Standard Operating Policy and Procedures (SOPP) 7

INFORMED CONSENT

Introduction

Federal Regulation 45 CFR 46.116-117 requires investigators to conduct an effective informed consent process with each potential human subject or his/her Legally Authorized Representative (LAR) before the subject may be enrolled in a research study. Informed consent is not a single event or a form to be signed but an ongoing process that takes place between researchers and prospective subjects. The basic elements of the process include full disclosure of the nature of the research and the subject's involvement, adequate comprehension on the subject's part, minimization of the possibility of coercion or undue influence, and the subject's voluntary choice to participate.

This policy sets forth the elements of the informed consent process, including exceptions and alternatives, the roles and responsibilities of the Principal Investigator (PI) and the Saint Joseph's University (SJU) Institutional Review Board (IRB), specific considerations for the consent of special populations, and the IRB's authority to approve a consent process that omits or alters some or all of the required elements of informed consent or to require specific information beyond standard requirements and/or third-party observation of the consent process.

1. Policy Statements
   - 1.1. Consent must be sought under circumstances that (a) provide the subject or the LAR sufficient information and opportunity to consider whether or not to participate voluntarily and (b) minimize the possibility of coercion or undue influence.
   - 1.2. Consent may not include any exculpatory language through which the subject or the LAR is made to waive or appear to waive any of the subject's legal rights or which releases, or appears to release, the PI, the sponsor, or SJU or its agents from liability for negligence.
   - 1.3. The PI must provide a detailed consent process in their application and submit appropriate documentation related to their informed consent process for ALL human subject research.
   - 1.4. Unless the IRB waives the requirement for signed consent, such as through 45 CFR 46.117(c), written consent must be given to and signed and dated by the subject or the subject's LAR (for special populations, see 4.6). An electronic signature on a consent document may be used if the procedures set forth by the PI for obtaining a

legitimate electronic signature are approved by the IRB. As noted by the Office of Human Research Protections (OHRP), "If properly obtained, an electronic signature can be considered 'original' for the purposes of recordkeeping."

1.5. During the course of a study, it may become necessary to change some of the information in the consent form. The PI is responsible for submission of all changes as an amendment or addendum, for review, approval, and decision regarding a need to re- consent by the IRB, before use.

1.6. All individuals designated by the PI to obtain informed consent must complete the required human subjects research training (CITI Program) and be listed as co investigator or research personnel on the IRB-approved protocol application before they may obtain informed consent.

1.7. The IRB has the authority to approve a consent process that omits or alters some or all of the elements of informed consent as set forth in this policy.

2. Elements of Informed Consent

Informed consent, no matter the form (written or oral) or language, must contain all nine federally-required elements, as set forth in 45 CFR 46.116. The IRB may require additional elements it believes necessary to ensure the health and welfare of the research subjects.

2.1. Standard Elements:

2.1.1. Research Statement

Each consent form must contain a statement indicating that the project is research, an explanation of the purpose of the research, the expected duration of participation in the research study, and a description of the procedures involved.

2.1.2. Foreseeable Risks

A consent form must contain a description of all foreseeable risks associated with the research project, including the likelihood of such risks and the potential consequences associated with each risk. For example, "Some questions asked during the interview may evoke negative emotions".

2.1.3. Foreseeable Benefits

A consent form must include all foreseeable benefits for the research subject and/or others (i.e., society). If there are no foreseeable benefits associated with the study, this should be stated within the consent form. Compensation for participation is not considered a benefit.

2.1.4. Appropriate Alternatives

A statement detailing any alternative procedures/course of treatment must be included in each consent form. If no alternatives exist, a statement should be included that informs the subject or LAR that the only alternative is not to participate in the research study.

2.1.5. Confidentiality

Statements regarding the extent to which research personnel will maintain/not maintain confidentiality of the subject's personal information/records must be

included in all consent forms. A description of the ways in which records will be protected must be included.

2.1.6. Compensation

The subjects must be informed of any compensation they will receive in exchange for participating in the research study. For studies deemed greater than minimal risk, subjects should be informed of any treatments that may be provided if an adverse event occurs.

2.1.7. Contact Information

Subjects must be provided with contact information for the PI, Faculty Advisor, and IRB Administrator. Contact information may include phone numbers, email addresses, and office locations. For questions about the research study, subjects should be advised to contact the research personnel. For questions regarding their rights, HSR, the IRB, or concerns about the research study, subjects should be advised to contact the IRB Administrator.

2.1.8. Voluntary Participation

Consent forms should inform subjects that participation in the research study is voluntary. Subjects should also be informed that refusal to participate will have no penalty or loss of benefits. The subject has the right to stop their participation at any time with no penalty or loss of benefits.

