RIRC Informed Consent

A. Purpose

The primary purpose of this procedure on informed consent is to outline the multiple requirements of the consent and assent process.

B. Applicable Regulations

21 CFR 50.25 45 CFR 46.116

QMC Policy 674-xx-708 on Informed Consent

QMC Policy SW-21-099 Interpreter Services for Foreign Language Speakers and the Hearing/Speech Impaired

DEFINITIONS

Assent: a child's affirmative agreement to participate in research. Assent may be verbal or in writing, depending on what the IRB approved protocol requires. Failure of the child to object to participating is not assent.

Guardian: An individual who is authorized by law to consent on behalf of a child to general medical care.

Informed Consent: A process by which a potential participant in a research project voluntarily agrees to participate in the study after having been informed of all aspects of the study relevant to the subject's decision to participate and having all questions answered to the participant's satisfaction. The process continues throughout the study and is documented by means of a written, signed, and dated informed consent form approved by the IRB.

Informed Consent Document: The written document, meeting all legal and regulatory requirements and approved by the IRB, which is signed by the participant or the participant's legally authorized representative demonstrating the participant's consent to participate.

Legally Authorized Representative: An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

Parent: A child's biological or adoptive parent.

Vulnerable Subjects: Individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of

refusal to participate. Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental, and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention. Other vulnerable subjects include patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors, and those incapable of giving consent. (ICH 1.61). Pregnant women, human fetuses and neonates, prisoners, terminally ill persons, economically and/or educationally disadvantaged, and cognitively impaired persons are also vulnerable populations.

Witness to Signature: A third party individual not involved in the study who witnesses the voluntary signature of research subject and/or legally authorized representative.

C. Process of Informed Consent

Informed consent is an on-going process that starts with the initial presentation of a research study to a prospective subject by the investigator and continues through the research activity until the subject ends his/her participation or the study closes.

1. Elements of Consent

    a. Informed consent is a primary ethical prerequisite to involving human subjects in research. It is based on the basic ethical principles of respect for persons, beneficence and justice as define in the Belmont Report (Appendix 1). Respect for person requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them. The consent process must involve the elements of information, comprehension and voluntariness. These 3 elements are described in full detail in the Belmont Report (Appendix 1).
    b. Informed consent is an ongoing process, it does not end with the signing of the consent. Research involves the constant re-evaluation of current information and procedures. The investigator is ethically obligated to keep subjects apprised of all issues related to their participation in the research.
    c. Informed consent is the knowing consent from an individual, or his/her legally authorized representative, who is able to exercise free power of choice without undue inducement or any element of force, fraud, deceit, duress or other form of constraint or coercion.
    d. The application submission must explain how informed consent will be obtained from the prospective research subject.
    e. It is the responsibility of the IRB to determine which of the procedures [45 CFR 46.117(b)] is appropriate for documenting informed consent in protocols that it reviews.

D. Assessing capacity to consent

Individuals in a wide variety of situations may have impaired decisionmaking capacity. For example, impairment may occur at times of great stress. Impaired capacity is not limited to individuals with neurologic, psychiatric, or substance abuse problems; conversely, individuals with neurologic, psychiatric, or substance abuse problems should not be presumed to be decisionally impaired. Some research questions may only be answered by research that involves persons with impaired decisionmaking capacity; precluding this research would contribute to needless suffering. The most severely impaired individuals have the greatest need for the benefits of research on etiology and treatment. While this area is controversial, limiting research to the least impaired individuals would hamper research on the underlying causes and potential therapies of many disorders. Not all research will directly benefit the individual participant but any offer future benefits to others who have or will develop the condition or disorder. While limited decisionmaking capacity should not prevent participation in research, it is important to keep in mind the need for additional scrutiny by the RIRC and the investigators when research involves this population.[1]

1. Conflicting roles and potential conflicts of interest.

   Potential and actual research participants, especially those with permanent or transient cognitive impairments, may find it difficult to understand the difference between research and treatment, and to understand researchers' multiple roles, making "therapeutic misconceptions" particularly problematic and possibly creating confusion among participants and their families.
   The consent form and the consent process must clearly indicate difference between individualized treatment and research and differences between clinician and clinical investigator.

