when an individual is present and could sign a paper form. Digital signatures may be considered for face-to-face and remote consent, but the technologies and processes used must be described in the protocol submission and approved by the PHRC.

There are two forms of digital signatures: (1) actual signatures on tablets or computers (where an individual uses a stylus or finger to make a representation of their signature, as available in many retail stores) OR (2) validated electronic signatures on platforms with password entry (such as those used to sign medical notes or electronically write prescriptions). Validated electronic signatures typically require one to "set up" an identity and password within an electronic system, and may not be easily and rapidly activated. Both forms of digital signature may be used in research in certain settings, but because of tracking, privacy and identity validation issues, this may be more challenging than it initially appears. Both 'digital signature' methodologies, if used entirely remotely, are generally approved only for low risk research because it is not always possible to validate the identity of the individual "on the other end of the computer." When a stylus is used to collect a signature in person, the usual methods of identity validation should be used (typically patient is asked to provide a picture identification card when they check in at the clinic). Note: Scanned signatures that are copied and pasted to a document are not acceptable "digital" signatures.

When validated password-protected signature platforms are proposed, investigators must use a Partners-approved platform, such as Adobe Esign or RedCap, and address the platform and identity validation in the submission. If alternative platforms are being considered, please discuss with the Research Information Security Officer prior to submitting the protocol to the PHRC.

Individuals Who Cannot Write or Are Physically Unable to Sign the Consent Form
When a person cannot write or is physically unable to sign the consent form, they can make their mark on the signature lline in the consent form. People who cannot make their mark on the consent form can indicate consent by other means, e.g., orally, nodding their head, etc. The means by which consent was given by the subject should be documented in the consent form and research record.

Documentation of the Consent Process
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 (or legally authorized representative) 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. Details about subject/child assent, and a description of the relationship of the surrogate should be added as appropriate. See Partners Human Research Quality Improvement (QI) Program template Documentation of the Informed Consent Process for Onsite Subject File.

Consent Form Storage

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. Lastly, a copy (or electronic scan/pdf) should be placed in the subject's medical record if relevant to the subject's ongoing medical care, or the subject is hospitalized when the research is initiated or hospitalization is expected (for example, an investigational device will be implanted during an upcoming procedure requiring hospitalization).

If the study involves sensitive research (e.g., alcohol or drug use, studies of illegal behaviors, and some genetic studies) a copy of the research consent form ordinarily should not be placed in the subject's medical record. Studies involving psychiatric illness, genetics and HIV infection should not automatically be presumed to be sensitive studies and excluded from the medical record. In the interests of subject safety, the IRB encourages sharing of information about research participation with treating clinicians, and has a high bar for excluding research documentation from the medical record. If a study has no medical interventions (for example, longitudinal exams and surveys of outpatients) investigators are not required to place copies (or electronic scan/pdf) of consent forms in medical records.

Converting Paper Consent Forms to Electronic Documents
The PHRC has developed guidance on Electronic Storage of Study Documents, including paper consent documents. The guidance document was developed with input from the Partners Human Research Quality Improvement Program and Research Computing. See also Partners HealthCare Policy PHS-1055 Guidelines on Retention of Research Data, Materials, and Records.

Waiver of Documentation of Informed Consent ("verbal or implied" consent)
A waiver of the requirement to obtain documentation of consent (signed consent forms) is not the same as a waiver of informed consent. Under a waiver of documentation of informed consent, subjects still interact with investigators and must agree to take part in the research, but a signed consent form is not required to document their agreement.

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;

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. Examples of such activities include completing surveys, performing an abbreviated physical exam, or providing a urine sample.

When the PHRC approves a waiver of the requirement to obtain a signed written 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 records.

When 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 (in person or remotely) about the study, answer their questions and obtain their verbal informed consent. In some instances a subject may be informed that completing a task, such as filling out a survey, suffices as consent and there is no verbal agreement - this is also called "implied consent." If written consent is waived, the PHRC usually requires the investigator to provide subjects with a written statement regarding the research, which could be provided in person, by mail, or electronically. Examples of information sheets are available on Research Navigator site under IRB Policy & Guidance. Investigators should specify in the submission how verbal or implied consent is documented, for example, by retaining a list of names of participants who completed a survey or participated in a focus group.

The PHRC requires the abbreviated HIPAA authorization statement below, be included in letters, statements, websites, or information sheets when investigators are collecting Protected Health Information (PHI) pursuant to verbal or implied consent. Note that this statement provides the link to the complete Partners HIPAA Privacy Notice available online, for those who want more information.