2.2. Additional Elements

When appropriate, inclusion of one or more of the following elements may be required by the IRB:

2.2.1. Unforeseeable Risks to Subjects, Embryos, or Fetuses

Subjects may be warned that some risks are currently not known or foreseeable 2.2.2. Investigator-Initiated Termination

A statement that describes any instances in which an investigator may terminate a subject's participation.

2.2.3. Additional Costs

A consent form may include a statement that describes any additional costs a subject may encounter.

2.2.4. Early Withdrawal

A PI may include procedures for withdrawal from a study (i.e., for subject's safety).

2.2.5. Significant Findings

Subjects may be told of any new findings that may affect their willingness to continue in the research.

2.2.6. Number of Subjects

An explanation of the approximate number of subjects to be enrolled in the study may be included in the consent form

2.2.7. Profit

Subjects may be informed that their 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.

2.2.8. Return of Individual Research Results

Subjects may be informed whether or not clinically relevant research results, including individual research results, will be disclosed to them and, if so, conditions for the return.

2.2.9. Whole Genome Sequencing

For research involving biospecimens, a statement indicating whether or not the research will (if known) or might include whole genome sequencing.

2.3. Institutional Requirements

2.3.1. Statement as to what audio or visual recording devices will be/were used, if any, how the recordings will be/were maintained, and what will be done with such recordings upon completion of the study. Except in the case that the IRB has approved the use of deception, the consent form must include a separate signature line for the participant to agree to be video or audio-taped or photographed.

2.3.2. Explain whether compensation of any kind is provided and any specific eligibility requirements for compensation.

2.3.3. IRB contact information and statement that the participant may contact the IRB at any time with questions, concerns or complaints.

3. IRB Review of Informed Consent

3.1. Submitted protocol applications are reviewed in accordance with SOPP 2: Submission Requirements and Procedures for Research That is Exempt from IRB Review and SOPP 3: Initial and Continuing Review by the IRB.

3.2. In assessing the informed consent process proposed by the PI, the IRB may consider strategies for ensuring that subjects understand the risks and benefits of the protocol, particularly those that are complex or difficult to comprehend. Such strategies could include (but are not limited to):

3.2.1. Providing an ongoing consent process that allows subjects to re-consider participation at critical junctures.

3.2.2. Using neutral, "culturally competent" (i.e., can speak the subjects' language and/or relate to their culture), and "protocol-competent" (i.e., can understand the protocol and discuss areas of difficulty) third parties to walk the subjects through the consent form and to document the informed consent process.

3.2.3. Ensuring comprehension of the protocol by administering a questionnaire to subjects

3.2.4. Familiarize subjects with the research environment and procedures, or even have them chat with past or present subjects, before they consent.

3.3. The IRB may at any time request that the informed consent process be observed and/or monitored. This activity may be carried out by a member of the Office of Research Services (ORS), an IRB member(s), or another individual selected by the IRB.

3.4. Once a protocol is approved by the IRB, an approval and expiration date will be established for the protocol. IRB-approved versions of the consent process/ documentation must be used during the consent process, as they are the only versions considered valid. Dates of approval and expiration are provided to the PI on all approval documentation.

3.5. The Research Compliance Coordinator (RCC) will document the outcome of any IRB

discussion relating to the consent process or documents, including but not limited to:

3.5.1. Use of non-English documents
3.5.2. Use of a translator
3.5.3. Use of consent from a LAR
3.5.4. Consent requirements relating to subjects from vulnerable populations
3.5.5. Waiver of documentation of consent
3.5.6. Waiver of consent
3.5.7. Letter of tribal support when research involves Native Americans or subgroup 4. Informed Consent Process

The process for obtaining informed consent is an ongoing exchange of information between the PI and the subject, which begins with the recruitment of the subject and continues through to the completion of the study.

4.1. Role of the PI

4.1.1. The PI must provide the IRB with a description of the consent process, including any precautions that will be taken to reduce undue influence. 4.1.2. Documents relating to informed consent should be submitted as part of the protocol application, including written information sheets; written consent/assent forms; consent short forms; oral consent/assent scripts; and/or appropriately translated consent documents for any non-English speaking subjects. A translator must attest in writing to the accuracy of any translations.

4.1.3. The PI does not have to obtain consent personally, but s/he bears the ultimate responsibility for the informed consent process. The PI must confirm to the IRB in the protocol or amendment application that s/he has trained co-investigators and key study personnel to be sufficiently knowledgeable about the study to answer study-related questions posed by potential subjects and/or their LARs. Only co-investigators or key study personnel who are capable of providing sufficient information about the research and have submitted their CITI Training completion report as part of an IRB-approved protocol have the authority to obtain consent from potential subjects.