2. Evaluating capacity to consent.

   Individual's capacities, impairments, and needs must be taken into account. Methods to assess capacity to consent are clearly needed. A clear understanding of the implications of various cognitive impairments, along with a careful consideration of proposed clinical research methodology is required. Assessment is complex; simply answering a certain number of factual questions about a protocol may not be an adequate assessment. A key factor in participants' decisionmaking is their appreciation of how the risks, benefits and alternatives to participation in the study apply to them personally.

   a. Limited decision making covers a broad spectrum. A healthy person in shock or a woman in labor may be temporally

decisionally impaired. Another may be severely retarded since birth, while yet a fourth who has schizophrenia may have fluctuating capacity. Investigators are required to be sensitive to differing levels of capacity and use evaluating methods tailored to the specific situation. The timing of the assessment must be considered to avoid periods of increased vulnerability when individuals may not be able to provide informed consent.

b. RIRC and the investigator are required to keep in mind that decisionmaking capacity may fluctuate, requiring ongoing assessment during the course of the research. The consent process must be ongoing.

3. Responsibility of the RIRC

Not all research projects proposing to involve decisionally impaired persons should be approved by the RIRC, and not all such persons should be enabled to participate in research studies.

a. A significant responsibility of the RIRC is the review of the informed consent/assent document, the consent process and the research design as presented in the research proposal. The RIRC is required to exercise heightened vigilance in the review of protocols involving individuals with questionable capacity.

b. As impairment increases, along with risks and discomforts, safeguards should increase according to a sliding scale i.e., protections should be proportional to the severity of capacity impairment or to the magnitude of experimental risk or both. Provisions for additional safeguards should be in place prior to involving individuals with questionable decisionmaking capacity in research that poses greater than minimal risk.

4. Options for additional safeguards.

A sliding scale involving evaluation of risks, benefits, and capacity to consent can guide the RIRC decisions regarding additional safeguards. Many strategies are available as options for investigators as they develop their research protocols and for RIRC members as they evaluate them. Examples of strategies include, but are not limited, to the following:

a. <u>Use of an Independent Monitor</u>
When reviewing greater than minimal risk research involving individuals with questionable capacity to consent, a monitor can be present when investigators invite individuals with impaired decisionmaking capacity to participate in research. The consent process should be visible throughout. The RIRC also has the right to observe recruitment, assessment, the informed consent process

and debriefing of research participants (and/or their family/surrogates).

b. Use of a Surrogate
When permitted by law, individuals with impaired capacity many have a family member or other legally authorized representative serve as a surrogate for research decisions, with this role documented during the consent process. Surrogates should be informed of the risks, benefits, and alternatives to the research when they are providing permission for an individual to participate. Whenever possible, surrogates should make research decisions based on substituted judgement, reflecting the views of the individual expressed while decisionally capable. Best interest standards should be used if the values of the individual are not known. It is important that surrogates receive some education about their own role, the cognitive and health status of the research participant, as well as about the study in which the participant may be involved.

c. Use of Assent in Addition to Surrogate Permission
The autonomy of individuals with impaired decisionmaking capacity should be respected. Their assent to participation in research should be obtained whenever possible and their decision to withdraw from a study at any time should be honored.

d. Use of an Advance Directive
Use of an advance directive for research can be considered.

e. Use of Informational/Educational Techniques
Because informed consent is an ongoing process throughout the course of the protocol, assessing and enhancing comprehension at each stage is essential. Single sheet summaries of important information about key elements of a study may be useful when provided on a regular basis. Questions from potential participants and family members should be encouraged, and handouts of frequently asked questions and answers regarding specific human subject protections can be prepared.

f. Use of a Waiting Period
Individuals who are decisionally impaired may need more time to consider the information they are given about a research protocol. Information can be provided incrementally to facilitate understanding. Planning built-in waiting periods within the consent process also may be useful to allow potential participants time to consult with family members about whether or not to participate.

E. Types of Consent

1. Written consent

The written consent form is normally appropriate for all research above a minimal level of risk. The consent form must include information that subjects would reasonably want to know about the study and the extent of their involvement in it. The information required in the informed consent is listed below in Sections E, F, G, H, I, J, L and N.

