

8.0 THE INFORMED CONSENT PROCESS AND DOCUMENT - REQUIREMENTS AND FORMAT

8.1 The Informed Consent Process and Document - General Requirements

Informed consent is one of the primary ethical requirements underpinning research involving humans; it reflects the basic principle of respect for persons. It should always be remembered that informed consent is an ongoing process, not a single event. The informed consent process is designed to give individuals all of the relevant information that they need in order to decide whether to participate, or to continue participation, in a research study. The process should permit the potential research subject to ask questions and to exchange information freely with the study investigators. Moreover, investigators have an ethical and contractual responsibility to keep research subjects fully informed of any new information that may affect their willingness to continue study participation. Thus, rather than an endpoint, the consent document should be the basis for a meaningful exchange between the investigator and the potential research subject or study participant.

No investigator may involve an individual in a research study unless the investigator has obtained prospectively the legally effective, written informed consent of the individual or the individual's legally authorized representative (unless the IRB has granted exempt status to the research study or has specifically waived the requirement for written informed consent). Note that verbal or telephone consent is not acceptable (unless the IRB has specifically waived the requirement for a signed consent form); nor is deferred consent (i.e., obtaining consent after the initiation of study procedures).

The general requirements for informed consent are summarized below:

- 1) Signed, written informed consent must be obtained from the individual, or the individual's legally authorized representative, before the individual can be involved in any procedures performed for research purposes (unless the IRB has specifically granted a waiver to obtain informed consent or a waive to obtain a signed informed consent document - see sections 8.3.1 and 8.3.3.)
 - a) If the research study involves children (age < 18 years old) who will continue to undergo research interventions (including the collection of identifiable private information) after they become adults, the IRB research protocol should address a mechanism (e.g., addendum informed consent document with copy of originally signed consent form attached; new consent form) whereby direct consent for continued participation in the research study will be obtained from these individuals at the time they reach adult status.
 - b) For research studies wherein the nature of the subject population is such that an individual may not be capable of initially providing direct consent for study participation but may recover adequate decision-making capability for direct consent at a later time, the IRB research protocol/informed consent document should address a mechanism whereby direct consent for continued participation in the research study will be obtained from the individual at the time s/he regains adequate decision-making capability. (See example statements under section 8.2, Informed Consent Document - Specific Instructions and Requirements, 14. c.)
 - c) In addition to obtaining the signed, written informed consent document, it is recommended that a narrative note be written in the subject's research records documenting the corresponding informed consent process. It is recommended that such documentation should include who was present

during the informed consent discussion; the fact that risks were presented; a notation, if applicable, that significant issues of concern to the subject were addressed; and a statement that all questions were answered to the satisfaction of the subject. This narrative note should also indicate the date and time that the subject signed the informed consent document and be signed by the individual responsible for the respective documentation. Noting the time of consent, in addition to the date, is especially important if any research procedures will be performed on the same day that informed consent was obtained. (Note: Documentation, in the subject's research records, of the date and time that informed consent was obtained is a good clinical practice requirement for any research study involving the evaluation of a research intervention (e.g., drug, device) which falls under the jurisdiction of the U.S. Food and Drug Administration.)

- 2) The investigator must seek informed consent under circumstances that give the individual sufficient opportunity to consider whether to participate in the research study, and that minimize possible coercion or undue influence.

Informed consent to participate in a research study should be sought at a time separate from obtaining informed consent for procedures performed for the medical management of the patient (i.e., non-research procedures).

- 3) For certain research studies (e.g., studies involving questionnaires, surveys) it may be practical and acceptable to mail the informed consent document to the potential subject and to have the signed document returned by mail. If this approach is taken, there must also be provisions for a telephone interaction between the potential subject and investigators so as to ensure that the informed consent process has been appropriately addressed. The cover letter accompanying the mailed informed consent document and survey or questionnaire materials must clearly address this telephone interaction. The procedures for ensuring an appropriate informed consent process when the consent form is mailed to potential research subjects should be addressed in the recruitment section of the corresponding IRB research protocol.
- 4) The information given to potential research subjects must be understandable to them.
 - a) The informed consent document should be directed at an individual whose reading skills are at the 8th grade level. (Some current word-processing programs can automatically calculate the reading level necessary to comprehend a given document via the "Readability" function of the grammar check command.) Technical and medical terminology should be avoided or must be explained in lay language.
 - b) It is recommended that informed consent documents be written using the second person style, that is, the subject is addressed as "you" and the investigator(s) as "I/we." This approach helps to communicate that there is a choice to be made by the prospective subject. Use of the first person may be interpreted as presumption of consent (i.e., the individual has no choice). Changes from one style to another must be separated by a row of asterisks.
 - c) Non-English speaking persons must have the information presented in a language that they comprehend. For potential research subjects who are unable to understand English:
 - i) The research subject should be provided with a "short form" consent document, written in the potential subject's native language that summarizes the basic elements of informed consent. (Copies of such "short form" consent documents, translated into several commonly encountered foreign languages are available from the IRB Office.)

- ii) The standard (i.e., IRB-approved, full-description) informed consent document should be presented verbally to the subject in his/her native language and all questions answered.
- iii) With agreement to participate in the research study:
 - the subject should sign and date the "short form" consent document;
 - the witness to the informed consent process should sign and date both the "short form" consent document and the standard consent document;
 - the investigator obtaining informed consent should sign and date the standard informed consent document; and
 - copies of the signed "short form" consent document and standard informed consent document should be given to the subject with originals of both documents retained in the investigator's research records.
- 5) The informed consent document may not include exculpatory language through which the potential research subject waives or appears to waive any legal rights or releases; or which appears to release the investigator, the sponsor, the institution, or their agents from liability for negligence.
- 6) The principal investigator of the research study is ultimately accountable for assuring that all aspects of the study are at all times in compliance with applicable federal regulations and IRB policies, including but not limited to the entire informed consent process and the instruction and oversight of individuals who may be involved in this process.
 - a) For research studies which do not involve the use of a drug, device, or surgical procedure; the principal investigator or a co-investigator listed on the IRB-approved research protocol/informed consent document must be involved in the informed consent process (i.e., prior to the implementation of research procedures) and must sign the Investigator's Certification statement at the time of this involvement.
 - i) The IRB may grant an exception to this requirement for investigator involvement in the informed consent process based on adequate written justification (i.e., addressed in the recruitment section of the corresponding IRB research protocol) of the reason(s) why it could not be reasonably or practically met. However, exceptions to this requirement may only be granted for research studies of minimal risk. In requesting IRB approval for such an exception, the individual(s) who will be involved in the informed consent process and who will sign the Investigator's Certification statement must be specifically identified (i.e., by name and/or position).
 - ii) Under an IRB-approved exception to this policy, research subjects retain the right to request that their questions, concerns or complaints be addressed by the principal investigator or a co-investigator listed on the research protocol/informed consent document; and this right shall be specifically addressed in the informed consent document (Voluntary Consent section) using the following, or closely related, wording; and such requests shall be honored.

VOLUNTARY CONSENT

"The above information has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions, voice concerns or complaints about any aspect of this research study during the course of this study, and that such future questions, concerns or complaints will be answered by a qualified individual or by the investigator(s) listed on the first page of this consent document at the telephone number(s) given. I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator. I understand that I may contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations that occurred during my participation. By signing this form I agree to participate in this research study. A copy of this consent form will be given to me."

- b) For research studies which involve a drug, device, or surgical procedure; the principal investigator or a co-investigator who is (i) listed on the IRB-approved research protocol/informed consent document and (ii) is a physician shall be involved in the informed consent process (i.e., prior to the implementation of research procedures) and must sign the Investigator's Certification statement at the time of this involvement.
 - i) The IRB may grant an exception to this requirement for physician investigator involvement in the informed consent process based on adequate written justification (i.e., submitted in the respective IRB research protocol, section 4.3, Recruitment Procedures) of the reason(s) why this requirement could not be reasonably and practicably met. However, the IRB will only grant an exception to this policy if it is specified that the informed consent process will involve (i.e., prior to administration of the drug, device or surgical intervention) an individual who is (i) listed as a co-investigator on the respective IRB-approved research protocol/informed consent document, and (ii) is a licensed health care professional; and that such individual will sign the Investigator's Certification statement at the time of his/her involvement.
 - ii) Under an IRB-approved exception to this policy, research subjects retain the right to request that their questions, concerns or complaints be addressed by a physician investigator involved in the conduct of the research study; and this right shall be specifically addressed in the informed consent document (Voluntary Consent section) using the following, or closely related, wording:

VOLUNTARY CONSENT

"The above information has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions, voice concerns or complaints about any aspect of this research study during the course of this study, and that such future questions, concerns or complaints will be answered by a qualified individual or by the investigator(s) listed on the first page of this consent document at the telephone number(s) given. I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator. I understand that I may contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations that have occurred during my participation. By signing this form I agree to participate in this research study. A copy of this consent form will be given to me."

- 7) The investigator must retain the original signed informed consent document in his/her research records. A copy of the informed consent document must be provided to the subject. For hospital patients, a separate copy of the informed consent document must be appended to the patient's medical record.

8.1.1 Basic Elements of Informed Consent

In seeking informed consent, the following information shall be provided to each potential research subject: (See more detailed instructions and requirements under section 8.2, Informed Consent Document - Specific Instructions and Requirements)

- 1) A statement that the study involves research; an explanation of the purpose of the research and the reason why the potential subject is being asked to participate; the expected duration of study participation; a description of the procedures that will be followed; and identification of any procedures which are experimental.
 - a) It is important to explicitly state that the individual is being asked to participate in a research study so as to clearly differentiate (i) the relationship between patient-physician from the relationship between subject-investigator; and (ii) informed consent for participation in research from informed consent for invasive clinical treatment procedures.
 - b) For studies directed at evaluating the safety of investigational new drugs, devices or other experimental interventions, the informed consent document should specify that a purpose of the research study is to evaluate the safety of the experimental intervention. Statements indicating that the experimental intervention is safe or statements specifying that the safety of the experimental intervention has been established in other studies are not appropriate when the purpose of the study involves a determination of safety.
 - c) For studies directed at evaluating the effectiveness of an investigational new drug, device or other experimental intervention, the informed consent document should specify that a purpose of the study is to evaluate the effectiveness of the experimental intervention. Statements claiming effectiveness of the experimental intervention are not appropriate when the purpose of the study involves a determination of effectiveness.
 - d) For investigator's with a Significant Financial Interest, the conflict must be disclosed to the research participant.
 - e) For procedures performed for research purposes:
 - i) In general:
 - Avoid addressing, in the consent form, procedures that are or will be performed for the individual's medical care (i.e., the consent form should focus only on those procedures performed specifically for the purpose of the research study). If the outcome of procedures performed for the individual's medical care will be used in support of the research study, specify that participation in the research will involve the review and recording of identifiable medical record information by the study investigators.
 - Specify the approximate amount of time (i.e., on a per visit basis) that will be required for the completion of research procedures. (Investigators should also ensure, through

consent form statements or other mechanisms, that research participants are aware of the location where study procedures will be performed.)