4.1.4. The PI is responsible to ensure that only the most current version of the IRB approved consent form (and process) is used by the person who is conducting the informed consent process.

4.1.5. The PI and other key research personnel are responsible for continuing the informed consent process through the course of an individual's participation. This may involve providing on-going opportunities to re-affirm willingness to participate, reminding the subjects about important information and data collection points, and providing new information as it becomes available.

4.1.6. During the course of a study, it may become necessary to change some of the information in the consent form. All changes must be submitted to the IRB by the PI as an amendment for review, approval, and a decision regarding a need to re- consent before use.

4.1.6.1. The PI has a responsibility to inform research subjects of any new information that might affect a subject's willingness to continue participating in the research.

4.1.6.2. In cases where subjects have completed participation and new information is

discovered that may affect the subject, the subject must be informed of this new information.

4.1.6.3. Written documentation of the subject's receipt of new information and willingness to continue to participate via an IRB-approved revised consent form or addendum must be obtained IF there is a significant change to the protocol or risk/benefit ratio which directly affects what the subject is being asked to do. Written documentation of re-consent may be obtained by having the subject sign an IRB-approved updated version of the consent form or an addendum to the original consent form.

4.1.6.4. Written documentation of re-consent should also be obtained from subjects who were enrolled in research studies when they were minors but who have turned 18 years old while still participating actively in the study.

4.1.6.5. While IRB approval of minor changes is required, minor changes that do not significantly affect the risk/benefit ratio may only require notification to the subject, but not written informed re-consent, as determined by the IRB. Notification may be conveyed verbally or in writing, with the PI's documenting in the research file that s/he has done so. The notification should reiterate to the subject or LAR that the subject is free to

withdraw/be withdrawn from the research study at any time without penalty or loss of benefits to which the subject is otherwise entitled.

4.1.7. The PI is responsible for documenting interactions with a subject.

4.2. Documentation of Informed Consent

The IRB requires documentation of informed consent by use of a written informed consent form, approved by the IRB and signed by the subject or the subject's LAR. The research subject shall receive a copy of the consent form. Except as described below in Section 4.7, addressing waiver, such documentation of informed consent must be obtained before any research study involving human subjects is initiated. Documentation is required even when consent is obtained orally in accordance with Section 4.3. The IRB will not approve a waiver of documentation of informed consent for any research involving greater than minimal risk.

4.2.1. Documents that may be used in the informed consent process include: 4.2.1.1. Written Consent Form in the language of subjects anticipated to be enrolled. PIs may refer to the format and language provided in sample consent forms. The PI should ensure that all of the required elements of informed consent, set forth in Section 2 above, are included. If some or all subjects are members of a special population, the PI should consult Section 4.6 for specific consent considerations. The consent form format should be easy to read (e.g., adequate white space, paragraph headings, no fine print, and should not use assumptive language such as "you understand that" or "you have been told that," etc.). The consent form must be written in language understandable to the subject, preferably at the 8th-grade level for healthy adult volunteers. The use of a readability index is recommended to help prepare consent forms that are easy to read. Short, easy-to-read sentences are preferred. All necessary medical, scientific, or technical terms must be explained.

4.2.1.2. Short Form for Non-English-Speaking Subjects (See Section 4.5.3)

4.2.1.3. Information Sheet (for Exempt Research/Waiver)

4.2.1.4. Oral Consent Script

4.2.2. Signing of the Written Consent Form

4.2.2.1. Except when a waiver of documentation of informed consent has been approved by the IRB, all subjects must sign the current IRB-approved consent form prior to participating in any study-related activity.

4.2.2.2. The consent form must be signed and dated by the subject or the subject's LAR, the person obtaining the consent, the PI (if required by a funding agency), and a witness, when appropriate.

4.2.2.3. A witness may be required by the IRB when the subject or his or her LAR is illiterate, legally blind, or speaks a language different from the one used in developing the informed consent form. A witness is a person who is independent of the research team and cannot be unfairly influenced by people involved with the research, who does not have a coercive relationship with the subject, and who attends the informed consent process. A translator who participated in the informed consent process also may serve as the witness.

4.2.2.4. The form may be read to the subject or his or her LAR, but in any event, the PI shall give either the subject or the representative adequate opportunity to read it before it is signed.

4.2.2.5. The subject must be given a copy of the consent form. The original signed consent form is to be kept on file in a secure location by the PI.