2. **Short form (**Oral consent)
A short form written consent must state that the elements of informed consent (as required by 21 CFR 50.25) have been presented orally to the research subject or subjects representative. A witness must be present during the oral presentation to the subject. **The RIRC must approve a written summary of what is to be said to the subject/representative.** The subject must sign the short form written document. The witness and the principal investigator must sign both the short form document and the written summary. **The subject must be given copies of both the summary and the short form.**

3. Waiver of consent in emergency medicine research
In October 1996, a new regulation (Title 21 CFR 50.24) allowing a narrow exception to the requirement for informed consent from each human subject or his or her legally authorized representative prior to initiation of an experimental intervention was passed for use with research in emergency settings.

The RIRC must document that each of the following criteria of the rule are met:

a. <u>Human subjects are in a life-threatening situation</u>
This criteria does not require the condition to be immediately life-threatening or to immediately result in death. Rather the subjects must be in a life-threatening situation requiring intervention before consent from a legally authorized representative is feasible. Life-threatening includes diseases or conditions where the likelihood of death is high unless the course of the disease or condition is interrupted. This could include people with long-term or permanent coma, stroke and head injury who may survive for long periods but the likelihood of survival is not known during the therapeutic window of treatment. The rule would apply in such situations if the interventions must be given before consent is feasible in order to be successful. The consent waiver is not intended to apply to persons who are not in emergent situations.

b. <u>Available treatments are unproven or unsatisfactory</u>
Clinical equipoise must exist. When the relative benefits and risks of the proposed intervention, as compared to standard therapy are unknown or thought to be equivalent or better, there is clinical equipoise between the historic intervention and the proposed test intervention.

c. The collection of valid scientific evidence is necessary to determine the safety and effectiveness of a particular intervention.

d. Obtaining informed consent is not feasible because:

   i. *The subjects will not be able to give their informed consent as a result of their medical condition.*
   Subjects do not have to be comatose, but the medical condition under study must prevent obtaining valid informed consent.

   ii. *The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible.*

   iii. *There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.*
   If the RIRC determines that it is not appropriate to waive the requirement for informed consent because there is a reasonable way to identify prospectively the individuals likely to become eligible for the study, then this exception would not apply.

e. Participation in the research holds out the prospect of direct benefit to the subjects because:

   i. *Subjects are facing a life-threatening situation that necessitates intervention.*

   ii. *Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects*.

   iii. *Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.*

f. The clinical investigation could not be carried out without the waiver.

g. The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact legally authorized representatives and make this information available to the RIRC at the time of continuing review.

h. The RIRC has reviewed and approved informed consent procedures and an informed consent document consistent with

other requirements in this chapter. These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible. If feasible, this procedure provides for an opportunity for available family members to object to a potential subject's participation in a clinical investigation and provides an additional and an important protection to these individuals.

i. Additional protections of the rights and welfare of subjects will be provided including at least:
   i. *Consultation (including, where appropriate, consultation carried out by the RIRC) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn.*
   ii. *Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits.*
   iii. *Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population and its results.*
   iv. *Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation.*
   v. *If obtaining informed consent is not feasible and a legally authorized representative is not reasonable available, the investigator has committed, if feasible to attempting to contact within the therapeutic window the subject's family member who is not a legally authorized representative, and asking whether he or she objects to the subject's participation in the clinical investigation. The investigator will summarize efforts made to contact family members and make this information available to the RIRC at the time of continuing review.*

j. The RIRC is responsible for ensuring the procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available a family member of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document.

k. Protocols involving an exception to the informed consent requirement under this section must be performed under a separate

investigational new drug application (IND) or investigational device exception (IDE) that clearly identifies such protocols as protocols that may include subjects who are unable to consent.

l. If the RIRC determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided under this section or because of other relevant ethical concerns, the RIRC must document its findings and provide these findings promptly in writing to the investigator and to the sponsor of the investigation.

F. Principal Investigator Responsibility

1. The Principal Investigator is responsible and accountable for gaining participants' informed consent to participate in the study in accordance with federal and local law, rules, regulations and university policy.

2. The PI may delegate responsibility for the informed consent process to another qualified researcher or research personnel involved in the study, but may not delegate accountability. Examples of qualified researchers to whom the PI may delegate responsibility for obtaining informed consent include Co-Investigators, Sub-Investigators, Research Associates, Clinical Research Nurses, Research Assistants, and Regulatory Coordinators, as per Policy 674-xx-708.