- Address, if applicable, the general nature, purpose, and number of biological specimen collections; volume (in teaspoonfuls, tablespoonfuls, or ounces) of blood that will be withdrawn; the FDA approval status, route of administration, dosage and duration of dosing of drugs; the FDA approval status of, and frequency of exposure to, medical devices; the general nature (e.g., examples of questions) and frequency of study questionnaires, surveys, interviews, or other assessments.

ii) For screening procedures:

- Screening questionnaires or interviews performed specifically for the purpose of the research study are subject to the regulations governing human subject protections. If such screening questionnaires or interviews ask questions of a sensitive nature (e.g., potentially damaging to the individual's reputation, employability, or financial standing) and the recorded responses will be linked to the subject's identity, written informed consent of the individual must be obtained prior to his/her participation in the screening questionnaire or interview.
- For certain research studies it may be more efficient for the investigators, and less confusing for the potential research subjects, to have a separate consent form for screening procedures.
- If applicable, the research protocol and consent form should address what steps will be taken in the event that a clinically significant, unsuspected disease or condition is identified during the conduct of the screening procedures.

iii) For experimental procedures:

- Experimental procedures should be listed separate from procedures that will be performed to evaluate eligibility for study participation (i.e., screening procedures) and procedures performed to evaluate the outcome of the experimental procedures (i.e., follow up procedures).
- Procedures inherent to certain research study designs (e.g., randomization and placebo control) should be clearly explained to the potential research subject.
- If the research involves a Phase I study to ascertain the maximum tolerated dose of an experiment drug, the potential research subject should be clearly informed that the intent of the study is to identify that dose of the drug which produces significant adverse effects. Hence, the informed consent document should indicate that certain of the subjects are expected to suffer from significant adverse effects based on the design of the study.

2) A description of any reasonably foreseeable risks or discomforts.

- a) The risks of all procedures performed specifically for the purpose of the research study should be addressed in the consent document. Not only the risks of the experimental procedures, but also the

risks of procedures performed for screening and follow up should be addressed; especially for procedures that inherently possess a risk (even though the likelihood of such may be low) of significant morbidity or mortality.

- b) The explanation of risks should be reasonable and should not minimize the likelihood or severity of potential adverse effects.
 - c) The description of potential risks should incorporate information regarding the expected frequency of occurrence and the severity of possible side effects or adverse events.
 - d) The consent form should address steps that will be taken by the investigators and, if applicable, any steps that should be taken by the subjects so as to prevent or minimize the risks of study participation.
- 3) A description of any potential benefits to research subjects or to others which may reasonably be expected from the research
- a) The description of potential benefits should be clear and not overstated.
 - i) If there is no potential for direct benefit to research subjects, this should be explicitly stated.
 - ii) If it is possible that subjects may benefit directly from study participation, identify the possible benefit(s) and include the statement, "However, there is no guarantee that you will receive such a benefit."
 - iii) If applicable, indicate the general benefit (i.e., to future patients with the respective disease/condition, to society, to increased knowledge) of the conduct of the research study.
 - b) If the research study involves a placebo-controlled arm, state clearly that individuals assigned to the placebo group are expected to receive no direct benefit from study participation.
- 4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the potential research subject in lieu of participation in the research study.
- a) To enable a rational decision whether to participate in the research study, potential research subjects should be made aware of the full range of options available to them. Thus, the informed consent document should summarize any pertinent alternatives (including, if applicable, "no further or additional treatment") to entering the study. It is expected that such a disclosure will include more than just a list of alternatives, however it is recognized that a full risk/benefit explanation is likely beyond the scope of the informed consent document. As with other required elements, the consent document should contain sufficient information to ensure an informed decision by the potential research subject. The investigators should offer their availability to discuss alternatives to research study participation and to answer respective questions.
 - b) If the research study involves the evaluation of a drug or device currently approved by the FDA or a procedure commonly used in clinical practice, specify that access to the study drug, device or procedure is available outside of study participation.

- c) For many research studies, the only alternative to study participation is not to participate. Since this is adequately addressed in other sections of the informed consent document, the Alternative Treatment section may be omitted for such research studies.
- 5) Statements describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.
- a) See standard Confidentiality section statements under section 8.2, Informed Consent Document - Specific Instructions and Requirements.
 - b) Potential subjects should be informed of who will have access to their research records and the purpose of such access. For example:
 - i) For any study where a medical record is generated, indicate that a copy of the signed consent document will be scanned into the e-Record.
 - ii) For drug and device studies, required access to the subject's research data and corresponding medical record information by the study sponsor and FDA for the purpose of monitoring the accuracy and completeness of the research data.
 - iii) For research involving procedures performed in any UPMC facility indicate that copies of those test results as well as other research-related procedures may be placed in the participant's medical record.
 - c) Potential subjects should be informed of the specific procedures (e.g., coding of research data, storage of identifiable information in locked or limited access files) that will be employed to protect their confidentiality.
 - d) Potential subjects should be informed of possible exceptions to maintaining confidentiality of their research information. Such possible exceptions include:
 - i) Required reporting of suspected child or elderly abuse.
 - ii) Required reporting of communicable diseases to public health agencies.
 - iii) Possible audit of research by the University Research Conduct and Compliance Office.
 - iv) Possible subpoena of research data by the courts.
 - e) Federal Certificate of Confidentiality: Although few studies require a Federal Certificate Confidentiality, there are instances when data are being collected about sensitive issues such as illegal behavior, alcohol or drug abuse, or sexual practices or preferences, wherein it is important that the confidentiality of research records be enhanced. Federal Certificates of Confidentiality are granted by federal funding agencies and are directed at protecting research data from disclosure subsequent to subpoena by the courts.

Only those studies which are granted a Federal Certificate of Confidentiality are permitted to address the Certificate in the informed consent document. (See sample Certificate of Confidentiality statements included under section 8.2, Informed Consent Document - Specific

Instructions and Requirements) Should the investigator obtain a Federal Certificate of Confidentiality after initiation of the study s/he should request a modification of the consent document to include the appropriate statements addressing this Certificate.

- f) Specify the length of time that the research records will be maintained and what will happen to the research records once this time period has expired. (Note that it is University policy that all research records be maintained for a period of at least 6 years following final reporting or publication of a project.)
- 6) For research involving greater than minimal risk, an explanation addressing 1) who should be contacted in the event of a research related injury; and 2) whether any compensation and/or medical treatments are available in such an event, including what they consist of and/or where further information may be obtained.
 - a) See the standard Compensation for Injury section language under section 8.2, Informed Consent Document - Specific Instructions and Requirements.
 - b) This explanation may be omitted from the informed consent document for certain minimal risk protocols (e.g., psychosocial studies) wherein injury associated with study participation is highly unlikely.
- 7) A statement that participation is voluntary; that refusal to participate will involve no penalty or loss of benefits to which the potential research subject is otherwise entitled; and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.
 - a) If the research study involves the recruitment and study of patients, the statement should specify that refusal to participate in, or withdrawal from, the research study will have no effect on the individual's current or future care at a UPMC facility (or other clinical facility where the research is being conducted) or the individual's current or future status with the University of Pittsburgh.
 - b) If the research study involves primarily the recruitment of University students, the statement should specify that refusal to participate in, or withdrawal from, the research study will have no effect on the individual's current or future status with the University.
- 8) An explanation of whom to contact for answers to pertinent questions, concerns or complaints about the research and the rights of research subjects.
 - See the standard Voluntary Consent section statements under section 8.2, Informed Consent Document - Specific Instructions and Requirements.

8.1.2 Additional Elements of Informed Consent

When appropriate, one or more of the following elements of information shall also be provided to each potential research subject:

- 1) The approximate number of subjects involved in the study. If the number of subjects enrolled currently or previously in a study would be material to the individual's decision to participate, potential research subjects should be informed not only of the approximate number of such study subjects, but also why this information is

important. For example:

- a) a research study wherein the small number of subjects may compromise confidentiality.
 - b) a research study to evaluate the safety of an investigational drug or device wherein the number of subjects previously studied would be of importance in the decision to participate in the current study.
- 2) A statement that certain experimental interventions or procedures may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable.
- a) If applicable, incorporate the following standard statement to address unforeseeable risks to the research subject:

"As with any experimental procedure, there may be adverse events or side effects that are currently unknown, and certain of these unknown risks could be permanent, severe or life-threatening."
 - b) Potential research subjects, both women and men, need to understand the danger of receiving any investigational drug whose effects on the reproductive system or fetus are unknown. If relevant animal data are available, the significance of these data should be explained to potential research subjects. If applicable, informed consent documents should explain that animal studies of mutagenicity (the capability to induce genetic mutations) and teratogenicity (the capability to induce fetal malformations) have not yet been conducted/completed. Note, however, that the lack of such animal data should not constitute a valid reason for restricting entry of women of childbearing potential into a clinical trial of an investigational drug. Investigators should ensure that individuals who agree to enter a study fully understand the potential risks that the study poses.
 - c) If measures to prevent pregnancy are warranted, this should be fully addressed. See standard pregnancy and birth control language under section 8.2, Informed Consent Document - Specific Instructions and Requirements.
- 3) Anticipated circumstances under which a subject's participation may be terminated by the investigator without regard to the individual's consent.
- a) Note that a simple statement that the investigator and/or sponsor may withdraw subjects at any time without providing a further explanation of the possible reasons for subject withdrawal does not provide for adequate informed consent of the subject.
 - b) A statement that the investigator may withdraw subjects if they do not "follow study procedures" is inappropriate. Potential research subjects are not in a position to know all of the study procedures. Individuals may be informed, however, that they may be withdrawn if they do not follow the instructions given to them by the investigator.
- 4) The consequences of a subject's decision to withdraw from the research study and the procedures for orderly termination of participation by the subject
- a) When withdrawal from a research study may have deleterious effects on the subject's health or welfare, the informed consent document should address any withdrawal procedures that are necessary for the subject's safety and specifically indicate that participation in these procedures

are important to the subject's welfare. An unexplained statement that a subject will be asked to submit to tests prior to withdrawal does not adequately inform the potential research subject why the tests are necessary for the subject's welfare. Note also, that participation in the research (including follow up safety assessments) is voluntary; hence it is not acceptable to "require" participation in safety assessments should the subject decide to withdraw from study participation.

- b) If applicable, indicate what steps will be taken with regard to continued treatment of the subject's disease or condition should s/he be withdrawn or withdraw from study participation.
- 5) A statement that significant new findings identified during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject or the subject's representative.
- a) See standard New Information section statement under section 8.2, Informed Consent Document - Specific Instructions and Requirements.
 - b) This statement may not be applicable to certain research studies (e.g., psychosocial studies) and may, thus, be omitted from the respective informed consent document.
- 6) Any additional costs to the subject that may result from participation in the research study.
- a) See standard Costs section statement under Section 8.2, Informed Consent Document – Specific Instructions and Requirements.
 - b) Potential research subjects should be clearly informed if they, or their third-party insurance provider, will be billed for any procedures performed for the purpose of the research study. If applicable, potential research subjects should be informed that certain third-party insurance providers may not reimburse for procedures performed for research purposes and that, in such an event, the research subject will be held directly accountable for the charges which will require payment in advance. Since the policies of insurance providers vary, the services of a hospital financial counselor should be provided so as to permit an assessment of insurance coverage and a disclosure to the potential subject of any personal financial risk associated with study participation. The availability of this financial counselor should be addressed in the informed consent document, and an estimate of the financial risk associated with study participation should be provided to the potential subject prior to obtaining his/her consent for study participation.
 - c) For patients participating as research subjects, indicate that the patient-subject will be charged, in the standard manner, for any clinical procedures performed for his/her medical care.
 - d) For research studies involving the evaluation of a drug or device, specify if the experimental intervention will be available to the subject following study completion and, if so, who will be responsible for the cost of the intervention (or maintenance of the intervention) following study completion.