4.3. Oral Informed Consent. Oral consent is the process of obtaining consent without the use of a written document.

4.3.1. The IRB may approve the use of oral consent where the subject is (1) blind, (2) illiterate, (3) unable to write his or her name, or (4) when a written consent form is the only way to connect an individual to their participation, and the data is sensitive, or could be damaging to a subject if confidentiality were breached. The IRB may also approve oral consent for research conducted over the telephone or using approved conferencing software.

4.3.2. Oral consent must be documented by the individual obtaining consent. 4.3.3. The PI should provide to the IRB for review and approval the following documentation: (a) a written summary or script of what is to be said to the subject or his or her LAR, and (b) documentation that will be used to confirm that the elements of informed consent required by federal regulations and the IRB have been presented orally to the subject or the subject's LAR.

4.3.4. Documentation should be signed by (a) the person obtaining consent; and (b) a witness to the oral presentation, when appropriate, as determined by the IRB. A copy of the documentation shall be provided to the subject or the representative when possible. The IRB may also decide that oral consent be documented by another method such as audio or video recording.

4.4. Consent by LAR

A LAR is an individual or judicial body authorized under applicable law to consent to a prospective subject's participation in the procedure(s) involved in the research. For adults, this would be a person with a durable power of attorney for health care for the subject or some other court order authorizing him or her to be the legal representative for such matters.

4.4.1. For adult subjects who are incapable of providing effective informed consent due

to some cognitive or decisional impairment, there are two ways in which their participation may be allowed:

4.4.1.1. A LAR may consent to enrollment;

4.4.1.2. If there is no LAR, a family member who is involved with medical decision-making for the subject may permit the subject's enrollment in IRB approved research only if (a) the risk is minimal, regardless of whether the subject would derive any benefit, OR (b) the risk is greater than minimal, but the research potentially carries a direct benefit to the subject.

4.4.2. If neither a legal representative nor a family member is available, then a subject may NOT be enrolled in any research protocol.

4.5. Obtaining Informed Consent from Non-English-Speaking Subjects. The concept of "informed consent" requires that information be presented "in language understandable to the subject." The research study and all other elements of informed consent must be explained fully to subjects in a language they understand by either a member of the research team qualified to obtain consent, a translator for written consent, or an interpreter for verbal consent. The translator or interpreter must be proficient in both English and a language in which the subject is fluent.

4.5.1. The IRB must approve all foreign language versions of written or oral consent documents as a condition of approval under 45 CFR 46.117(b).

4.5.2. If it is known in advance that a potential subject or a significant percentage of the prospective subjects do not speak English, a written consent form in the language of the consenting subject(s) must be submitted to the IRB as part of the protocol application. The English consent form should be translated into the appropriate foreign language for review and approval by the IRB. A translator must attest in writing to the accuracy of the translations.

4.5.3. If the majority of anticipated research subjects are English speakers, but the PI identifies for enrollment an individual who does not speak and read the language of the approved consent form, he or she may use an IRB-approved "Consent Short Form" in the language that the subject knows fluently in cooperation with a translator who speaks English and the language of the research subject. Consent short forms may be used with an interpreter's oral explanation of consent form.

4.5.4. Where oral consent is appropriate, as set forth in Section 4.3, an interpreter fluent in both English and the subject's language should communicate the IRB approved English consent form orally to the subject in front of a witness. The interpreter may also serve as the witness. The IRB may require that the interpreter be a non- research team member.

4.6. Special Considerations for Special Populations. Although only certain categories of subjects are mentioned specifically in the regulations, researchers have a responsibility to consider and design research in a way that protects the rights of all potential subjects who have circumstances which might affect their ability to give informed and voluntary consent to participate in research, as set forth in 45 CFR 46.

4.6.1. Children

4.6.1.1. Federal law defines "children" as persons who have not attained the legal age for consent to treatments or procedures involved in the research under the applicable law of the jurisdiction in which the research will be

conducted. Under Pennsylvania law, persons under the age of eighteen (18) generally meet this definition (with the exception of emancipated minors). As a result, written permission of a child's parent(s) or legal guardian(s) must generally be obtained prior to the participation of that child in research.

4.6.1.2. In order to safeguard children's interests and to protect them from harm, federally-mandated considerations are in place for reviewing research involving children. Adding to the protection provided under the Common Rule (45 CFR 46), federal regulations (45 CFR 46, Subpart D) provide protections for children involved in research such as obtaining assent from the child and obtaining the permission of the parents/legal guardians for the child to be enrolled in the research protocol. More specific provisions, as set forth in 45 CFR 46, Subpart D are based on the degree of risk involved in the proposed research and the nature and degree of anticipated benefits.