3. Informed Consent of studies involving investigational product may only be signed by a licensed independent practitioner researcher who will prescribe or perform substantial and significant aspects of the device or procedure.

4. The PI and all research personnel who are involved in the informed consent process or in documenting informed consent must be able to demonstrate competency in understanding the ethical obligations of informed consent. Competency is demonstrated by satisfactorily completing QMC required human subjects protections education and training. The PI and individual(s) to whom informed consent is delegated shall have sufficient clinical training to understand and explain study related procedures to potential participants.

G. General Information for Obtaining Informed Consent

1. Only the most recently IRB approved, stamped and dated version of the informed consent document(s) may be used to consent potential participants.
2. A completed Informed Consent Document must be obtained from every participant who takes part in a study prior to performing any study-related activities, unless the RIRC has granted a waiver.
3. The process of obtaining informed consent/assent must be explained in the RIRC application.
4. A potential research subject is asked to sign the informed consent document only after all questions and concerns have been addressed and the consenter is satisfied that there is an understanding of the study.
5. The informed consent document must be signed, dated and/or timed* by the participant or legal representative, and a witness to signature, along with the

research team member or investigator obtaining consent. *It is important to place time when protocol-specified items will be conducted on same say as obtaining informed consent.

6. The original signed informed consent is kept in the patient's research folder and a copy placed in the patient's medical record (uploaded to Media Manager in CareLink)..
7. The participant is given a copy of the signed informed consent document.
8. A progress note documenting the informed consent process must be placed in the subject's study chart and signed by the investigator or research team member who consented the participant. At a minimum, the progress note must include:
    a. the name of the study,
    b. the person consenting the subject,
    c. a statement that the study was explained to the subject or the subject's representative,
    d. a statement that the subject was given the opportunity to ask questions,
    e. documentation that consent was obtained before any subject procedures were performed
    f. that a signed consent was provided to the subject
    g. description of any changes in consenting process
9. The signed signatory page(s) are faxed, sent, or sent from a queens.org email address to the Research Regulatory Office (rirc@queens.org) within 24 hours of signing, or no later than 1 week later. RA# and name must be legible.

H. Other Considerations Involving Informed Consent

1. Obtain consent only under circumstances that provide the prospective subject or his/her representative sufficient opportunity to consider whether or not to participate.
2. The investigator must minimize the possibility of coercion or undue influence.
3. The consent process may not involve the use of exculpatory language through which the subject or representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, sponsor, institution or agents from liability for negligence.
4. Information in the informed consent must be in lay language understandable to the subject or the representative between a 6 to 8th grade reading level.
5. The QMC RIRC/designee or other compliance official may observe the consent process for any study.

H-. Requirements for Informed Consent Content

1. Key Information

i. The informed consent must begin with a concise and focused presentation of key information. Refer to posted consent form template(s).

2. **A statement that the trial involves research**
    i. The ethical principle of respect for persons requires the subject be informed that the activity is research. There is a difference between the patient-physician relationship, and the subject-investigator relationship.
3. **The purpose of study**
    i. The purpose should provide a clear and accurate statement of the scientific purpose, the objectives of the study, the reasons why the research is being conducted and a description of the background supporting the study.
4. **The expected duration and time involved of subject's participation and approximate number of subjects expected to be enrolled in the trial.**
5. **The trial treatment and the probability for random assignment to each treatment.**
    i. A clear account of the difference between standard care and experimental treatment. When a study involves randomization, this activity is considered a research maneuver and should be described as a procedure of the study. The probability of assignment to each treatment or condition is needed in the consent form.
    ii. If study drugs are involved, the subject is entitled to know dosages.
    iii. If questionnaires or survey tools are to be used, an estimate of the length of time needed to complete the activity, and a description of what the tools will ask.
6. **The trial procedures to be followed, including all invasive procedures.**
    i. A clear description of all the procedures that will be followed during the course of the study.
    ii. This includes the subject's responsibilities of participation.
7. **The aspects of the trial that are experimental**
    i. A procedure or treatment that is experimental in a study must be clearly delineated from what is standard or routine medical care.
8. **Reasonable foreseeable risks, discomforts or inconveniences to the subject, and, when applicable, to an embryo, fetus or nursing infant.**
    i. All potential risks and discomforts whether minor or major must be described. The likelihood and severity of such risks should be estimated and the reversibility of adverse reactions should be described. If appropriate, a statement should be included that participation may result in currently unforeseeable risks to the subject (or embryo, fetus).
    ii. Include if any studies have been done (animal or human), and their results.
    iii. Explain any measure to be taken to prevent pregnancy for women and men.
9. **Reasonably expected benefits to subject or society (when there is no intended clinical benefit to the subject, the subject should be made aware of this).**