8.2 Informed Consent Document - Specific Instructions and Requirements (See also the Example Informed Consent Document on the IRB website (www.irb.pitt.edu)).

- 1) General Requirements:
 - a) Place the first page on appropriate division, department, school, or center letterhead.

CHAPTER 8 (PAGE 8-12) REVISION REQUESTED – REMOVAL OF REQUIREMENT TO HAVE PARTICIPANT INITIAL EACH PAGE OF THE CONSENT DOCUMENT

- b) FOR PAPER SUBMISSIONS: Specify, in the upper right corner of every page, *“University of Pittsburgh, Institutional Review Board”*, and include a space to indicate the IRB approval date, renewal date and IRB number assigned to the research study. Please see the Sample Consent Form on the IRB website for the format. It is also suggested that a version number of the consent form be included somewhere on the page to ensure that the most up-to-date consent form is used.
- FOR OSIRIS SUBMISSIONS: Include the watermark from the OSIRIS system onto the consent document.
- c) Specify *“CONSENT TO ACT AS A PARTICIPANT IN A RESEARCH STUDY”* at the top, center of the first page (i.e., under the division, department, school, or center letterhead).
- d) If applicable, separate changes in second- to first-person style using a row of asterisks.
- e) **Note:** it is acceptable to use standard section headings (e.g., DESCRIPTION, RISKS, BENEFITS), in all capital letters, or standard explanatory questions (e.g., ***Why is this research being done?***), in bold italics, in the consent form. However, both should not be used.
- 2) TITLE: The title on the consent form must be identical to the title listed on the research protocol, unless a specific justification (e.g., confidentiality issue, planned deception) for a different title is addressed in the research protocol.
- 3) INVESTIGATORS:
- a) List the PRINCIPAL INVESTIGATOR and all CO-INVESTIGATORS.
- b) Include either an address and telephone number for each listed investigator or a common department, division, school, or center address and telephone number, if applicable.
- 4) SOURCE(S) OF SUPPORT: List all sources of support for the research study.
- 5) DESCRIPTION (**Note:** In lieu of incorporating this standard section heading, the standard question format, outlined below, may be used. Regardless of the option selected, all of the information addressed below should be included in this section of the consent form.)
- a) Incorporate (in bold italics) the standard question, ***“Why is this research being done?”*** and address the following:
- i) The purpose of conducting the research.
- ii) The FDA approval status of drugs or devices, if applicable.
- iii) If an investigator has a Significant Financial Interest, please include the following standard language: *“One or more of the investigators conducting this research has a financial interest in or a patent for the development of this (ADD STUDY SPECIFIC INFORMATION). This means that it is possible that the results of this study could lead to personal profit for the individual investigator(s) and/or the University of Pittsburgh. This project has been carefully reviewed to*

ensure that your well-being holds more importance than any study results. Any questions you might have about this will be answered fully by Dr. (ENTER THE NAME AND TELEPHONE NUMBER OF THE PI OF THE RESEARCH STUDY) or by the Human Subjects Protection Advocate of the University of Pittsburgh (1-866-212-2668).

- b) Incorporate (in bold italics) the standard question, "***Who is being asked to take part in this research study?***", and address the following:
- i) The reason why the potential subject is being asked to participate in the research study..
 - ii) The number of subjects to be studied at the University of Pittsburgh or UPMC and/or, if applicable, the number of subjects to be studied at non-local or multi-center sites. If the number of subjects to be enrolled in the research study is material to the individual's decision to participate, address why the number of subjects should be a consideration.
- c) Incorporate (in bold italics) the standard question, "***What procedures will be performed for research purposes?***", and address the following:
- i) Include the following standard statement: "*If you decide to take part in this research study, you will undergo the following procedures that are not part of your standard medical care.*", or, for potential subjects who are not patients, "*If you decide to take part in this research study, you will undergo the following procedures*".
 - ii) **Screening Procedures:** If applicable, list the screening procedures that will be performed specifically for the purpose of the research study.
 - Precede this listing with the standard statements: "*Procedures to determine if you are eligible to take part in a research study are called "screening" procedures. For this research study, the screening procedures include:*"
 - Do not address procedures performed for the potential subject's routine medical care, even if the results of such clinical procedures will be used to determine subject eligibility.
 - Specify, if applicable, that screening for study eligibility will involve the review and collection of information from the subject's medical record.
 - If applicable, indicate the volume (in teaspoonfuls, tablespoonfuls, or ounces) of blood that will be withdrawn for the screening procedures.
 - Specify the approximate duration of time (i.e., on a per study visit basis) required for completion of the screening procedures. (Investigators should also ensure, through consent form statements or other mechanisms, that research participants are aware of the location where study procedures will be performed.)
 - If applicable, address what steps will be taken in the event that a clinically significant, unsuspected disease or condition is identified during the conduct of the screening procedures.

Note: For certain research studies it may be more efficient for the investigators, and less confusing for the potential research subjects, to have a separate consent form for screening

procedures. This is acceptable to the IRB.

Note: Screening questionnaires or interviews performed specifically for research purposes are subject to the regulations governing human subject protections. If such screening questionnaires or interviews ask questions of a sensitive nature (e.g., potentially damaging to the individual's reputation, employability, or financial standing) and the recorded responses will be linked to the subject's identity, written informed consent of the individual must be obtained prior to his/her participation in the screening questionnaire or interview.

Note: Written informed consent of potential research participants must be obtained prior to sending identifiable X-rays, specimens, or other private (e.g., medical) information to external sponsors for a determination of study eligibility.

- iii) Experimental Procedures: List, in sequence, the experimental interventions that will be performed for the purpose of the research study.
- Precede this listing with the standard statement: *"If you qualify to take part in this research study, you will undergo the following experimental procedures:"*.
 - Do not address procedures performed for the potential subject's routine medical care.
 - Please attempt to list the experimental intervention(s) separate from the procedures that will be performed to evaluate the outcome of the experimental intervention(s) (see next heading).
 - If applicable, address:
 - the route of administration, dosage and duration of dosing for each experimental drug intervention;
 - the number of exposures and/or duration of exposure for each experimental device intervention;
 - the nature, purpose, volume, and number of all experimental biological specimen collections; and/or
 - the general nature (e.g., example of questions) and frequency of experimental tests, questionnaires, surveys, interviews or other experimental assessments.
 - Specify the approximate duration of time (i.e., on a per study visit basis) required for completion of the experimental intervention(s). (Investigators should also ensure, through consent form statements or other mechanisms, that research participants are aware of the location where study procedures will be performed.)
- iv) Monitoring/Follow-up Procedures: If applicable, list the monitoring/follow-up procedures that will be performed specifically for the purpose of the research study.
- Precede this listing with the standard statements: *"Procedures performed to evaluate the safety and effectiveness of the experimental procedures are called "monitoring" or "follow-up" procedures. For this research study, the monitoring/follow-up procedures include:"*.

- Do not include procedures performed for the potential subject's routine medical care, even if the results of such clinical procedures will be used to monitor the safety and/or effectiveness of the experimental intervention(s).
 - Specify, if applicable, that monitoring/follow-up will involve the review and recording of information from the subject's medical record.
 - If applicable, indicate the volume (in teaspoonfuls, tablespoonfuls, or ounces) of blood that will be withdrawn for the monitoring/follow-up procedures.
 - Specify the approximate duration of time required for completion of the monitoring/follow-up procedures (i.e., on a per-visit basis).
- 6) **RISKS** (**Note:** In lieu of incorporating this standard section heading, the standard question format, outlined below, may be used. Regardless of the option selected, all of the information addressed below should be included in this section of the consent form.)

Incorporate (in bold italics) the standard question, "***What are the possible risks, side effects, and discomforts of this research study?***", and address the following:

- a) Identify all reasonably foreseeable risks (e.g., physical, psychological, legal, or economic) and discomforts that may be associated with the screening procedures, experimental interventions, or monitoring/follow-up procedures performed specifically for the purpose of the research study.
- b) Provide quantitative and severity information re. the expected frequency of occurrence of the listed, possible side effects or adverse events. The following format is recommended:

"Likely - Occurs in more than 25% of people (more than 25 out of 100 people):

Common - Occurs in 10-25% of people (10 to 25 out of 100 people):

Infrequent - Occurs in 1-10% of people (1 to 10 of 100 people):

Rare - Occurs in less than 1% of people (less than 1 out of 100 people):"

Under each frequency of occurrence category, list possible adverse events in order of most severe to less severe.

- c) If applicable, address possible side effects (e.g., bruising, soreness, or rarely, infection at the site of venipunctures; spasm with loss of blood flow and possible nerve damage at the site of arterial puncture) of needle insertions for blood withdrawal or drug administration.
- d) If the research involves a Phase I study to ascertain the maximum tolerated dose of an experiment drug, the potential research subject should be clearly informed that the intent of the study is to identify that dose of the drug which produces significant adverse effects. Hence, the informed consent document should indicate that certain of the subjects are expected to suffer from significant adverse effects based on the design of the study.
- e) For research studies involving the evaluation of an experimental drug, device, or surgical

procedure, incorporate the following standard statement:

"As with any experimental procedure, there may be adverse events or side effects that are currently unknown and certain of these unknown risks could be permanent, severe or life-threatening."

- f) If the procedures (i.e., screening procedures, experimental procedures, or follow-up procedures) performed for the purpose of the research study involve exposure to ionizing radiation, incorporate the following standard radiation risk statements:

- For procedures that result in radiation exposures to the whole body (e.g., radioactive drugs, whole body DEXA):

"Participation in this research study will involve radiation exposure associated with the (specify procedure). The amount of whole body radiation exposure that you will receive from this procedure is about (specify amount of radiation exposure) rem (a unit of radiation exposure). For comparison, radiation workers are permitted, by federal regulation, a maximum whole body radiation exposure of 5 rems per year. There is no minimum amount of radiation exposure that is recognized as being totally free of the risk of causing genetic mutations (abnormal cells) or cancer. However, the risk associated with the amount of radiation exposure that you will receive from taking part in this study is felt to be low and comparable to everyday risks."