4.6.1.3. Federal regulations require the IRB to classify research involving children into one of three categories:

4.6.1.3.1. Research not involving greater than minimal risk.

4.6.1.3.2. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.

4.6.1.3.3. Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.

4.6.1.4. Unless the IRB has approved a waiver of written consent, assent must be obtained from children, as appropriate based on their age, in addition to parental/guardian consent.

4.6.1.4.1. For adolescents (junior/senior high school age), assent must be obtained in writing, with supplementary verbal explanations as needed.

4.6.1.4.2. For children (elementary school age), assent should be obtained in a form which the child can understand and a signed assent form must be obtained from children old enough to render a signature.

4.6.1.4.3. For very young children, the explanations of research should match their level of understanding.

4.6.1.5. An IRB may waive the requirement for obtaining parental or guardian permission if it deems that the waiver meets the spirit of the principles of the Belmont Report and is in accordance with the provisions of 45 CFR 46.116 and 408(c).

4.6.2. Prisoners

4.6.2.1. Under the federal regulations, prisoner means "any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal

prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing." The definition applies to minors as well as adults. When persons under the age of 18 are involved, the PI and the IRB must apply the additional protections outlined in Section 4.6.1. 4.6.2.2. Prisoners are a "special" population because their lack of physical liberty raises the issue of whether they have the ability to make a truly voluntary and un-coerced decision to participate in research. The respect for persons elaborated in the Belmont Report requires that the decision to participate in research be wholly informed and voluntary. A secondary issue is

whether confidentiality of participation and of data can be adequately maintained in the prison facility, along with the risk of other prisoners knowing that the research subject may have unique characteristics (HIV status, mental status, etc.). It is essential for the investigator to understand and consider the unique challenges of confidentiality in a prison setting.

4.7. Waiver of Documentation of Informed Consent. Documentation of informed consent may be waived partially or entirely by approval of the IRB Chair, the IRB Chair's designee, or the convened IRB if either:

4.7.1. The only record linking the subject and the research would be the consent form and thus the principal risk would be potential harm resulting from a breach of confidentiality, OR

4.7.2. The research presents no more than minimal risk of harm to the subjects (including risk of breach of confidentiality); and the research does not involve any procedure for which written consent is normally required outside the research context. In cases where the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research that includes some or all of the requirements of informed consent described in Section 2.

4.8. Waiver of Informed Consent. The IRB may approve a consent process that omits or alters some or all of the elements of informed consent set forth above in Section 2 (Elements of Informed Consent), provided that the IRB finds and documents that:

4.8.1. The research involves no more than minimal risk to the subjects; 4.8.2. The waiver or alteration will not adversely affect the rights and welfare of the subjects;

4.8.3. The research could not practicably be carried out without the waiver or alteration; and

4.8.4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

OR

4.8.5. The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:

4.8.5.1. Public benefit or service programs;

4.8.5.2. Procedures for obtaining benefits or services under those programs; 4.8.5.3. Possible changes in or alternative to those programs or procedures; or 4.8.5.4. Possible changes in methods or levels of payment for benefits or services under those programs, and the research could not practicably be carried out without the waiver or alteration.

5. Regulations and Guidance Applicable to Informed Consent

5.1. 45 CFR 46.109(b), (c) & (e): IRB Review of Research, stating that (1) "[a]n IRB shall require that information given to subjects as part of informed consent is in accordance with §46.116. The IRB may require that information, in addition to that specifically mentioned in §46.116, be given to the subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects;" (2) "[a]n IRB shall require documentation of informed consent or may waive documentation in accordance with §46.117;" and (3) "[a]n IRB shall have the authority to observe or have a third party observe the consent process and the research."

5.2. 45 CFR 46.111(a)(4), (a)(5) & (b): Criteria for IRB approval of research, mandating that (1) informed consent "will be sought from each prospective subject or the subject's LAR, in accordance with, and to the extent required by §46.116," and "appropriately documented, in accordance with, and to the extent required by §46.117;" and (2) "[when some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects."

5.3. 45 CFR 46.116: General requirements for informed consent

5.4. 45 CFR 46.117: Documentation of informed consent.

5.5. 45 CFR 46, Subpart D, addressing additional protections for children involved as subjects in research

5.6. 45 CFR 46, Subpart C, addressing additional protections for prisoners involved as subjects in research

5.7. OHRP Guidance: 11/09/95, Obtaining and Documenting Informed Consent of Subjects Who do not Speak English.

5.8. OHRP Guidance on the Involvement of Prisoners in Research, May 23, 2003

5.9. The Belmont Report