i. The potential benefits of participation for the subject, the general benefits for science, the population at large or other patients with similar diseases should be described.

10. Alternative procedure(s) or course(s) of treatment

i. Any alternatives to participation in the study must be explained to the subjects. This section should make clear what possible choices are available if the individual chooses not to participate in the study. The alternative can be no treatment, standard therapy, other experimental treatments or some or all of the protocol treatment without participating in the study.

11. **The extent to which confidentiality of records identifying the subject will be maintained and the possibility of who may inspect records.**

i. Other individuals or groups may access the subjects data or records. A statement indicating that the monitor(s), sponsor, research staff, RIRC, and the regulatory authorities, in particular FDA, will be granted direct access to the subject's original medical records for verification of clinical trial procedures and/or data without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations, and that by signing a written informed consent form, the subject or subject's legally authorized representative is authorizing such access.

ii. If study results are published, the subject's identity will remain confidential.

12. The compensation and/or treatment available to the subject in the event of trial related injury, what they consist of and where information can be obtained.

i. A statement regarding Emergency Care and Compensation for Injury is required in the consent form of all research that involves more than minimal risk.

ii. A statement must indicate whether subjects will be billed for such medical treatment.

13. Anticipated payment, if any, to the subject for participation in the trial

i. Money given to subjects for participation in a research study needs to be listed in dollar amounts in the consent form. If the full amount of payment is not to be granted if the subject does not complete the research, the consent must state how much of the payment they will receive.

14. Anticipated expenses, if any, to the subject for participation in the trial

i. When participation in the study may result in any costs whatsoever, clear information must be provided in the consent explaining these costs.

15. Participation and withdrawal

i. Regulations require a statement indicating that the trial is voluntary and the subject may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the subject is otherwise entitled

ii. If subject withdraws, explain if they will be asked to follow-up and /or what procedures are required for subject safety.

16. **That the subject or the subject's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the subject's willingness to continue participation in the trial;**
17. **The person(s) to contact for further information regarding:**
    i. the research,
    ii. the rights of research subjects (provide RIRC address and phone), **and**
    iii. whom to contact in the event of research-related injury (there should be a phone number that is available 24 hours a day)
18. **The foreseeable circumstances and/or reasons under which the subject's participation in the trial may be terminated;**
19. A **statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;**
20. A **statement regarding whether clinical relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions;**
21. **For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (ie.sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen);**
22. **The version or date of the consent form.**

I. State of Hawaii and The Queen's Medical Center Informed Consent Requirements

1. The name, address and telephone number of the investigator. For studies that are more than minimal risk, the subject should be given a telephone number that is available 24 hours a day.
2. Signature, time and date lines to be completed by the investigator, the subject or when appropriate, the guardian, and witnessed by a non-research staff person;
3. The signature page must be on a separate page and addressograph with the patients identification or the patient's name printed if it is not readable;
5. Enough space on the first and last page of the consent form for placement of the QMC Date of Approval/Expiration Stamp. The stamped version of the consent form is to be used in all studies.
6. Fax or mail to Research Regulatory Office (UT505 or fax: 691-7897), or email via a queens.org email address ot rirc@queens.org the signed page of consent form within 24 hours of signature.