- For procedures that result in radiation exposures to limited body areas (e.g., CT studies, X-rays, angiography):

"Participation in this research study will involve radiation exposure associated with the (specify procedure). The amount of radiation exposure that you will receive from this procedure is about (specify amount of radiation exposure) rem (a unit of radiation exposure) to the (specify area of body) with minimal exposure of other body areas. For comparison, radiation workers are permitted, by federal regulation, a maximum radiation exposure of 50 rems per year to any single body organ. There is no minimum amount of radiation exposure that is recognized as being totally free of the risk of causing genetic mutations (abnormal cells) or cancer. However, the risk associated with the amount of radiation exposure that you will receive from taking part in this study is felt to be low and comparable to everyday risks."

- g) If study participation involves reproductive risks, include the following language:

"Animal studies to determine the effects of the (specify research procedure) on the fetus (unborn child) have not been done (or summarize results). To avoid risk to the fetus, it is important that you (for female participants) or your female sexual partner (for male participants) not become pregnant while you are participating in this research study. Avoiding sexual activity is the only certain method to prevent pregnancy. However, if you choose to be sexually active, you should use an appropriate "double barrier" method of birth control (such as female use of a diaphragm, intrauterine device (IUD), or contraceptive sponge, in addition to male use of a condom) or the female should be using prescribed "birth control" pills, injections, or implants. Such birth control methods should be used for (specify duration) prior to beginning your participation in the research study and continue for (specify duration) after your final study visit. If you choose to be sexually active during this study, you understand that even with the use of these birth control measures pregnancy could still result. The risks of receiving the (specify research procedure) while pregnant

include potential loss of pregnancy or possible birth defects.

If you are a women of child-bearing potential, you will undergo a pregnancy test prior to your exposure to the (specify research procedure). (If applicable, address repeat pregnancy testing performed at defined intervals during study participation.) If you become aware that you or your sexual partner is pregnant during the course of your participation in this research study, you must, if applicable, discontinue immediately the (specify research procedure) and contact, as soon as possible, the principal investigator listed on the first page of this form."

- h) Indicate the steps that will be taken by the investigators and, if applicable, any steps that should be taken by the subjects so as to prevent or minimize the risks of study participation.
- 7) **BENEFITS** (**Note:** In lieu of incorporating this standard section heading, the standard question format, outlined below, may be used. Regardless of the option selected, all of the information addressed below should be included in this section of the consent form.)

Incorporate (in bold italics) the standard question, "***What are the possible benefits from taking part in this research study?***", and address the following:

- a) If applicable, state explicitly that subjects will receive no direct benefit from study participation.
- b) If it is possible that subjects may benefit directly from study participation, identify the possible benefit(s) and include the statement, "*However, there is no guarantee that you will receive such a benefit.*"
- c) If the research study involves a placebo-control arm, state clearly that subjects assigned to the placebo group are expected to receive no direct benefit from study participation.
- d) If applicable, indicate the general benefit (i.e, to future patients with the respective disease/condition, to society, to increased knowledge) of the conduct of the research study.

Note: Do not overstate the potential benefits of study participation so as to be coercive to participation.

- 8) **ALTERNATIVE TREATMENTS** (**Note:** In lieu of incorporating this standard section heading, the standard question format, outlined below, may be used. Regardless of the option selected, all of the information addressed below should be included in this section of the consent form.)

Incorporate (in bold italics) the standard question, "***What treatments or procedures are available if I decide not to take part in this research study?***", and address the following:

- a) If applicable, disclose any currently available treatments or procedures that may be of potential benefit to the potential subject in lieu of participation in the research study.
- i) If the research study involves the evaluation of a currently approved drug or device, indicate that the study drug or device is available outside of study participation.
- ii) If applicable, include "no further or additional treatment" as an alternative to study participation.
- b) Offer the availability of the investigators to discuss and answer questions regarding alternatives to research study participation.

Note: For many research studies, the only alternative to study participation is not to participate. For such studies, this section of the informed consent document may be omitted.

- 9) **NEW INFORMATION** (**Note:** In lieu of incorporating this standard section heading, the standard question format, outlined below, may be used. Regardless of the option selected, all of the information addressed below should be included in this section of the consent form.)

Incorporate (in bold italics) the following standard question, "***If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?***"

- Incorporate the standard statement "*You will be promptly notified if any new information develops during the conduct of this research study which may cause you to change your mind about continuing to participate.*"

Note: These statements may not be applicable to certain research studies (e.g., psychosocial research). For such studies, this section of the informed consent document may be omitted.

- 10) **COSTS and PAYMENTS** (**Note:** In lieu of incorporating this standard section heading, the standard question format, outlined below, may be used. Regardless of the option selected, all of the information addressed below should be included in this section of the consent form.)

Incorporate (in bold italics) the standard question, "***Will I or my insurance provider be charged for the costs of any procedures performed as part of this research study?***", and address the following:

Any additional costs to the subject that may result from participation in the research study.

- a) Potential research subjects should be clearly informed if they, or their third-party insurance provider, will be billed for any procedures performed for the purpose of the research study. If applicable, potential research subjects should be informed that certain third-party insurance providers may not reimburse for procedures performed for research purposes and that, in such an event, the research subject will be held directly accountable for the charges which will require payment in advance. Since the policies of insurance providers vary, the services of a hospital financial counselor should be provided so as to permit an assessment of insurance coverage and a disclosure to the potential subject of any personal financial risk associated with study participation. The availability of this financial counselor should be addressed in the informed consent document, and an estimate of the financial risk associated with study participation should be provided to the potential subject prior to obtaining his/her consent for study participation.

The following wording should be incorporated if the research subject or his/her health insurance provider will be responsible for any costs associated with the research:

"If you participate in this research study, the cost of the experimental (**device or drug, as applicable**) and/or the costs of certain procedures performed for the purpose of the research study may be billed to your health insurance provider. You will be notified, in advance of undergoing the research procedures should your health insurance provider refuse to cover certain or all of these research costs and if any of these uncovered research costs will be billed directly to you. In this situation, you will be provided with a price estimate for the uncovered research costs that will be billed to you. If you decide to continue your participation in this research study, you will be required to meet with a hospital financial counselor to

arrange for your advance payment of these uncovered research costs. If you do not have health care insurance, you will be provided with a price estimate for the research costs that will be billed to you. If you decide to continue your participation in this research study, you will be required to meet with a hospital financial counselor to arrange for your advance payment of these research costs."

- b) If applicable (i.e., for patients participating as research subjects), indicate that the subject will be charged, in the standard manner, for any procedures performed for his/her routine medical care.
- c) For research studies involving an evaluation of a drug or device, specify if the experimental intervention will be available to the subject following study completion and, if so, who will be responsible for the cost of the experimental intervention (or maintenance of the intervention) following study completion.

Incorporate (in bold italics) the standard question, "***Will I be paid if I take part in this research study?***", and address the following:

- a) Specify if the subjects will or will not be paid for study participation. If the subjects will be paid for study participation:
 - i) address the total payment for completion of all parts of the research study, and
 - ii) address a payment schedule for only partial completion of the research study.

Note: Neither the total payment for study completion or the payment schedule for partial study completion should be coercive to initial or continuing participation in the research study. It is acceptable, however, for the payment schedule to include a non-coercive, payment bonus for the completion of all parts of the study.

- b) Specify any other incentives (e.g., reimbursement for travel, parking expenses, non-monetary rewards, course credits, etc.) to the subjects associated with their participation in the research study. Address both the overall incentives for total study completion and how the incentives will be distributed in the event of only partial study completion.

11) COMPENSATION for INJURY (Note: In lieu of incorporating this standard section heading, the standard question format, outlined below, may be used. Regardless of the option selected, all of the information addressed below should be included in this section of the consent form.)

Incorporate (in bold italics) the standard question, "***Who will pay if I am injured as a result of taking part in this research study?***"

- a) For research that is NOT commercially sponsored but is conducted at Pitt or UPMC facilities, incorporate the following standard statements addressing current institutional policy regarding the treatment and the costs of treating an injury that occurs as a result of research participation:

"If you believe that the research procedures have resulted in an injury to you, immediately contact the Principal Investigator who is listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-

related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. At this time, there is no plan for any additional financial compensation.

- b) For research that IS commercially sponsored and the protocol is provided by the sponsor, the sponsor should, at a minimum, provide adequate compensation for subject harm directly resulting from the research intervention that requires any emergency care. Some sponsors have plans for monetary compensation for non-emergency treatment, and, if they do, that additional compensation for harm should be included in the informed consent, but it is the responsibility of the investigator to ensure that the compensation for injury statement is consistent with the signed sponsor's agreement. This should be addressed in the consent form as well as the IRB application. While some sponsors may not wish to provide any compensation for subject harm, the University of Pittsburgh will require, for studies involving its faculty or facilities, that sponsors at least provide emergency care.

Note: This section of the informed consent document may be omitted from certain minimal risk research studies (e.g., research limited to questionnaires/surveys) wherein injury associated with study participation is unlikely to occur.

- 12) CONFIDENTIALITY (**Note:** In lieu of incorporating this standard section heading, the standard question format, outlined below, may be used. Regardless of the option selected, all of the information addressed below should be included in this section of the consent form.).

Incorporate (in bold italics) the standard question, "***Who will know about my participation in this research study?***" and include the following standard statements and information:

"Any information about you obtained from or for this research study will be kept as confidential (private) as possible. [Specify the procedures (e.g., coding of research data, storage of linkage code information in separate locked files) that will be used to protect the confidentiality of the research subjects. If records will be maintained in such a manner that it may be possible to link directly the research data with the subject's identity, this must be explicitly stated. In this circumstance, additional protections (e.g., password controlled access to the research database) to protect subject confidentiality should be described.] You will not be identified by name in any publication of the research results unless you sign a separate form giving your permission (release)."

Incorporate (in bold italics) the standard question, "***Will this research study involve the use or disclosure of my identifiable medical information?***"

Include the following standard statements and information if the research study involves the collection of the subjects' current or future identifiable medical information:

"This research study will involve the recording of current and/or future identifiable medical information from your hospital and/or other (e.g., physician office) records. The information that will be recorded will be limited to information concerning [specify the nature of the data that will be recorded]. This information will be used for the purpose of [specify the purpose of the research use of the current and/or future identifiable medical information]."

If research tests or procedures are being conducted at UPMC facilities and are generating laboratory test results or other clinical information, the UPMC testing facility will likely generate an

electronic medical record of those results – even if the research subject is not an in- or out-patient at any UPMC facility. Research subjects must be informed in the consent form of this eventuality. The following suggested language may be utilized:

"This research study will result in identifiable information that will be placed into your medical records held at [specify the name of the applicable institution or physician's office]. The nature of the identifiable information resulting from your participation in this research study that will be recorded in your medical record includes [specify the type research data which may or will be recorded in the subject's medical record]."

Include the following standard statement if this research study does not involve the use or disclosure of the subjects' identifiable medical information:

"This research study will not involve the use or disclosure of your identifiable medical information."

Incorporate (in bold, italics) the standard question, "***Who will have access to identifiable information related to my participation in this research study?***" and include the following standard statements:

"In addition to the investigators listed on the first page of this authorization (consent) form and their research staff, the following individuals will or may have access to identifiable information (which may include your identifiable medical information) related to your participation in this research study:

Authorized representatives of the University of Pittsburgh Research Conduct and Compliance Office may review your identifiable research information (which may include your identifiable medical information) for the purpose of monitoring the appropriate conduct of this research study.