We are required by the Health Insurance Portability and Accountability Act (HIPAA) to protect the privacy of health information obtained for research. This is an abbreviated notice, and does not describe all details of this requirement (see Partners Privacy Notice). During this study, identifiable information about you or your health will be collected and shared with the researchers conducting the research. In general, under federal law, identifiable health information is private. However, there are exceptions to this rule. In some cases, others may see your identifiable health informatioin for purposes of research oversight, quality control, public health and safety, or law enforcement. We share your health information only when we must, and we ask anyone who receives it from us to protect your privacy.*

*Partners HealthCare Notice for Use and Sharing of Protected Health Information

Waiver of Documentation of Informed Consent ("electronic" consent)
As noted above, the PHRC may waive the requirement to obtain a signed written consent form for minimal risk studies and approve a consent procedures that doesn't require a signature. Investigators may choose to provide subjects with information about the research in an electronic environment and ask the subject to check a digital checkbox to indicate whether they agree or decline to participate.

All subjects must be afforded an opportunity to ask questions prior to agreeing to participate and study contact information should be provided. This consent discussion could take place in person, by phone, by email, by videoconference or live chat but the investigator is reminded that communication portals or software may need to be vetted by Partners Research Information Security.

Subjects should also be asked to provide demographic information such as name and date of birth and contact information unless the study is an anonymous one-time interaction, and no follow-up contact is planned. It is recommended that a copy of the study information should be securely emailed to the subject, or the subject may be directed to print study-specific information for their records.

Comprehension and teaching aids such as videos, graphics, online resources may be used, but require prospective IRB review and approval. Investigators are advised to draft "standard operating procedures" to describe and document the consent procedures, and to ensure study staff are trained on the procedures and methods used to obtain informed consent.

When the PHRC approves a waiver of the requirement to obtain a signed written consent form based on consideration (2), the investigator should consider how s/he will track and record who provided verbal or implied consent. When completing a simple survey, a simple spreadsheet of subjects' names, date, time, and individual obtaining consent may be adequate. In more complicated settings, a more detailed note as described previously in this Policy under Documentation of the Consent Process should be considered.

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 waives 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 HIPAA and the Privacy Rule, see Waiver and Alteration of Informed Consent and Authorization for Research.) Note: An alteration or waiver of elements of informed consent is NOT the same as a waiver of the requirement for written documentation of informed consent.

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. New information can and should be added to a full study consent form, especially if new participants are still enrolling. In some instances one might consider a "consent form addendum," which focuses solely upon the new information. Subjects should also be notified of a change of principal investigator or contact information; however, in most cases this type of change can be adequately communicated by other means. 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 of subjects previously enrolled and actively participating 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.

- 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.

Subjects should be given the information above 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.

Industry sponsors have varying policies and requirements, and investigators are advised to discuss with them when and if formal written "re-consent" is desired when information that is new, but not of major importance, is added to a consent form. The PHRC does NOT recommend annual "re-consent" or new consent simply because the study consent form has been "re-approved" at the time of continuing review. Rarely, the Committee may advise annual "re-consent" - for example, if a subject is enrolled in a transplantation study where a significant waiting period is anticipated. Investigators are also encouraged to consult with the PHRC as needed on these topics.

Examples of when the PHRC may approve a letter being sent to notify the subject of changes 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 Human Research 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. Investigators are advised to consider various

options at the outset of the study and contemplate how they will convey these options and record the subject's wishes.

An investigator may ask a subject who is withdrawing whether s/he wishes to allow 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 collection of associated clinical outcome information, such as medical course or laboratory results obtained through medical record review, and address the maintenance of privacy and confidentiality of the subject's information. In some situations, subjects may agree to surveys or observational follow-up, but not wish to receive study drug or other interventions or attend study visits. If the subject agrees to more limited observational follow-up, 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. In some instances a menu of choices may be appropriate. If the subject does not agree, the investigator must not access the subject's medical record or other confidential records for purposes related to the study. 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.

APPENDIX I
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.

When seeking informed consent for applicable clinical trials, as defined in 42 U.S.C. 282.(j)(1)(A), the following statement shall be provided to each clinical trial subject, "A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."

Other Applicable Partners HealthCare Policies:

References:

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:

Development and Consultation:

Original Review Date	Reviewed By	Reviewer Approval Date
	Human Research Office	
	Office of the General Counsel	

Policy Revision History:

Policy Version	Authors	Reason for Revision	Revision Date	Reviewed By	Original Review Date	Revision Approval Date
						04/10/2017

Policy External Link:

https://grcarcher.partners.org/default.aspx?requestUrl=..%2fGenericContent%2fRecord.aspx%3fid%3d336261%26moduleId%3d65