J. HIPAA Specific Requirements

1. **The core elements to include for authorizations:**
    - **Description of information to be used**

- **Who is authorized to use the information**
- **Who can receive or see the protected health information**
- **The purpose of the use/disclosure**
- **An expiration date or an expiration event (May use "end of the research study" or "none")**
- **Signature of individual/representative and date.**
- **A statement that individual still has a right to revoke the authorization in writing**

2. **The authorization for the use or disclosure of protected health information for research may be combined with a consent to participate in the research or with any other legal permission related to the research study.**
3. **The individual's right to access protected health information may be temporarily held if:**
    - **Protected health information was obtained by during the course of the clinical study.**
    - **The individual agreed to the temporary hold of access when consenting to participate in the study. (must include on consent form)**
    - **The study is still in progress**
    - **The consent process must state that the individual's right to access to protected health information will be reinstated once the research is complete.**

K. Research Involving Investigational Drugs or Devices Informed Consent Requirements

1. Name of the drug (or device), dosage, how administered, frequency, for what duration, possible side effects, and cautionary statements on the concurrent use of alcohol or other drugs.
2. For use of placebo, or single- or double-blind procedure, a statement of what the chances are that the subject may receive a placebo.
3. A general statement to the effect that "As with any drug (or device), there may be unanticipated adverse effects."
4. Instructions for action to be taken in the event of adverse effects.
5. For subjects who are not hospitalized, an emergency around-the-clock telephone number for subjects to call in the event of an adverse effect.
6. Relevant cautionary statements about the operation of machine or motor vehicles while experiencing effects of the drugs.
78. A statement that indicates the phase of testing (e.g. phase 2 of an investigational new drug) and whether the number of subjects is limited; and that the FDA has allowed use of this drug (or device) for research.
9. A statement as to whether the drug (or device) will be available at the conclusion of the study if it is found to be effective for the subject, if known.

10. A statement indicating the possibility that the FDA may inspect the records of the research and the subjects' medical record.

L. Research Involving Radiation Informed Consent Requirements

An estimate of the hazard of radiation in terms readily understandable to the layman (e.g. comparable to exposure to one chest x-ray).

M. Research Involving Prisoners

A statement that participation in the research project will have no effect on the inmate-participant's release date or parole eligibility.

N. Deception or withholding information

It is recognized that in some research it is not possible to fully inform the subject of the experimental procedures without destroying the validity or the research. While it is recognized that informed consent need not be based on full disclosure of information in the consent for these type studies, it is the responsibility of the RIRC to set limits to the incompleteness of such information. In studies with planned deception, the RIRC has the responsibility of assessing whether this violates the rights or welfare of subjects, and if such violation exists the RIRC must set limits on these studies.

If the subjects are misled or deceived during data collection, it is particularly important to insure that debriefing includes both a detailed description of the deception and a description of its need and the role it played within the experiment.

N. Assent and parental permission for participation of children

When children or minors are involved in research, the regulations require the assent of the child or minor and the permission of the parent(s), in place of the consent of the subjects. Given that children have not reached their full intellectual and emotional capacities and are legally unable to give valid consent, involving children in research requires the permission of their parents or legally authorized representatives.

1. For children under seven years of age.
   In the child is under the age of 7, only a Parental Permission form is required. This form should follow all applicable requirements of informed consent as outline in this manual.
2. For children from 7-12 years of age.

If the child is 7-12 years of age, a child assent form is required in addition to the parental permission form. This form should be brief and study specific and contain language this both appropriate to the child's maturity and age. The assent form should have a simple format that is easy to read and when possible, limited to one page. The use of larger type and simple pictures will facilitate the child's understanding of the text.

3. Youth assent form from 13-18 years of age.
   If the child is 13-18 years of age, a Youth Assent Form is required in addition to a parental permission form. The youth assent form may follow the format provided for adult consent but is required to contain simple language written at the appropriate educational level of the youngest prospective subject in the youth age range.
4. The RIRC will make the determination of whether assent is required and whether informed consent must be obtained by 1 or both parents/guardians as per 45 CFR part 46 subparts A, B,C,D.
5. If the parents' consent but the child does not wish to participate, the researcher must contact the IRB before including the child in the research.
6. The IRB may require additional protections when minors participate in research, such as requiring that an independent third party or an advocate of the child be present during the informed consent process.
7. Individuals who are "mature minors" or "emancipated minors" under the law of the state may be able to give informed consent. If a participant is a mature minor or emancipated minor, the researcher should contact the IRB before allowing the minor to give informed consent for participating in the study.