In unusual cases, the investigators may be required to release identifiable information (which may include your identifiable medical information) related to your participation in this research study in response to an order from a court of law. If the investigators learn that you or someone with whom you are involved is in serious danger or potential harm, they will need to inform, as required by Pennsylvania law, the appropriate agencies."

Note: Remove references to "*(which may include your identifiable medical information)*" from the previous standard statements if this research study does not involve the use and disclosure of the subjects' identifiable medical record (i.e., hospital).

Include the following standard statements and information if an external sponsor of the research study will have access to the subjects' identifiable research information and/or identifiable medical information for study monitoring or data analysis purposes:

"Authorized representatives of the sponsor of this research study, [specify name of sponsor and/or contract research organization], will review and/or obtain identifiable information (which may include your identifiable medical information) related to your participation in this research study for the purpose of monitoring the accuracy and completeness of the research data and for performing required scientific analyses of the research data. [Include if applicable - "Authorized representatives of the study sponsor may also be present during your participation in certain research procedures."] While the

study sponsor understands the importance of maintaining the confidentiality of your identifiable research and medical information, the UPMC and University of Pittsburgh cannot guarantee the confidentiality of this information after it has been obtained by the study sponsor.

The investigators involved in the conduct of this research study may receive funding from the sponsor to perform the research procedures and to provide the sponsor with identifiable research and medical information related to your participation in the study."

Note: Remove references to "*(which may include your identifiable medical information)*" and "*and medical*" from the previous standard statements if this research study does not involve the use and disclosure of the subjects' identifiable medical information.

Include the following standard statements and information if the research study involves an evaluation of any article (e.g., drug, device, electronic product, food additive) regulated by the U.S. Food and Drug Administration:

"Authorized representatives of the U.S. Food and Drug Administration may review and/or obtain identifiable information (which may include your identifiable medical information) related to your participation in this research study for the purpose of monitoring the accuracy of the research data. While the U.S. Food and Drug Administration understands the importance of maintaining the confidentiality of your identifiable research and medical information, the University of Pittsburgh and UPMC cannot guarantee the confidentiality of this information after it has been obtained by the U.S. Food and Drug Administration."

Note: Remove references to "*(which may include your identifiable medical information)*" and "*and medical*" from the previous standard statements if this research study does not involve the use and disclosure of the subjects' identifiable medical information.

Include the following standard statements and information if the research study (or any aspect of the research study) will involve the utilization of hospital or health care services (e.g., laboratory tests, diagnostic procedures); hospital or health provider care of the patient-subject; or hospital or health provider billing activities:

"Authorized representatives of the UPMC hospitals or other affiliated health care providers may have access to identifiable information (which may include your identifiable medical information) related to your participation in this research study for the purpose of (1) fulfilling orders, made by the investigators, for hospital and health care services (e.g., laboratory tests, diagnostic procedures) associated with research study participation; (2) addressing correct payment for tests and procedures ordered by the investigators; and/or (3) assessing internal hospital operations (i.e. quality assurance)."

Include the following information, if applicable:

[Identify any other individuals who may or will have access to the identifiable research or medical information related to the subjects' participation in this research study and the indicate the purpose of such access.]

Incorporate (in bold, italics) the standard question, "***For how long will the investigators be permitted to use and disclose identifiable information related to my participation in this research study?***" and include the following standard statements and information:

"The investigators may continue to use and disclose, for the purposes described above, identifiable information (which may include your identifiable medical information) related to your participation in this research study for [specify the length of time that identifiable research information will be maintained. Note that it is acceptable to specify "indefinitely". Note also that it is a University policy that all research records must be maintained for at least 6 years following final reporting or publication of a project.

Note: Remove reference to "*(which may include your identifiable medical information)*" from the previous standard statements if this research study does not involve the use and disclosure of the subjects' identifiable medical information.

If applicable (i.e., if the research study will result in the generation of information that will be placed in the subjects' medical records), incorporate (in bold, italics) the following standard question, "***May I have access to my medical information that results from my participation in this research study?***" and include the standard statement:

"In accordance with the UPMC Notices of Privacy Practices document that you have been provided, you are permitted access to information (including information resulting from your participation in this research study) contained within your medical records filed with your health care provider unless otherwise specifically stated below."

Include the following information if it is your intention to restrict research subject access to any medical information that results from his/her participation in this research study:

[Specify any restrictions on the patient's-subject's access to medical information generated as a result of research participation. Indicate that such access will be granted at the end of the research study. Note that the UPMC does not generally permit investigators to include restrictions on patient-subject access to medical record information held by the UPMC or affiliated health care providers. The principal investigator must petition the Privacy Officer, UPMC, on a study-specific basis, if s/he wishes to restrict respective patient-subject access to his/her own medical record information. If the Privacy Officer, UPMC, grants such restrictions, it will be the principal investigator's responsibility to clearly communicate to the involved UPMC hospital(s) or affiliated health care providers the restrictions that have been granted. This communication must include documentation of the Privacy Officer's permission along with a copy of this signed consent form/authorization.]

If a federal Certificate of Confidentiality has been obtained for the research study, incorporate (in bold, italics) the standard question, "***What additional confidentiality (privacy) protections are provided by a federal Confidentiality Certificate?***" and include the following standard statements mandated by the DHHS:

"To further help to protect your privacy, the investigators have obtained a Confidentiality Certificate from the U.S. Department of Health and Human Services (DHHS). With this federal Certificate, the investigators cannot be forced (for example, by court order) to disclose information that may identify you in any federal, state, or local court; administrative; legislative; or other proceeding. Disclosure will be necessary, however, upon the request of the DHHS (for example, for audit or program evaluation purposes).

You should understand that this federal Certificate does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research study. Note, however, that if an insurer or employer learns about your study participation and obtains your consent to receive your identifiable research information, then the investigators may not use the Certificate to withhold this information from the insurer or employer. This means that you or your family must also actively protect your privacy. Finally, you should also understand that this federal Certificate does not prevent investigators from taking steps, including reporting to appropriate authorities, to prevent serious harm to yourself or others."

Note: If these standard statements related to a federal Confidentiality Certificate are included in the consent form, the following standard statements appearing under the standard question, "***Who will have access to identifiable information related to my participation in this research study?***", should be omitted:

"In unusual cases, the investigators may be required to release identifiable information (which may include your identifiable medical information) related to your participation in this research study in response to an order from a court of law. If the investigators learn that you or someone with whom you are involved is in serious danger or potential harm, they will need to inform, as required by Pennsylvania law, the appropriate agencies."

- 13) RIGHT TO PARTICIPATE or WITHDRAW FROM PARTICIPATION (Note: In lieu of incorporating this standard section heading, the standard question format, outlined below, may be used. Regardless of the option selected, all of the information addressed below should be included in this section of the consent form.)

Incorporate (in bold, italics) the standard question, "***Is my participation in this research study voluntary?***" and include the following standard statements:

"Your participation in this research study, to include the use and disclosure of your identifiable information for the purposes described above, is completely voluntary. (Note, however, that if you do not provide your consent for the use and disclosure of your identifiable information for the purposes described above, you will not be allowed to participate in the research study.) Whether or not you provide your consent for participation in this research study will have no effect on your current or future relationship with the University of Pittsburgh. Whether or not you provide your consent for participation in this research study will have no effect on your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with a health care insurance provider."

For investigators who recruit potential subjects from their own patient populations, address the conflict-of-interest inherent to the dual role of clinician and research investigators by incorporating the following standard statements:

"Your doctor is involved as an investigator in this research study. As both your doctor and a research investigator, s/he is interested both in your medical care and the conduct of this research study. Before agreeing to participate in this research study, or at any time during your study participation, you may discuss your care with another doctor who is not associated with this research study. You are not under any obligation to participate in any research study offered by your doctor."

Incorporate (in bold, italics) the standard question, "***May I withdraw, at a future date, my consent for***

participation in this research study?", and include the following standard statements and information:

"You may withdraw, at any time, your consent for participation in this research study, to include the use and disclosure of your identifiable information for the purposes described above. (Note, however, that if you withdraw your consent for the use and disclosure of your identifiable information for the purposes described above, you will also be withdrawn, in general, from further participation in this research study.) Any identifiable research or medical information recorded for, or resulting from, your participation in this research study prior to the date that you formally withdrew your consent may continue to be used and disclosed by the investigators for the purposes described above.

Note: Remove reference to "*or medical*" from the previous standard statements if this research study does not involve the use and disclosure of the subjects' identifiable medical information.

To formally withdraw your consent for participation in this research study you should provide a written and dated notice of this decision to the principal investigator of this research study at the address listed on the first page of this form.

Your decision to withdraw your consent for participation in this research study will have no effect on your current or future relationship with the University of Pittsburgh. Your decision to withdraw your consent for participation in this research study will have no effect on your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with a health care insurance provider."

- a) Address, if applicable, any dangers that may be associated with a decision to withdraw suddenly from study participation. Indicate, for example, that in the interest of the subject's safety, s/he is requested to participate in study termination laboratory tests or other monitoring procedures. **Note:** the consent form cannot include statements that mandate that subjects who desire to withdraw from study participation must complete certain study withdrawal procedures.
- b) Address other study termination requests such as the return of unused study drug or supplies.

Incorporate (in bold, italics), if applicable, the standard question, "**If I agree to participate in this research study, can I be removed from the study without my consent**", and address the following:

- a) Specify possible reasons why a subject may be withdrawn from study participation by the investigators.
- b) If applicable, indicate what steps will be taken to ensure the subject's safety upon his/her termination from study participation.
- c) If applicable, indicate the steps that will be taken with regard to continued treatment of the subject's disease or condition should s/he be withdrawn from study participation.
- d) Specify that any identifiable research or medical information recorded for, or resulting from, the subject's participation in this research study prior to the date that s/he was withdrawn from participation may continue to be used and disclosed by the investigators for the purposes described.

14) VOLUNTARY CONSENT

- a) Incorporate the following standard statements:

"The above information has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions, voice concerns or complaints about any aspect of this research study during the course of this study, and that such future questions, concerns or complaints will be answered by a qualified individual or by the investigator(s) listed on the first page of this consent document at the telephone number(s) given. I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator. I understand that I may contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations in the event that the research team is unavailable. By signing this form I agree to participate in this research study. A copy of this consent form will be given to me."

- b) For adults (age \geq 18 years old) capable of providing direct consent, incorporate the following standard statements and signature lines:

"By signing this form, I agree to participate in this research study. A copy of this consent form will be given to me."

Participant's Signature

Date

- c) For adults (age \geq 18 years old) determined to be decisionally-impaired and, thus, unable to provide direct consent, incorporate the following standard statements and signature lines:

Participant's Name (Print)

The above-named individual is unable to provide direct consent for study participation because

Therefore, by signing this form, I give my consent for his/her participation in this research study.

Representative's Name (Print)

Representative's Relationship to Participant

Representative's Signature

Date

Witness Signature

Date

Incorporate the following statements if the potential subject is capable of exercising some judgment concerning the nature of the research study and whether s/he desires to participate.

VERIFICATION OF EXPLANATION

I certify that I have carefully explained the purpose and nature of this research study to the above-named participant in appropriate language. He/she has had an opportunity to discuss it with me in detail. I have answered all his/her questions and he/she has provided affirmative agreement (i.e., assent) to participate in this study.

Investigator's Signature

Date

For research studies wherein the nature of the subject population is such that an individual may not be capable of initially providing direct consent for study participation but may recover adequate decision-making capability for direct consent at a later time, also incorporate the following standard statements and signature lines:

CONSENT FOR CONTINUED RESEARCH PARTICIPATION

I understand that I am currently participating in a research study. I further understand that consent for my participation in this research study was initially obtained from my authorized representative as a result of my inability to provide direct consent at the time that this initial consent was requested. I have now recovered to the point where it is felt that I am able to provide direct consent for continued participation in this research study.

"The above information has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions, voice concerns or complaints about any aspect of this research study during the course of this study, and that such future questions, concerns or complaints will be answered by a qualified individual or by the investigator(s) listed on the first page of this consent document at the telephone number(s) given. I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator. I understand that I may contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations in the event that the research team is unavailable. By signing this form I agree to participate in this research study."

By signing below, I agree to continue my participation in this research study. A copy of this consent form will be given to me.

Participant's Signature

Date

- d) For children (age 0-17 years), incorporate the following standard statements and signature lines:

"I understand that, as a minor (age less than 18 years), the above-named child is not permitted to participate in this research study without my consent. Therefore, by signing this form, I give my consent for his/her participation in this research study."

Parent's Name (Print)

Relationship to Participant (Child)

Parent's Signature

Date

(Note: For certain research studies involving children, the signature of both parents is required. See section 6.1.5 of the IRB Reference Manual)

ASSENT:

I certify that I have carefully explained the purpose and nature of this research study to the child-subject in age appropriate language. He/she has had an opportunity to discuss it with me in detail. I have answered all his/her questions and he/she has provided affirmative agreement (i.e., assent) to participate in this study.

Investigator's Signature

Date

Investigator's Printed Name

For children ages 14-17 or children less than 17 who are developmentally able to sign his/her name include the following language:

This research has been explained to me, and I agree to participate.

Signature of Child-Subject

Date

Printed Name of Child-Subject

- e) For an individual who agrees to participate in the research study but is unable to sign his or her name, the individual should make his/her "mark" on the Participant Signature line. The signature of a witness to this "signature/mark" of the study participant should be included on the respective informed consent document.

- 15) CERTIFICATION of INFORMED CONSENT: Incorporate the following standard statement and signature line:

"I certify that I have explained the nature and purpose of this research study to the above-named individual(s), and I have discussed the potential benefits and possible risks of study participation. Any question the individual(s) have about this study have been answered, and we will always be available to address future questions, concerns or complaints as they arise. I further certify that no research component of this protocol was begun until after this consent form was signed."

Printed Name of Person Obtaining Consent

Role in Research Study

Signature of Person Obtaining Consent

Date

8.3 Waivers and Exceptions of Informed Consent Requirements

8.3.1 Waiver of Informed Consent for Minimal Risk Research Studies (Research Activities)

The IRB can approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent, or may waive the requirement to obtain informed consent from some or all of the research subjects provided that each of the following criteria 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.

To be considered for such a waiver, the principal investigator must, in the recruitment section of the corresponding IRB research protocol, request a waiver of the requirement to obtain informed consent for some or all of the research subjects and must address each of the above criteria including a justification of its applicability to the proposed research and/or the subject population for whom the waiver of consent is being requested.

8.3.1.1 Model Request for Waiver of Informed Consent to Use Medical Record Information (PHI) to Identify Potential Research Subjects: Researcher Who Accesses and Uses Medical Record Information for this Purpose is Involved Directly in Providing Health Care to the Respective Patients – Question 4.3 in OSIRIS

The IRB will consider a waiver of informed consent for the use of medical record information to identify potential research subjects under the circumstance wherein the researcher is also the potential subjects' personal physician. With IRB approval of such a waiver request, the physician-researcher and other members of the potential subjects' health care provider staff would be permitted to access medical record information to identify potential subjects for subsequent contact to determine their interest in study participation. Note that this limited waiver of informed consent directed at the use of medical record information for subject identification and recruitment purposes does not constitute a waiver of informed consent for participation in the research study. This consideration is based on the fact that there is no breach of privacy or confidentiality of the patients' (i.e., potential subjects') medical record information since the personal physician-researcher (health care provider staff-researcher) already has knowledge of and access to this information.

In order for the IRB to address such a waiver request, it must find that the researcher has addressed and appropriately justified each of the Federal Policy criteria (45 CFR46.116(d)) for

granting a waiver of informed consent for this minimal risk research activity. (Note that the Office for Human Research Protections has determined that the use of medical record information to identify potential research subjects constitutes "human subject research" and is therefore subject to prior written informed consent of the involved patients-subjects or IRB waiver of this informed consent requirement. Involved researchers are not, however, required to obtain a waiver of the requirement for written HIPAA Authorization for this activity since the Office of Civil Rights has determined that the use of identifiable medical record information by the members of the respective covered entity for purposes of identifying and recruiting potential research subjects can be performed under the Preparatory to Research provisions of the HIPAA Privacy Rule.)

In addition, please note the following:

1. The waiver applies specifically to the personal physician or a member of the personal physician's health care staff who is directly involved in the health care of the patient and not to any colleagues who are not involved directly in the care of the patient.
2. The "use" refers to recording only identifiable information necessary to accomplish the purpose of the waiver, to identify potential research subjects for recruitment (e.g., to develop a mass mailing).
3. The waiver is not intended to serve the purpose of performing a full review of the medical records to determine complete eligibility. The waiver is only to help in initial recruitment efforts.

Federal Policy Criteria

1. Criterion: "The research [research activity] involves no more than minimal risk."

Justification: The research activity for which this waiver of informed consent is being requested is limited to accessing and using patient medical record information for the purpose of identifying potential research subjects. There are no physical or psychological risks associated with this research activity.

To ensure that the risk to the privacy and confidentiality of the involved patients remains minimal:

- (1) *any identifiable health information recorded for the purpose of identifying patients for subsequent research study recruitment will be stored in a secure manner (e.g., locked file cabinet, password protected database) accessible only to research study investigators who are also involved directly in the health care of the respective patients; and*
- (2) *the recorded identifiable health information of any given patient will be destroyed immediately after (a) determining that the patient does not, in fact, qualify for participation in the research study; or (b) contacting the patient for discussion of the research study and his/her interest in study participation.*

We hereby provide our assurance that any identifiable health information recorded for the purpose of identifying patients for subsequent research study recruitment will not be used

by or disclosed to any research study investigator who is not also involved directly in the care of the involved patients. We also provide our assurance that this identifiable health information will not be reused or disclosed to any other person or entity, except as required by law or for authorized oversight of the research study.

2. Criterion: "The waiver will not adversely affect the rights and welfare of the subjects."

Justification: Consistent with this waiver request, access to, and the use of patient medical record information for the purpose of identifying potential research subjects will be limited to research study investigators who are also involved directly in the care of the respective patients. Since these investigators would already have knowledge of and access to the patients' identifiable medical record information, granting of this waiver will not adversely affect the privacy of the involved patients or the confidentiality of their medical record information.

3. Criterion: "The research [research activity] could not practicably be carried out without the waiver."

Justification: It is not possible to conduct this research study unless we are able to identify and recruit potential research subjects. If the identification and recruitment of patients who meet research study eligibility criteria must rely on waiting until such time that these individuals schedule a clinic visit, this will result in considerable delays in our ability to accrue study participants and likely result in the sponsor's termination of the clinical trial [or termination of grant funding] before our research subject accrual projections [or requirements for statistical significance] are met. Research study recruitment efforts involving mass mailings directed at all patients seen in our clinic, the majority of whom would not meet study eligibility requirements, is not only impractical but would impinge on the privacy of especially non-eligible patients. Thus, to practically conduct this research study requires that we be able to access and use patient medical record information to identify prospectively our patients who meet study eligibility criteria and to focus our recruitment efforts at these patients.

The mechanism recommended by the IRB and UPMC for the identification and recruitment of potential research subjects involves the use of an honest broker system/process to (1) perform an independent (i.e., independent of the research investigators) review of medical record information to identify patients who meet study eligibility criteria; and 2) to provide the names of these potentially eligible research subjects to their personal care givers for subsequent contact to introduce the research study and ascertain the patient's preliminary interest in study participation. The first of these steps (i.e., involvement of an honest broker system/process) is necessary so as to avoid a violation of the patients' privacy and medical record confidentiality by the research investigators. However, consistent with this waiver request, the research investigators who will access the patient medical record information to identify potential research subjects are also involved directly in the care of the patients, thus obviating the privacy and confidentiality concerns. The second of these steps (i.e., involvement of the patient's personal care givers in potential subject recruitment) is necessary so as to avoid "cold-calling" which is prohibited by the IRB. However, consistent with this waiver request, the honest broker would be providing the identities of the potential subjects to care givers who are also the research investigators. In so doing, the care giver-investigators would be obtaining identifiable private information about the patients for research purposes without

the patients' consent; a violation of the Federal Policy regulations unless the IRB grants a waiver of the consent/authorization requirements for this research activity.

In summary, this research activity (i.e., use of patient medical record information to identify potential research subjects) could not practically be conducted without a waiver of the informed consent requirements.

4. Criterion: "Whenever appropriate, the subjects will be provided with additional pertinent information after participation."

Justification: Note that we are requesting a waiver of the requirements to obtain informed consent for the limited purpose of allowing research investigators to access and use patient medical record information to identify their patients who may be eligible for participation in this research study. The informed consent of these patients will be obtained for actual study participation/collection of their medical record information for study purposes.

To be considered for such a waiver, the principal investigator must, in the recruitment section of the corresponding IRB research protocol, request a waiver of informed consent to use medical record information (PHI) to identify potential research subjects.

Investigators who have previously approved protocols who wish to request this waiver may do so by submitting an expedited modification to modify the recruitment section of the corresponding IRB research protocol.

8.3.2 Waiver of the Requirement to Obtain a Signed Informed Consent Document for Participation in a Research Study [Research Activity] – Question 4.6 in OSIRIS

The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all of the research procedures if either:

- 1) 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; or
 - If a waiver is granted based on this criterion, each subject must be asked whether s/he wants documentation linking her/him with the research, and the subject's wishes will govern.)
 - **Please note that a waiver to document cannot be approved under Category #1 if the respective research study is subject to FDA regulations (21 CFR Parts 50, 56) governing human subject protections (i.e., the research study involves an evaluation of any article [e.g., drug, device, food, electronic product] regulated by the FDA).**
- 2) 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.

To be considered for such a waiver, the principal investigator must, in the recruitment section of the corresponding IRB research protocol, request a waiver of the requirement to obtain a signed informed

consent document for some or all of the research procedures and must address whichever of the above criteria is applicable to the research procedures for which the waiver is being requested to include an appropriate justification for its applicability.