O. Revised Informed Consents and Re-consenting

1. If, during the course of the trial, the protocol has been modified in such a way that changes are made to the Informed Consent, participants who have already given their informed consent are to be re-consented using the updated form. All participants currently enrolled in the study must sign the updated informed consent form to acknowledge the changes, unless approved otherwise by the IRB. The participant may be re-consented at the next patient contact unless otherwise stated by the IRB or study sponsor.

2. For potential participants who are not yet enrolled in the study, the revised Informed Consent replaces all previous versions for the Informed Consent and is used in its clean format. Informed Consent is obtained as described above.

3. Document reconsent as per Section G.

P. Genetic Research Consent Requirements (see also Administrative Policy #610-00-198 Genetic Research)

1. The primary risks to the subjects of genetic research include psychological (anxiety, confusion) and social (damage to familial relations, inability to

obtain employment or insurance) if the results become available to insurance companies, employers, or unauthorized personnel.

2. The subject's family members, who may not have had informed consent, may be subject to the same risks.
3. The explanation of the actual risks/benefits of a specific research study during the informed consent process and the procedures to protect subjects from those risks is critical in the RIRC approval process.
4. The principal investigator must present the scientific and/or clinical risks/benefits to subjects during the informed consent process and must include a full discussion of those risks/benefits in the submission to the RIRC.
5. Information on expected outcomes and unexpected outcomes (such as non-paternity) generated during the course of the study must be clearly stated in the informed consent form. If the research includes a medical history or family history, any expected sensitive personal information must be clearly stated.
6. If family members are to be studied, the investigator must describe methods to protect subjects against disclosure (direct disclosure or derivable by inference) of medical or personal information about themselves or family members.
7. The investigator must clearly describe implications of the study results for the subject's family and discuss with the patient (and the family if appropriate), possible means to address those implications.
8. The subject must be informed if information generated in the course of the research including any clinical laboratory tests, will be included in the subject's medical record or otherwise disclosed to healthcare providers or others.
9. The following must be included in the informed consent form:

"The Genetic Information Nondiscrimination Act (GINA) is a Federal law that prohibits discrimination in health coverage and employment based on genetic information. This Federal law generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that is obtained from research.
- Health insurance companies or health plan administrators engaged in research may not use the information obtained to discriminate against you.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information from research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

All health insurance companies and group health plans must follow this law by May 21, 2010. All employers with 15 or more employees must follow this law as of November 21, 2009.

Limitations (The following are not all inclusive, but the main limitations of GINA):

- The law does not exclude life insurance companies from using genetic information to make decisions.
- The law does not protect an individual if they already have a disease. It only protects an individual that has a genetic predisposition to a disease.

For more detailed information regarding the provisions of GINA see:
http://www.genome.gov/Pages/PolicyEthics/GeneticDiscrimination/GINAInfoDoc.pdf"

Q. Federal Certificate of Confidentiality

In research carried out on sensitive issues such as illegal behavior, alcohol or drug abuse, or sexual practices or preferences, a Federal Certificate of Confidentiality can be granted by the Department of Health and Human Services for the protection of confidentiality of the subjects involved in sensitive research. These certificates are available to protect the identity of the research subjects from Federal, state, or local civil, criminal, administrative, or legislative proceedings. If a Certificate of Confidentiality is to be used, a statement to its purpose is written into the consent form. Certificates of Confidentiality are automatically given for federally funded research.

R. Request for a Waiver of Informed Consent or waiver of Documenting Informed Consent

A waiver of informed consent, may be requested through IRB forms. The IRB must determine that all criteria are met. Justification must be provided for the following:

a. The research in its entirety involves no greater than minimal risk
b. The waiver of informed consent or alteration will not adversely affect the rights and welfare of the subjects.
c. It is not practicable to conduct the research without the waiver/alteration.
d. Whenever appropriate, subjects will be provided with additional pertinent information after their participation, and what information will be provided.
e. If research uses identifiable private information or identifiable biospecimens, why the use of such information/biospecimen in an identifiable format is necessary to carry out the research.

A request for waiver of informed consent can be made by the investigator, however, the RIRC has final authority. Even with the waiver, the RIRC may

require the investigator provide subjects with a written statement regarding the research.