Note that if the IRB grants a waiver of the requirement to obtain a signed consent form for some or all of the research procedures, this does not eliminate the requirement to obtain the informed consent of the subject for participation in the respective research procedures. Thus, accompanying this waiver request should be a script of the information that will be provided to potential subjects in obtaining their verbal consent for participation in the respective research procedures. This verbal consent process should include all of the basic and additional, applicable elements of informed consent addressed under sections 8.1.1 and 8.1.2, above. The waiver request should also address (i.e., within the recruitment section of the corresponding IRB research protocol, the mechanism that will be used by the investigators to document that the verbal consent of subjects has, in fact, been obtained.

8.3.3 Exception of the Requirement to Obtain Informed Consent for Research Involving the Evaluation of Emergency Care Interventions – Question 4.8 in OSIRIS

The Federal Policy and FDA regulations permit individuals to be enrolled, without their legally effective informed consent (or the consent of their authorized representative), in research studies directed at the evaluation of emergency care interventions provided that certain basic conditions are met:

- 1) Potential subjects are in a life-threatening situation, and:
 - a) available treatments are unproven or unsatisfactory; and
 - b) collection of scientific data is required to determine the safety and effectiveness of the experimental intervention.
- 2) Obtaining informed consent is not feasible because:
 - a) the potential subject is not able to consent due to his/her medical condition;
 - b) the intervention must be administered before consent from the potential subject's authorized representative is feasible; and
 - c) there is no reasonable way to identify prospectively potential eligible subjects.
- 3) Participation in the research study holds out the prospect of direct benefit to the subjects because:
 - a) the subjects are facing a life-threatening situation;
 - b) appropriate pre-clinical and prior clinical research studies support the potential for direct benefit; and
 - c) the risks associated with the research are reasonable relative to the risks of the subjects' condition and the risk/benefit ratio of standard therapy for the condition.
- 4) The research could not be practically carried out without the waiver.

In addition to meeting the above basic conditions, there are multiple additional requirements that must be addressed before the IRB can grant exceptions to the requirement to obtain informed consent for research

involving the evaluation of emergency care interventions. The investigator should address the following information in the protocol:

- 1) Define, based on scientific evidence, the maximum length of time before which the intervention(s) must be initiated (i.e., a "therapeutic window").
- 2) Define what attempts will be made to contact, within this "therapeutic window", a legally authorized representative for each subject and, if feasible, to asking this representative for consent for the subject's participation.
- 3) In the event of the unavailability of a legally authorized representative of the subject, define what attempts will be made, if feasible, to contact, within this "therapeutic window", a member of the subject's family and asking whether s/he objects to the subject's participation.
- 4) Address standard informed consent procedures (i.e., to address subject enrollment with direct consent, if applicable, or with consent of the subject's authorized representative, if available) and includes an informed consent document that meets applicable regulatory and IRB guideline requirements).
- 5) Address procedures to inform, at the earliest feasible opportunity the subject (i.e., if his/her condition improves), a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member of the subject, of the subject's inclusion in research, the details of the research, and the right to discontinue the subject's participation at any time without penalty or a entitled benefits; and
- 6) Address appropriate procedures and information to be used in providing an opportunity for a family member to object to a subject's participation in the research.
- 7) Address procedures to provide information about the research to the subject's legally authorized representative or family member should a subject enrolled into the study without consent die before such individuals can be contacted.
- 8) Address an independent data monitoring committee to exercise oversight of the research (see Appendix L for additional requirements related to data and safety monitoring committees/plans).
- 9) Address prior, specific IND or IDE approval (i.e., as research involving an emergency consent waiver) of the research by the Food and Drug Administration (i.e., for research involving investigational or approved drugs or devices).
- 10) Address the requirement for consultation with representatives of the community (communities) in which the research will be conducted and from which the subjects will be drawn. The University of Pittsburgh currently utilizes the Pittsburgh Human Relations Commission as its community consultation committee. Contact Jeannie Barone, Assistant Director for Regulatory Affairs, at 412-383-1480 for assistance with this requirement. A summary of comments/concerns raised by the community must be presented to the IRB prior to final approval being granted.
- 11) Address a plan, including draft copy, for public disclosure/notification of the research to the community (communities) in which the research will be conducted and from which the subjects will be drawn. This could include meetings with focus groups, church or community organizations, newspaper articles, etc. A summary of comments/concerns raised during public disclosure/notification must be presented to the IRB prior to final approval being granted.

Investigators involved in the development or implementation of such research studies, wherein an exception to the requirement to obtain informed consent is an anticipated necessity, are advised to engage the assistance of the IRB Office as early as possible in the development or implementation process. Please contact Jeannie Barone, Assistant Director for Regulatory Affairs, at 412-383-1480 for assistance.

8.3.4 Model Request for Waiver of the HIPAA Authorization Requirement for the Sharing of Contact Information (i.e., Linked to Study-Specific Health Information [subject's medical diagnosis or condition]) for the Purpose of Recruiting Potential Research Subjects – Question 2.14 in OSIRIS

To facilitate the identification and recruitment of potential research subjects, researchers will frequently employ the services of physicians and health care staff members (referring health care providers), who are independent of the research study, to introduce the research study to their patients who may be eligible for study participation. For those patients who indicate an interest in study participation, the referring health care provider will obtain the verbal permission of the patient to transfer the patient's name and contact information (linked to medical diagnosis or condition) to the researcher. The Office of Civil Rights has specified that this research subject identification and recruitment activity may proceed (i.e., under the Preparatory to Research provisions of the HIPAA Privacy Rule) without the requirement for a valid HIPAA Authorization provided that the referring health care provider and the researcher who receives this contact information work for the same covered entity (e.g., hospital system, physician's office). (One of the conditions of the Preparatory to Research provision of the HIPAA Privacy Rule is that the identifiable health information may not be removed from the covered entity.) Thus, this exception to the requirement for a valid HIPAA Authorization would apply when, for example, both the referring health care provider and the researcher who receives the contact information work for UPMC. Examples of situations where this exception would not apply include the following:

- the researcher who receives the contact information is an employee of UPMC, but the referring health care provider does not work for UPMC
- the referring health care provider works for UPMC, but the researcher (e.g., a listed investigator or research study coordinator) who receives the contact information is an employee of the University (i.e., not an employee of UPMC).

In these latter situations where the exception to the requirement for a valid HIPAA Authorization does not apply, the referring health care provider must either 1) obtain the written HIPAA Authorization of the patient to share the patient's contact information (i.e., linked to medical diagnosis or condition) with the researcher (see model HIPAA Authorization for Sharing Health Information under the HIPAA page [Forms and Documents] of the IRB web site [www.irb.pitt.edu]); or 2) a HIPAA privacy board or IRB must grant a waiver of this HIPAA Authorization requirement. Note that the HIPAA Privacy Rule does not include provisions for obtaining the verbal HIPAA Authorization of patients.

Prior to the HIPAA Privacy Rule, the IRB permitted this research subject identification and recruitment activity to proceed without the requirement for the written informed consent of the patient, provided that the referring health care provider appropriately documented the patient's verbal permission to provide the patient's contact information to the researchers. This previous policy was consistent with the Office of Human Research Protection guidance concerning situations wherein an institution is or is not "engaged" in the conduct of human subject research

(see *Engagement of Institutions in Research*, OHRP (OPRR), January 26, 1999).

The University IRB will consider a waiver of the requirement for a written HIPAA Authorization for the sharing of contact information (linked to medical diagnosis or condition) for the purposes of subject identification and recruitment in the following limited circumstance:

- The researchers who receive the patient's/potential subject's contact information either (1) do not work for the covered entity (e.g., are University employees); or (2) work for a different covered entity than the referring health care provider(s).

In addition, please note the following:

1. As per the previous discussion, there is no requirement for a written HIPAA authorization if both the referring physician and the researcher who receives the patient's/potential subject's contact information work for the same covered entity (e.g., both work for UPMC), and the referring health care provider appropriately documents the patient's verbal permission to provide his/her contact information to the researcher.
2. The University IRB may grant such a waiver of the requirement for a written HIPAA Authorization for the sharing of contact information (linked to medical diagnosis or condition). However, there is no guarantee that the covered entity to which the referring health care provider reports will accept the University IRB's waiver approval decision if the University IRB does not currently serve, based on a contractual relationship, as the IRB-of-record for that covered entity. (Refer to the Preface of the IRB's *Reference Manual for the Use of Human Subjects in Research* for a listing of those covered entities for which the University is currently the IRB-of-record.
3. This waiver of the HIPAA Authorization requirement applies only to the sharing of the patient's/potential subject's contact information (linked to medical diagnosis or condition). If the researchers wish to access and review the patient's/potential subject's medical record information for the purpose of determining study eligibility, they will need to obtain prospectively the written informed consent of the patient for this activity or IRB approval of a waiver of this informed consent requirement (see section 8.3.1.1).

Below is a template for requesting a waiver of the requirement for a written HIPAA Authorization for sharing contact information (linked to medical diagnosis or condition) for the purposes of subject identification and recruitment:

HIPAA Waiver Criteria and Respective Justifications

1. Criterion: "The use or disclosure of protected health information involves no more than a minimal risk to the privacy of individuals based on (a) an adequate plan to protect the identifiers from improper use and disclosure; (b) an adequate plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research (unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law); and (c) adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of protected health information would be permitted by this subpart."

Justification: The sharing of the patient's/potential subject's contact information (linked to medical diagnosis or condition) between the referring health care provider and the researchers involves no more than a minimal risk to the privacy of the patient since the referring health care provider, who introduces the research study to his/her patient, will obtain and appropriately document the verbal permission of the patients to provide the patient's contact information to the researchers.

To further ensure that the risk to the privacy of the involved patients remains minimal:

- (1) the patient's/potential subject's recorded contact information will be stored by the researchers in a secure manner (e.g., locked file cabinet, password protected database) accessible only to the researcher who was provided this information and other members of the research team involved in the conduct of the research study (studies) for which this information was originally provided; and*
- (2) the patient's recorded contact information will be destroyed immediately after the researchers have contacted the patient to discuss the research study (studies) for which this information was originally provided; unless, upon such contact, the patient/potential subject indicates a further interest in study participation.*
 - For patients/potential subjects who indicate a further interest in study participation, the patient will be engaged in an informed consent process to further determine research study eligibility and/or study interest. The patient's recorded contact information will be destroyed immediately after ascertaining that the patient is not eligible for or declines participation in the research study (studies).*

We hereby provide our assurance that the recorded patient contact information will not be reused or redisclosed to any other person or entity (i.e., other than the members of the research team involved in the conduct of the research study [studies] for which the contact information was originally provided) except as required by law or for authorized oversight of the research study.

2. Criterion: "The research [research activity] could not practically be conducted without the waiver or alteration."

Justification: It is not possible to conduct this research study unless we are able to identify and recruit potential research subjects. To avoid "cold-calling" it is recommended by the University IRB that the research study be first introduced to patients/potential subjects by an individual involved directly in their health care (i.e., referring health care provider). If the patient/potential subject is interest in study participation, s/he can be given the contact information for the researchers and asked to contact the researchers directly. However, this approach has been routinely shown to result in a very low rate of patient/potential subject follow up. A much more effective alternative is for the health care provider, who introduced the research study to the patient, to obtain the permission of the patient/potential subject to provide the patient's contact information to the researchers. While it may be possible for this permission to be documented in the form of a valid written HIPAA Authorization, such is reasonably practical only in those situations wherein the respective health care provider and patient interaction occurs face-to-face (e.g., during

a clinic visit). It is not reasonably practical to obtain a valid written HIPAA Authorization if the research study is introduced to the patient/potential subject via a letter from the patient's health care provider or via a telephone interaction between the patient and health care provider. Even in the situation where the respective health care provider and patient interaction occurs face-to-face, the requirement for the patient to sign a valid (at minimum 2 page) HIPAA Authorization to document the patient's permission to simply provide his/her contact information to the researchers is considered to be excessive by both the involved health care providers and the patients/potential subjects; thus impacting substantially on the willingness of these individuals to participate in this research subject recruitment activity.

In summary, this research activity (i.e., the sharing of the patient's interest in research study participation and the patient's contact information [linked to medical diagnosis or condition] between referring health care providers and the researchers) could not practically be conducted without a waiver of the HIPAA authorization requirement.

3. Criterion: "The research [research activity] could not practically be conducted without access to and use of the protected health information."

Justification: It is not possible to conduct this research study unless we are able to identify and recruit potential research subjects. To avoid "cold-calling" it is recommended by the University IRB that the research study first be introduced to patients/potential subjects by an individual (e.g., a referring health care provider) involved directly in their health care. If a patient is interested in study participation, his/her contact information (linked to medical diagnosis or condition) must be provided by the referring health care provider to the researchers in order to provide an effective mechanism to follow up on this interest and to recruit subjects into this research study.

8.3.5 Model Request for a Waiver of the Requirements to Obtain HIPAA Authorization/Informed Consent to Access, Record, and Use Protected Health Information/Patient Medical Record Information for a Retrospective Research Study: Investigator(s) Who Accesses (Access) and Uses (Use) Such Information for Research is (are) Involved Directly in Providing Health Care to the Respective Patients

Retrospective research studies involving investigator access to and the recording of identifiable medical record information are subject to both 1) the requirement for the respective patients' signed, written authorization in accordance with the HIPAA Privacy Rule; and 2) the requirement for the respective patients' signed, written informed consent in accordance with the Federal Policy regulations governing human research subject protections. The IRB will consider a waiver of the HIPAA authorization and informed consent requirements for retrospective research studies involving access to and the recording of identifiable medical record information under the circumstance wherein the researcher(s) who accesses (access) and use such information is (are) involved directly in providing health care to the respective patients. This consideration is based on the fact that there is no breach of privacy or confidentiality of the patients' (i.e., subjects') medical record information since the personal health care provider(s)-researcher(s) already has (have) knowledge of and access to this information.

In order for the IRB to grant such a waiver request, it must find that the researcher has addressed and appropriately justified each of the HIPAA criteria for granting a waiver of the written HIPAA authorization requirement and each of the Federal Policy criteria for granting a waiver of informed

consent requirement for this minimal risk research activity. Below is a template for requesting a waiver of these requirements.

A. HIPAA Waiver Criteria and Respective Model Justifications

1. Criterion: "The use or disclosure of protected health information involves no more than a minimal risk to the privacy of individuals based on (a) an adequate plan to protect the identifiers from improper use and disclosure; (b) an adequate plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research (unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law); and (c) adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of protected health information would be permitted by this subpart."

Justification: Access to and the use of protected health information by the research investigator(s) who is (are) also involved directly in the care of the respective patients involves no more than a minimal risk to the privacy of these patients since these investigator(s) already has (have) knowledge of and access to the patients' identifiable health information. Moreover, the protected health information that will be accessed, recorded and used by this (these) investigator(s) will be limited to that information which is related to the investigator's (investigators') area of medical practice. To further ensure that the risk to the privacy of the involved patients remains minimal:

- (1) *the protected health information collected for the purpose of this research study will be assigned a research code number and any obvious patient identifiers (name, social security number, hospital record number) will be removed from this information. Both the anonymized health information and the information linking the research code numbers to the patients' identities will be stored in a secure manner (e.g., locked file cabinet, password protected database) accessible only to the research study investigator(s) who is (are) also involved directly in the health care of the respective patients. The information linking the research code numbers to the patients' identities will be stored separate from the anonymized health information.*
- (2) *the information linking the research code numbers to the patients' identities and the anonymized health information will be destroyed (1) immediately after a determination has been made to not publish the respective research study; or (2) at 7 years following the publication of the respective research study (i.e., in accordance with University policies).*

I (We) hereby provide my (our) assurance that any protected health information recorded for the purpose of this research study will not be used by or disclosed to any other person or entity, except as required by law or for authorized oversight of the research study.

2. Criterion: "The research could not practically be conducted without the waiver or alteration."

Justification: It is not possible to conduct this research study without access to and the use of protected health information. In accordance with the Federal Policy regulations governing human subject protections, the process of accessing identifiable medical record information for the purpose of identifying eligible patients for this research study so as to permit the subsequent obtaining of their HIPAA authorization, itself, requires the prior informed consent of the involved patients. The patients, whose protected health information will be accessed under this waiver request, have not previously provided informed consent for this research activity. Thus, obtaining the HIPAA authorization of these patients for the research use of their health information is impractical. In the absence of obtaining the HIPAA authorization of the patients for the use of their protected health information for research, the IRB and UPMC recommend the involvement of an honest broker system/process to perform an independent (i.e., independent of the research investigators) collection of the protected health information and its subsequent de-identification (in accordance with HIPAA "safe harbor" or "limited data set" standards) prior to providing the information to the research investigators. Such involvement of an independent honest broker system/process is cumbersome and adds expense to the study, but is typically necessary so as to avoid a violation of the patients' privacy and medical record confidentiality by the research investigators. However, consistent with this waiver request, the research investigators who will access and use the protected health information are also involved directly in the care of the respective patients, thus obviating the privacy and confidentiality concerns.

In summary, this research study could not practically be conducted without a waiver of the HIPAA authorization requirement.

3. Criterion: "The research could not practically be conducted without access to and use of the protected health information."

Justification: Access to and the collection and analysis of protected health information is necessary in order to conduct this research study. Consistent with the "minimum necessary standard" of the HIPAA privacy rule, I (we) will only access and collect the specific health information necessary to complete this research study.

B. Federal Policy Criteria and Respective Model Justifications

1. Criterion: "The research involves no more than minimal risk."

Justification: This research study is limited to accessing, collecting and analyzing existing medical record information. There are no physical or psychological risks to the human subjects (i.e., the respective patients) associated with the conduct of this research study.

Access to and the collection and analysis of identifiable medical record information for this research study involve no more than a minimal risk to the confidentiality of the respective patients private information based on (a) an adequate plan to protect the identifiers from improper use and disclosure; (b) an

adequate plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research; and (c) adequate written assurances that the recorded medical record information will not be reused or disclosed to any other person or entity, except as required by law or for authorized oversight of this research study (see HIPAA Waiver Criteria and Respective Justifications).

2. Criterion: "The waiver will not adversely affect the rights and welfare of the subjects."

Consistent with this waiver request, access to and the recording and use of identifiable medical record information for the purpose of this research study will be limited to an investigator(s) who is (are) also involved directly in the care of the respective patients. The medical record information that will be accessed, recorded and used by this (these) investigator(s) will be limited to that information which is related to the investigator's (investigators') area of medical practice. Since this (these) investigator(s) would already have knowledge of and access to such identifiable medical record information for his/her (their) patient care responsibilities, granting of this waiver will not adversely affect the privacy of the involved patients or the confidentiality of their medical record information.

3. Criterion: "The research could not practicably be carried out without the waiver."

Justification: It is not possible to conduct this research study without access to and the use of the patients' medical record information. In accordance with the Federal Policy regulations governing human subject protections, the process of accessing identifiable medical record information for the purpose of identifying eligible patients for this research study so as to permit the subsequent obtaining of their informed consent, itself, requires the prior informed consent of the involved patients. The patients, whose protected health information will be accessed under this waiver request, have not previously provided informed consent for this research activity. Thus, obtaining the informed consent of these patients for the collection and use of their identifiable medical record information for the purpose of this research study is impractical. In the absence of obtaining the informed consent of the patients for the use of their identifiable medical record information for research, the IRB and UPMC recommend the involvement of an honest broker system/ process to perform an independent (i.e., independent of the research investigators) collection of the requisite medical record information and its subsequent de-identification prior to providing the information to the research investigators. Such involvement of an independent honest broker system/process is cumbersome and adds expense to the study, but is typically necessary so as to avoid a violation of the patients' privacy and medical record confidentiality by the research investigators. However, consistent with this waiver request, the research investigator(s) who will access and use the patients' identifiable medical record information is (are) also involved directly in the care of the patients, thus obviating the privacy and confidentiality concerns.

In summary, this research study could not practically be conducted without a waiver of the HIPAA authorization requirement.

4. Criterion: "Whenever appropriate, the subjects will be provided with additional pertinent information after participation."

Should the analysis of the medical record information collected for the purpose of this research study reveal a situation that may impact on the health of a patient, the investigator(s), who is (are) also involved in the care of the respective patient, will promptly notify the patient and offer the availability of care.

To be considered for such a waiver, the principal investigator must, in the recruitment section of the corresponding IRB research protocol (submitted in accordance with the requirements for expedited IRB review), request a waiver of HIPAA authorization/informed consent for access to and the recording of identifiable medical record information; to include the respective HIPAA and Federal Policy waiver criteria and model justifications addressed above.

8.3.6 Request for a Waiver of the Requirement to Obtain HIPAA Authorization to Access, Record, and Use Protected Health Information/Patient Medical Record Information for a Retrospective Research Study: Investigator(s) Who Accesses (Access) and Uses (Use) Such Information for Research is (are) Involved Directly in Providing Health Care to the Respective Patients

This waiver request is completed within the exempt form for retrospective medical record review at: <http://www.irb.pitt.edu/Exempt/RetrospectiveMedRev.htm>. The principal investigator (P.I.) of the research study must have legitimate access to the desired medical information insofar as he or she is a UPMC staff member and/or has been granted UPMC privileges and provides related care (i.e., related to the information desired) to the patients, or is in the position to provide related care (including treatment, and/or diagnostic services) to the patients.

For example, any health professional providing patient care to a particular set of patients (e.g., all patients treated in the Emergency Department; all patients with aphasia; all patients undergoing CT scans), would ordinarily have access to the related medical record information of those patients as part of his or her current or future job responsibilities, and hence would be in a position to serve as the P.I. of a research study involving a retrospective review of those medical records (regardless of whether he or she actually provided direct care to those particular patients).

Note that the University IRB will not approve a retrospective medical record research study with such a waiver request if the medical record information desired is not in some way related to the patient care responsibilities of the listed P.I.

In order for the IRB to grant such a waiver request in the exempt form for retrospective medical record review, it must find that the researcher has addressed and appropriately justified each of the HIPAA criteria for granting a waiver of the written HIPAA authorization requirement.