A waiver of the documentation of consent (meaning waiving the requirement to get a signed consent form) for some or all subjects is requested through IRB forms. This waiver still requires the investigator to provide information about the research to each subject. A written script or information sheet must be submitted to the IRB; these are typically basic elements of the informed consent. Justification for at least one of the 2 criteria must be met. Each criteria has 2 items to address::

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. Subjects will be asked whether they want documentation linking them to the research, and the subject's wishes will govern;
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.

Even if the waiver is granted, the RIRC may require other conditions, such as requiring the researcher to provide subjects with an information sheet (written summary) about the research.

S. Request for a waiver of the documentation of consent

Two types of request for waiver of HIPAA Authorization may be granted:

1. Use/disclosure of existing data for the entire study (for example, retrospective record review/archived specimens)
2. Use/disclosure for subject prescreening purposes only (for example, to allow a study coordinator access to the medical record to verify specific eligibility criteria prior to informed consent/authorization)

The type of PHI being waived must be described. In addition the following criteria must be met for consideration of approval:

a. The research could not be practicably conducted without access to and use of protected health information.
b. The research could not practicably be conducted without the waiver or alteration.
c. The rights or welfare of subjects will not be adversely affected by the waiver
d. Specifying the data fields that are the minimum necessary to be used under the HIPAA waiver.
e. There is 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 project, or for other research for which the use or disclosure of protected health information would be permitted.

f. There is an adequate plan to protect the identifiers from improper use and disclosure.
g. There is 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.

T. Non-English Speaking Subjects

Qualified interpreter services are as per SW-xx-099 policy in the use of MARTTI. A family member of the subject may not be the interpreter.

The informed consent form should be in language understandable to the subject/representative. When the study subject population or the investigator or RIRC anticipates that the consent process will be conducted in other language from English, the RIRC will require a translated consent document. The translated document must have assurances of accuracy (back translation from other than who provided translation).

An authorized interpreter must assist in the the consent form process, however, the translation should not be substituted for a written consent form.

If a non-English speaking subject is encountered unexpectedly, the investigator must carefully weigh the ethical/legal ramifications of enrolling subjects when a language barrier exists.

As a short tem alternative, the oral presentation of informed consent with a SHORT FORM written consent document may be used. The oral presentation and the short form written document must be in language understandable to the subject; the RIRC-approved English language informed consent document (ICD) may serve as the summary, and the witness and interpreter must be fluent in both English and the language of the subject.

- The subject/representative sign the short form document,
- The summary (ICD) is signed by the person obtaining consent, and
- The short form document and summary (ICD) is signed by the witness. (The interpreter may serve as the witness.)

In addition to the documentation requirements covered under Section G, note that the informed consent was discussed in language understandable to the subject with assistance of an interpreter, and that a short form was used./signed.

Future study visits must consider the ongoing continued communication of informed consent to ensure understanding of all study elements. An interpreter must be used for all study visits and interactions.

The RIRC must receive and approved all foreign language versions of the short form document.

Use of a short form is limited to 2 subjects per study. If the study expects to enroll others in the same language, a full translated informed consent must be submitted along with a plan for communication and use of any other patient-facing document.

U. Illiterate English-Speaking Subjects:

A person who speaks and understands English, but does not read and write, can be enrolled in a study by "making their mark" on the consent form

A person who can understand and comprehend spoken English, but is physically unable to talk or write, can be enrolled in a study if they are competent and able to indicate approval or disapproval by other means, if:

- The person retains the ability to understand the concepts of the study and evaluate the risk and benefit of being in the study when it is verbally explained, and
- The person is able to indicate approval or disapproval.

The consent form should document the method used for communication and the specific means the prospective subject communicated agreement to participate. The person obtaining informed consent should read through the consent document, review the study with the subject, and provide opportunities to ask questions. An impartial third party should witness the entire consent process and sign the consent. A video tape of the consent interview is recommended.

V. Posting of clinical trial consent form

1. For each clinical trial conducted or supported by a Federal department or agency, one (1) IRB-approved informed consent form that is used to enroll subjects must be posted by the awardee or the Federal department or agency component conducting the trial on a publically available Federal Web site (that this will be established as a repository)
2. If the Federal department or agency supporting or conducting the clinical trial determines that certain information should not be made publically available on a Federal Web site (e.g. confidential commercial information), such Federal department or agency may permit or require redactions to the information posted.
3. The information must be posted on the Federal Web site after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol.