SOP 10: INFORMED CONSENT OPTIONS, PROCESSES, AND DOCUMENTATION

1. Subject of Policy & Procedure

The IRB requires investigators to conduct an effective informed consent process with each and every potential human research participant or his or her legally authorized representative before the participant may be enrolled in a research study. The exceptions to this requirement are limited and must be approved by the IRB before the commencement of the study. Informed consent reflects the basic principle of respect for persons elaborated in the Belmont Report by ensuring that prospective participants understand the nature of the research in order to decide knowledgeably and voluntarily whether to participate. The elements required to be included in the informed consent process are enumerated in the consent form, which documents the informed consent process. While there are a few circumstances in which the IRB may grant a waiver or provide for an alternative to the informed consent process, the principle of obtaining legally effective informed consent is the standard for all research with human participants.

To be clear, informed consent is not a single event or form to be signed, but an educational and ongoing process that takes place between the Protocol Principal Investigator (Protocol PI) and the prospective participant. It is the process by which the research study is explained to the potential participant and the participant asks questions and then voluntarily agrees to participate in the research. The process involves the ongoing, interactive exchange of information, beginning with the recruitment of the participant and ending with the completion of the study. The basic elements of this process are: full disclosure of the nature of the research and the participant's involvement; adequate comprehension on the participant's part; minimization of the possibility of coercion or undue influence; and the participant's voluntary choice to participate.

The IRB has the final authority as to the content of the consent form presented to the prospective study participants. The IRB may require that the form include, in addition to the information required by the regulations and/or the Sponsor, information adjudged by the IRB to add meaningfully to the protection of the participants' rights and welfare. The IRB also has the authority to observe, or to charge a third party to observe, the consent process.

2. Scope of Policy & Procedure

This Policy & Procedure applies to all on-going and future human participant research projects conducted by CCC-UPR faculty, staff, or students or by anyone conducting a research activity supported by CCC-UPR or where CCC-UPR is considered to be engaged in the research.

3. Terms and Definitions

All parties to whom this policy applies (*e.g.*, faculty, students, staff, IRB members) should consult the IRB Glossary.

4. See Also

Affected researchers and employees should also consult:

1. CCC UPR Federalwide Assurance Registration
2. Sample Consent Form

5. Regulations 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 legally authorized representative, 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) "[w]hen 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. OHRP Guidance: 11/09/95, Obtaining and Documenting Informed Consent of Subjects Who do not Speak Spanish.

5.6. American Geriatrics Society: 2017 Position Statement re Informed Consent for Research on Human Subjects with Dementia, and Informed consent for dementia research from the Alzheimer Europe available at the following websites: https://aspe.hhs.gov/system/files/pdf/256696/Session%205%20Background.pdf; https://www.alzheimer-europe.org/Ethics/Ethical-issues-in-practice/2011-Ethics-of-dementia-research/Informed-consent-to-dementia-research#fragment1

6. Elements of Informed Consent

Informed consent, no matter the form (written or oral) or language (English, Spanish, or other), must contain all federally required elements of informed consent, as set forth in 45 CFR 46.116. The IRB may also require additional elements it believes necessary to ensure the health and welfare of the research participants. New York State law does not provide for an emergency exemption from informed consent to participate in research that would normally require consent (*i.e.*, research that involves more than minimal risk).

6.1. Required Conditions

1. Consent must be sought under circumstances that (a) provide the participant or the legally authorized representative sufficient opportunity to consider whether or not to participate, and (b) minimize the possibility of coercion or undue influence.
2. Consent may not include any exculpatory language (a) through which the participant or the legally authorized representative is made to waive or appear to waive any of the participant's legal rights, or (b) which releases, or appears to release, the investigator, the Sponsor, or CCC-UPR or its agents from liability for negligence.

6.2. Standard Elements

Building upon the federally required elements of informed consent specified in the federal regulations (45 CFR 46), the IRB has identified a set of standard elements that all researchers should include in their informed consent process.

Requirements for Informed Consent, new subsection 46.116(a)(5)(i) (**new requirement**)

New with the revised 2018 Common Rule is the requirement that the consent document begin with a "concise and focused" presentation of **key information** that will help potential participants or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension, and provide sufficient information that a "reasonable person" would want to have.

1. Key information *is a summary of the study. The revised final Common Rule lists five (5) factors as suggested.*

Modified from www.citiprogram.com

2. Statement that the study involves research (including prominent use of the term "research")
3. Explanation of the purposes of the research, including the name of the study and who is conducting the study. The IRB can waive or alter this element if the study involves. deception, as long as there is a debriefing session after the research has been conducted.
4. Description of the procedures to be followed/what will happen to the participant.
5. Expected duration of the participant's involvement, including the time commitment for each component of the study and the total expected time to complete the study.
6. Identification of any procedures that are experimental, if any.
7. Description of any reasonably foreseeable risks, side effects, or discomforts to the participant.
8. Description of any benefits to the participant or others which may be reasonably expected from the research.
9. Disclosure of appropriate alternative procedures or courses of treatment/therapy, if any, that might be advantageous to the participant.
10. Description of the manner and extent to which the confidentiality of records identifying the participant will be maintained.
11. Statement as to what audio or visual recording devices will be used, if any, and what will be done with such recordings upon completion of the study. The consent form should include a separate signature line for the participant to agree to be video- or audio-taped or photographed.
12. Explanation as to whether and what compensation is provided.
13. When appropriate, contact information and emergency contact information for the participant in the event of a research-related injury to the participant.
14. When appropriate, information regarding available medical treatments for research-related injuries, payments for these treatments, and contact information for additional information about these issues.
15. Name and contact information of the Protocol PI for answers to pertinent questions by the participant about the research and his or her rights as a participant, at any time before or during the research.
16. Statement that participation is voluntary, that refusal to participate will not involve any penalty or loss of benefits to which the participant is otherwise entitled, and that the participant may discontinue participation at any time without penalty or loss of benefits to which the participant is otherwise entitled.
17. IRB contact information and statement that the participant may contact the IRB at any time with any questions or complaints.
18. Statement that the participant shall be offered a copy of the consent form.

6.3. <u>Additional Elements that may be Required by the IRB</u>

1. Statement that the particular treatment or procedure may involve currently unforeseeable risks to the participant (or to the embryo or fetus if the participant is or may become pregnant).

2. Statement of anticipated circumstances under which the participant's participation may be terminated by the Protocol PI or the Sponsor without regard to the participant's consent
3. Description of what will be done with the data once the study is completed.
4. Statement of any additional costs to the participant which may result from his or her participation in the research.
5. Description of the consequences of a participant's decision to withdraw from the research and procedures for orderly termination of participation.
6. Statement that the participant will be notified of significant new findings, should they develop during the course of the research, which may relate to the participant's willingness to continue participation.
7. Indication of the number of participants planned to be enrolled in the study.
8. All informed consent of the CCC-UPR must have to include the next paragraph (choose one of the following paragraphs):

6.4 When reviewing research subject to the revised Common Rule, the CCC-UPR IRB will evaluate the provisions for informed consent as described in the CCC-UPR IRB SOP Manual with the below variations. Investigators conducting research subject to the revised Common Rule must adhere to these requirements.

6.4.1 General Requirements for Informed Consent [§__.116(a)]

In addition to the requirements for obtaining informed consent and the consent process described in the CCC-UPR IRB SOP Manual, the following specific requirements for consent, whether written or oral, apply to research subject to the revised Common Rule:

1. Before involving a human subject in research, an investigator shall obtain the legally effective informed consent of the subject or the subject's legally authorized representative (LAR) (reworded slightly for clarity that consent must be obtained before involving a subject in research)

2. An investigator shall seek informed consent only under circumstances that provide the prospective subject or the LAR sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence (importantly, added "to discuss"; reworded slightly)

3. The information that is given to the subject or the LAR shall be in language understandable to the subject or the LAR (slight rewording – added "legally authorized" to "representative")

4. The prospective subject or the LAR must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information (**new requirement**)

5. Except for broad consent (See Section 8.3):
    a. Informed consent must begin with a concise and focused presentation of the key

information that is most likely to assist a prospective subject or LAR in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension (**new requirement**)

i. Generally, the beginning of an informed consent should include a concise explanation of the following:

1. The fact that consent is being sought for research and that participation is voluntary;

2. The purposes of the research, the expected duration of the prospective subject's participation, and the procedures to be followed in the research;

3. The reasonably foreseeable risks or discomforts to the prospective subject;

4. The benefits to the prospective subject or to others that may reasonably be expected from the research; and

5. Appropriate alternative procedures or courses of treatment, if any that might be advantageous to the prospective subject.

However, based upon the facts of an individual protocol, the IRB may require that different (or additional) information be presented at the beginning of an informed consent to satisfy this requirement.

b. Informed consent as a whole must present information in sufficient detail relating to the research, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or LAR's understanding of the reasons why one might or might not want to participate (**new requirement**)

6.4.2 No informed consent may 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 releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.

6.5. Additional Elements of Consent are required by the revised common rule

In addition to the elements of informed consent described in the CCC-UPR/IRB SOP Manual, the following additional elements are required for research subject to the revised Common Rule. The requirements for Broad Consent are described in Section 8.3.

6.5.1 Basic Elements [§__.116(b)]

1. One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:

a. A statement that identifiers might be removed from the identifiable private information

or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility; or

b. A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

6.5.2 Additional Elements (must be included when appropriate) [§__.116(c)]

1. 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;

2. A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions;

3. For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

6.5.3 *DAMAGE RELATED TO INVESTIGATION*

"If you suffer a physical or mental injury as a result of receiving the study drug or any medical procedures required by the study, you will be reimbursed by the sponsor for reasonable and customary fees and medical expenses actually incurred to treat such injury, but only to the extent such fees and expenses are not paid by your health insurance or governmental coverage. You will not be offered any financial compensation from the Comprehensive Cancer of the UPR. Your health insurance may not pay costs of treating a research related injury. No other provision has been made for payments of any other forms of compensation for a research related injury, such as for lost wages, lost time, or discomfort. By signing this consent form you do not give up any legal rights."

OR

"In the case of any physical or mental damage related to the study, you must notify the staff immediately. A plan will be created to address your immediate needs if Principal Investigator, (name of the PI), determines that the damage is directly related to the study procedures. You will receive treatment for problems related to the study directly by the study staff or you will be informed where you can get additional treatment from you.

There are no additional funds from the Comprehensive Cancer Center at UPR or the US National Institutes of Health for research-related damages, no compensation is available for physical damage such as loss of work, pain, and suffering. Both you and your insurer will continue to be responsible for medical expenses incurred outside the study or medical expenses

that are determined to be not directly related to study procedures. You will not lose your legal rights to sign this consent."

7. Broad Consent [§__.116(d)]

(If an organization is not adopting the option for broad consent or only permitting under limited circumstances, this section may be eliminated, or language added to reflect the organization's constraints or requirements for use.)

Broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens (collected for either research studies other than the proposed research or non-research purposes) is permitted under the revised Common Rule. Broad consent is not currently recognized in FDA regulation or guidance.

When obtaining broad consent, the general requirements for informed consent described in Section 8.1 apply except as noted. The following elements of broad consent [§__.116(d)] shall be provided to each subject or the subject's LAR:

1. A description of any reasonably foreseeable risks or discomforts to the subject;

2. A description of any benefits to the subject or to others, which may reasonably be expected from the research;

3. A statement describing the extent, if any, to which confidentiality of records identifying the subject must be maintained;

4. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled;

5. For research involving biospecimens, 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;

6. For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen);

7. A general description of the types of research that may be conducted with the identifiable private information or identifiable biospecimens. This description must include sufficient information such that a reasonable person would expect that the broad consent would permit the types of research conducted;

8. A description of the identifiable private information or identifiable biospecimens that might be used in research, whether sharing of identifiable private information or identifiable biospecimens

might occur, and the types of institutions or researchers that might conduct research with the identifiable private information or identifiable biospecimens;

9. A description of the period of time that the identifiable private information or identifiable biospecimens may be stored and maintained (which period of time could be indefinite), and a description of the period of time that the identifiable private information or identifiable biospecimens may be used for research purposes (which period of time could be indefinite);

10. Unless the subject or legally authorized representative will be provided details about specific research studies, a statement that they will not be informed of the details of any specific research studies that might be conducted using the subject's identifiable private information or identifiable biospecimens, including the purposes of the research, and that they might have chosen not to consent to some of those specific research studies;

11. Unless it is known that clinically relevant research results, including individual research results, will be disclosed to the subject in all circumstances, a statement that such results may not be disclosed to the subject; and

12. An explanation of whom to contact for answers to questions about the subject's rights and about storage and use of the subject's identifiable private information or identifiable biospecimens, and whom to contact in the event of a research-related harm.

(The following two paragraphs are examples of procedures an organization could choose to adopt, organizations should customize as appropriate to reflect their own practices.)

Investigators must include information regarding the circumstances under which broad consent will be obtained, the proposal for tracking of responses, and the proposed consent form(s) (or oral script if a waiver of documentation of consent is sought) and any other consent materials (e.g., information sheet, audiovisual materials, etc.) in their submission to the IRB. The Comprehensive Cancer Center- UPR IRB will review the information provided with the aid of a checklist to ensure that all requirements are satisfied. The outcome of the IRB's review will be communicated to the investigator in writing following the procedures described in the Comprehensive Cancer Center- UPR [CCC-UPR/IRB SOP Manual].

When investigators propose research involving the use of identifiable private information and/or identifiable biospecimens research for which broad consent was obtained, the investigators must include documentation of the IRB approval for the storage or maintenance of the information or specimens and a copy of the consent form and/or other materials. The Comprehensive Cancer Center- UPR IRB will review the information provided with the aid of a checklist to ensure that all requirements are satisfied.

The outcome of the IRB's review will be communicated to the investigator in writing following the procedures described in the Comprehensive Cancer Center- UPR [CCC-UPR/IRB SOP Manual].

8. Process for Obtaining Informed Consent

As explained in Section 1: Subject of Policy & Procedure, the process for obtaining informed consent is not a one-time information session, but an ongoing exchange of information between the Protocol PI and the participant which begins with the recruitment of the participant and continues to the completion of the study.

8.1. Role of the Protocol PI

The Protocol PI does not have to obtain the consent personally, but he or she bears the ultimate responsibility for the informed consent process. Any co-investigators or key study personnel capable of providing sufficient information about the research and listed on the protocol or added to the study by an amendment has the authority to obtain consent from potential participants.

The Protocol PI is responsible for making sure that only the most current version of the IRB approved consent form is used by the person who is conducting the informed consent process. To do so, the Protocol PI may insert a computerized watermark into the document, stamp it, or otherwise mark it to make clear that it is the most current, IRB-approved version.

The Protocol PI and other key research personnel are responsible for continuing the informed consent process through the course of the participant's participation. This involves providing on-going opportunities to re-affirm the willingness to participate, reminding the participants about important information and data collection points, and providing new information as it becomes available. For example, the Protocol PI could arrange periodic meetings where participants are encouraged to ask questions and raise concerns about the study and their participation. The Protocol PI is also responsible for implementing any other precautions the IRB deems appropriate to ensure a complete informed consent process. All interactions with a participant are to be documented as appropriate.

8.2. Role of the Protocol IRB

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, IRB member(s), or another individual selected by the IRB.

In assessing the informed consent process proposed by the Protocol PI in the protocol application, the IRB may consider strategies for ensuring that participants really understand the risks and benefits of the protocol, particularly those that are complex or difficult to comprehend. Such strategies could include, as appropriate:

1. Requiring a waiting period during which participants can carry out a list of suggestions to help them understand the protocol better or to consult with family or clergy about their decision to participate.
2. Providing an ongoing consent process that allows participants to re-consider participation at critical junctures.
3. Using neutral, "culturally competent" (*i.e.* can speak the participants' language and/or relate to their culture) and "protocol-competent" (*i.e.* can understand the protocol and probe areas of difficulty) third parties to walk the participants through the consent form and to document the informed consent process by signing the consent form.
4. Ensuring comprehension of the protocol by administering a questionnaire to participants
5. Familiarizing participants with the research environment and procedures, or even having them chat with past or present participants, before they consent.
6. Limiting the target group to persons with the expertise and background to understand the protocol and informed consent procedures (as long as this would not skew results or result in a participant population over which the researcher has special influence).

8.3. Training for Persons Obtaining Consent

All persons designated by the Protocol PI to obtain informed consent must complete all required IRB training and be listed as a co-investigator or research personnel on the protocol at the time of the protocol application submission or added later via an amendment before they may obtain informed consent. All personnel, including those who will obtain informed consent, must complete the same IRB training required of Protocol PIs, which is set forth in SOP 3: Initial and Continuing Review by the IRB, Section 6.1.

The Protocol PI must confirm to the IRB in the protocol or amendment application the completion of this training by these key personnel and that he or she has trained them to be sufficiently knowledgeable about the study to answer study-related questions posed by potential participants and/or their legally authorized representatives.

8.4. Duties of Persons Obtaining Consent

1. Sign the consent form as "the person obtaining consent."
2. Obtain the signature of the participant or his or her legally authorized representative on the consent form; ensure that the signatory enters the date of signing next to their name and prints out their name on the form; ensure that the signatory initials each page of the consent form where required.
3. Ensure that all participants or their representatives receive a copy of the consent form, unless documentation of informed consent is waived or altered by the IRB.
4. Ensure that no person be involved in the study as a participant unless and until informed consent has been obtained *and* documented.

8.5. Outline of Steps in the Consent Process

1. The potential participant is provided with general information about the nature of the study and why he or she might be suited to participate. Recruitment fliers, websites, and phone scripts might be part of this process. All study-specific recruitment materials must be reviewed and approved by the IRB *before* use, in accordance with SOP 11: Recruitment of Study Participants.
2. The potential participant indicates an interest in joining the study.
3. Details are presented to the potential participant by study personnel who are knowledgeable about both the study and the IRB requirements for the informed consent process.
4. Adequate information concerning the research is given to the potential participant via the IRB-approved consent form. The information should be clearly presented in nontechnical, easily understandable language.
5. Ample time and opportunity are provided for the potential participant and/or his or her legally authorized representative to ask about the details of the study, to consider other available options, and to decide whether to participate.
6. All questions by the participant and/or the legally authorized representative are answered to their satisfaction.
7. It has been ensured to the degree possible that the potential participant and/or the legally authorized representative have comprehended the information provided about the research.
8. The potential participant and/or the legally authorized representative have provided voluntary consent by signing the consent form or other IRB-approved mode of authorization.
9. A copy of the consent form, as well as other documentation about the research (*e.g.*, calendars, instructions), are provided to the participant and/or the legally authorized representative. All documents so provided must first be approved by the IRB.
10. The person obtaining consent must document that the informed consent process has occurred. This may be done by a narrative note in the medical or research record, or by an entry onto a research worksheet kept in each participant's research file.

8.6. Waiver or Alteration of Informed Consent [§__.116(e) and (f)]

When reviewing research subject to the revised Common Rule, the CCC-UPR IRB will evaluate requests for waivers or alterations of informed consent in accordance with the requirements and criteria specified in the revised rule and summarized below. The IRB's determination will be documented in the IRB record and communicated to the investigator as described in the CCC-UPR/IRB SOP Manual.

8.6.1. General Waiver or Alteration of Consent

In order to approve a request from an investigator to waive the requirement for informed consent, or to omit or alter one or more basic or additional element of consent (an "Alteration"), under this provision

the Comprehensive Cancer Center- UPR IRB must determine and document that the below criteria are satisfied.

1. The research involves no more than minimal risk to the subjects;

2. The research could not practicably be carried out without the requested waiver or alteration;

3. If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;

4. The waiver or alteration will not adversely affect the rights and welfare of the subjects; and

5. Whenever appropriate, the subjects or LARs will be provided with additional pertinent information after participation.

Investigators may be asked to provide justification, or additional information or documentation, to support that the above criteria are satisfied.

Restrictions:

1. Waivers
   a. If an individual was asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens in accordance with the requirements in Sections 7.0 and 6.0, and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.

2. Alterations –
   a. An IRB may not approve a request to alter or omit any of the general requirements for informed consent described in Section 6.5

   b. If a broad consent procedure is used, an IRB may not alter or omit any of the elements described in Section 8.3

8.6.2. Waiver or Alteration of Consent in Research Involving Public Benefit and Service Programs

In order to approve a request from an investigator to waive the requirement for informed consent, or to omit or alter one or more basic or additional element of consent (an "Alteration"), under this provision the CCC-UPR IRB must determine and document that the below criteria are satisfied.

1. 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:
   a. Public benefit or service programs;

b. Procedures for obtaining benefits or services under those programs;

c. Possible changes in or alternatives to those programs or procedures; or

d. Possible changes in methods or levels of payment for benefits or services under those programs; and

2. The research could not practicably be carried out without the waiver or alteration.

Restrictions:

1. Waivers –

a. If an individual was asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens in accordance with the requirements in Sections 8.1 and 8.3, and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.

2. Alterations –

a. An IRB may not approve a request to alter or omit any of the general requirements for informed consent described in Sections 8.1 and 6.4.1

b. If a broad consent procedure is used, an IRB may not alter or omit any of the elements described in Section 6.0

8.63 Waiver of Documentation of Informed Consent

1. 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:

a) The only record linking the participant and the research would be the consent form (and thus the principal risk would be potential harm resulting from a breach of confidentiality).

OR

b) The research presents no more than minimal risk of harm to the participants (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.

*A survey is an example of a type of study that would qualify for a waiver of documentation of informed consent, as return of the survey could be considered documentation of consent.

2. In cases where the documentation requirement is waived, the IRB may require the investigator to provide participants with a written statement of information regarding the research that includes some or all of the requirements of informed consent described in Section 6. In essence, the statement is considered documentation of a waiver of informed consent.

8.7 Screening, Recruiting, or Determining Eligibility [§__.116(g)]

The revised Common Rule removes the requirement for partial waivers of consent for the use of information or specimens for the purposes of screening, recruiting, or determining the eligibility of prospective subjects for inclusion in the research. Pursuant to the revised rule, the [INSERT ORGANIZATION] IRB may approve a research proposal in which an investigator will obtain information or biospecimens for these purposes without the informed consent of the prospective subject or the subject's LAR if either of the following conditions is met:

1. The investigator will obtain information through oral or written communication with the prospective subject or LAR, or

2. The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.

When research is subject to the revised Common Rule, and the above conditions are met, investigators do not have to request waivers of consent for the purposes of screening, recruiting, or determining eligibility but do have to describe the activities in the application or protocol submitted to the IRB. The above does not negate the requirements of other rules, such as HIPAA, when applicable. It also does not negate the requirement to obtain consent, or a waiver of consent, before involving a subject (including the use of their identifiable private information or biospecimens) in other research activities.

8.7.1. 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 6, provided that the IRB finds and documents in its minutes that:

1. 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:
    i. Public benefit or service programs;
    ii. Procedures for obtaining benefits or services under those programs;
    iii. Possible changes in or alternative to those programs or procedures; or
    iv. Possible changes in methods or levels of payment for benefits or services under those programs.

AND

2. The research could not practicably be carried out without the waiver or alteration.

OR

8.7.2. 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 6, provided that the IRB finds and documents in its minutes that:

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

Examples of research that might qualify for a waiver of informed consent include, but are not limited to, retrospective chart reviews and observation of public behavior.

Note: Informed consent *cannot* be waived for research involving FDA-regulated products.

9. Consent by a Legally Authorized Representative or Family Member

There are circumstances in which informed consent for participation in an IRB-approved research study may be sought from a legally authorized representative of the participant, or even a family member.[1] To be clear, this section does not refer to surrogate consent for emergency research or procedures, but to consent for participation in research already approved by the IRB.

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

The term family member includes the following legally competent persons: spouses; parents; children, including adopted children; siblings; siblings' spouses; and any person related by blood or affinity whose close association with the participant equates to a family relationship.

Generally, for research involving human participants at the CCC-UPR, the informed consent of a legally authorized representative or the permission of a family member may be required where cognitive impairment has rendered the potential participant(s) incapable of giving true informed consent. Again, the protocol must receive IRB approval before consent and enrollment can be sought by the Protocol PI.

[1] A family member who is not a legally authorized representative technically does not provide true informed consent, but rather permission based on a failure to object. A legally authorized representative, however, does provide true informed consent.

Informed consent must be obtained from all adult participants who are mentally capable of providing their effective informed consent to participate in the proposed research. For adult participants 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:

1. A legally authorized representative may consent to enroll a participant in any research protocol that has been approved by the IRB.
2. If there is no legally authorized representative, a family member who is involved with medical decision-making for the participant, may permit the participant's enrollment in IRB approved research *if*
   (a) the risk is minimal, regardless of whether the participant would derive any benefit; OR
   (b) the risk is greater than minimal, but the research potentially carries a direct benefit to the participant.

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

The requirements and procedures for obtaining the consent of a legally authorized representative on behalf of a cognitively impaired individual are detailed in SOP 10: Informed Consent, Enrollment, and Other Considerations for Research Involving Cognitively Impaired Participants.

9.1. Obtaining Written Informed Consent via Fax

Situations may arise where it is appropriate to obtain informed consent from participants via fax. The following are such appropriate situations:

1. The informed consent process takes place in person, and the potential participant then takes the document home for consideration.
2. The consent process takes place over the phone.
3. The consent is obtained from a legally authorized representative.

In each situation, the person obtaining the informed consent should sign the consent form and make appropriate notes in the participant's records upon completion of the informed consent discussion. The participant or legally authorized representative may then fax a signed copy of the consent form to the research site. The participant or legally authorized representative should return the signed original consent form to the research site at his or her earliest opportunity, either at the next visit or via mail. Upon receipt of the faxed consent form, the Protocol PI or appropriate designee should sign and date the faxed form as acknowledgment of its receipt and make appropriate notes to the participant's record. After receiving the signed original consent form, the appropriate recipient should then sign and date it, file it with the faxed copy, and make appropriate notes to the participant's record.

Research participants who have verbally indicated that they have signed the consent form and will return it at some future date are not eligible to participate in the research project. Only after the PI or his/her representative has the original signed consent form or a faxed copy of the original signed consent form, is the participant eligible to participate in the research protocol.

The notes coinciding with the dates and signatures on the consent forms provide the source documentation that confirms and details the consent process. All documents will be maintained by the Protocol PI in the protocol file.

9.2. Obtaining Written Informed Consent via Mail or Email

This option is used when it is not possible to complete the consent process in person. Generally, this option is used when the study is a minimal risk study or there has been a change to the informed consent that may affect the participant and the participant is not scheduled for a study visit. Two copies of the consent form must be mailed so that the participant has a copy to keep and another to mail back to the site. An e-mail from the participant's account is also acceptable. It is strongly encouraged that a follow-up phone call be placed to ensure that the participant understands the changes in the informed consent. Once the signed consent form is received at the research site, it should be signed with the date it is received by a research team member authorized to obtain informed consent. Appropriate notes to the file must document the changes and if a phone call was made to answer any questions by the participant about the changes.

9.3 Obtaining Electronic Informed Consent

E-consent can help sites provide information to patients and continue enrollment during a time of site closures, quarantines, travel limitations, nature disastres and more. This is just one of many ways the FDA Guidance recommends anticipating and adapting to these challenges to maintain patient safety and data integrity. Many researchers are already altering study workflows, updating protocol and conducting virtual clinic visits.

E-Consent Costs And Requirements

Clinical research is possible because of patients who voluntarily provide their informed consent to participate in trials. The FDA requires a written consent form that is approved by the IRB and signed and dated by the patient or their legally authorized representative at the time of consent (21 CFR 50.27(a)). Remote methods and electronic informed consent (e-consent) have been weighed in recent years to reduce inefficiencies and improve the ability to share new information with currently enrolled patients.

Now more than ever, e-consent could allow for continued enrollment for many trials that have been halted during the pandemic.

E-consent may require up-front costs for design and implementation of a compliant electronic system, plus training study staff and IRB approval. An e-consent must contain all elements required by HHS and/or FDA regulations (45 CFR 46.116 and 21 CFR 50.25). In addition, the e-consent process may include interactive electronic-based technology, diagrams, images or graphics, videos, and possibly narration.

If you are developing an e-consent for your clinical trial, you can find answers in Questions Surrounding Electronic Informed Consents based on the FDA Guidance on the Use of Electronic Informed Consent.

While patients typically experience the informed consent process in-person during discussions with study personnel, e-consent could be obtained through:

- Electronic messaging
- Telephone calls
- Video conferencing

Live chat with a remotely located investigator or study personnel from a confidential space at home
While in-person visits may be currently restricted due to COVID-19, remote communication with patients at any time can be cost-effective for all parties.

Preparing To Implement E-Consent
For clinical trials not yet open to accrual, consider the following steps:

Determine if your Electronic Database Capture (EDC) system has the capability of e-consent, or if a separate system is needed.

Confirm the system and signature process is compliant with 21 CFR Part 11, especially for FDA regulated research. Not all commercially available e-consent solutions are Part 11 compliant.

Obtain IRB approval for use of e-consent with the specific e-consent system. Of note, some IRBs have preferred vendors.

Define how the sponsor and its representatives will have access to review the signed e-consent.

When the above steps are complete and questions have been answered, consider the following:

Document the plan for e-consent implementation in the site and sponsor records.

10. Documentation of Informed Consent

The revised Common Rule modifies the requirements for documentation of consent as described below. When reviewing research subject to the revised Common Rule, the Comprehensive Cancer Center- UPR IRB will apply the requirements summarized below. Unless the requirement for documentation of consent is waived by the IRB, informed consent must be documented by the use of written informed

consent form (ICF) approved by the IRB and signed (including in an electronic format) by the subject or the subject's LAR. A written copy must be given to the person signing the ICF.

The ICF may be either of the following:

1. A written consent document that embodies the basic and required additional elements of informed consent. The investigator shall give either the subject or the subject's LAR adequate opportunity to read the informed consent form before it is signed; alternatively, this form may be read to the subject or the subject's legally authorized representative; or

2. A short form written consent document stating that the elements of informed consent have been presented orally to the subject or the subject's LAR and that the key information required by §__.116(a)(5)(i) (See Section 8.1 #5.a) was presented first to the subject, before other information, if any, was provided. When this method is used:

a. The oral presentation and the short form written document should be in a language understandable to the subject; and

b. There must be a witness to the oral presentation; and

c. The IRB must approve a written summary of what is to be said to the subject (the approved full consent document may serve as this summary); and

d. The short form document is signed by the subject;

e. The witness must sign both the short form and a copy of the summary; and

f. The person actually obtaining consent must sign a copy of the summary; and

g. A copy of the summary must be given to the subject or representative, in addition to a copy of the short form.

10.1. Informed Consent Documents

The documents used in the informed consent process and referenced in this SOP include:

1. Written consent form in the language of participants (English or Spanish) anticipated to be enrolled
2. Written statement of information regarding the study
3. Oral consent script

10.2. Format of Written Consent Form

1. In drafting the written consent form, Protocol PIs may refer to the format and language provided in the sample consent form, provided.

   The Protocol PI should ensure that all of the required elements of informed consent, outlined in Section 6 above, are included. If some or all of the participants are members of a vulnerable population, the Protocol PI should consult the SOP addressing that population for specific consent requirements.

2. The consent form format should be easy to read (*e.g.*, adequate white space, paragraph headings, no fine print).
3. The consent form should not use assumptive language such as "you understand that" or "you have been told that," *etc*.
4. The consent form must be written in language understandable to the participant, preferably at the 8th-grade level.
5. Ordinary language, as opposed to technical jargon, should be used as much as possible. Short, easy to read sentences are preferred. All necessary medical, scientific, or technical terms must be explained.
6. The consent form may not contain any exculpatory language through which the participant waives or appears to waive legal rights or releases, or appears to release, the Protocol PI, the Sponsor, or CCC-UPR from liability or negligence.
7. The consent form should make clear the role of the Protocol PI, emphasizing that the PI is not assuming the role of a healthcare provider concerning the participant.

10.3. Ensuring Use of Current, IRB-Approved Consent Form

The final approved consent form must contain the date of approval and date of expiration established for the protocol by the IRB. The expiration date will be no longer than 364 days after the last review by the IRB or its representatives. If a revision to the consent form is approved by the IRB before the expiration of the previous version, all previous versions must be destroyed. The Protocol PI should take steps to ensure that only the most current, IRB-approved version of the consent form is used to obtain consent. These steps may include the insertion of a computerized watermark, the use of a stamp, or the making of some other mark to indicate that the consent form is the final, IRB-approved version.

10.4. Signing of the Written Consent Form

The consent form must be signed and dated by the participant or the participant's legally authorized representative, the person obtaining the consent, the Protocol PI (if the Sponsor so requires), and a witness (when appropriate).

The IRB has the authority to waive documentation of informed consent. However, a request for waiver of informed consent itself (*i.e.*, the purpose of the study will not be known) requires that the protocol be reviewed by the IRB as a deception study.

A witness may be required by the IRB when the participant or his or her legally authorized representative 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 participant, and who attends the informed consent process. A translator who participated in the informed consent process also may serve as the witness.

The form may be read to the participant or his or her legally authorized representative, but in any event, the Protocol PI shall give either the participant or the representative adequate opportunity to read it before it is signed.

All participants must sign the current IRB-approved consent form prior to participating in any study-related activity.

The participant must be given a copy of the consent form. The original signed consent form is to be kept on file in a locked file cabinet at the Protocol PI's site for audit purposes.

10.5. Consent Form Revisions

During the course of a study, it may become necessary to change some of the information in the consent form. This can be done by a (1) consent form revision, (2) addendum, or (3) notification to the study participant or his or her legally authorized representative. Any changes must be submitted to the IRB as an amendment for review, approval, and a decision regarding the need to re-consent before use. *See* SOP 3: Initial and Continuing Review by the IRB, Section 11, setting forth procedures for submission and review of amendments. *See also* Section 9.6 below in this SOP for information concerning the re-consenting of participants.

When there have been changes made to the consent form, the revised version that is stamped "approved" must be used when enrolling new participants in the study.

Immediate hazards or issues of safety, however, should be communicated to the participant upon receipt of the new information or as directed by the Sponsor. The new information communicated to the participant or his or her legally authorized representative must be reported to the IRB as soon as possible. *See* SOP 4: Unanticipated Problems Involving Risk to Human Research Participants or Others: Procedures for Reporting to and Review by the IRB.

10.6. Re-Consenting Participants

The Protocol PI has a responsibility to inform research participants of any new information that might affect a participant's willingness to continue participating in the research. While some new information may require re-consenting all participants with a revised consent form or addendum (*e.g.*, discovery of a previously unknown serious side effect), other changes may require only

notification to active participants (*e.g.*, grammatical corrections, minor changes not affecting the risk/benefit ratio). The timeliness and method of informing participants and the necessity of re-consenting will depend on the seriousness of the new information and will be decided and communicated to the Protocol PI when the IRB approves the revisions.

In cases where participants have completed active study or follow-up procedures and new safety information is discovered that may affect a participant's further participation or long-term risks from the treatment, the participant must be informed of this new information.

10.6.1. Written documentation of the participant's receipt of new information and willingness to continue to participate, via an IRB-approved revised consent form or addendum (*see* Section 9.5 above for procedures), must be obtained if there is a significant change to the protocol or risk/benefit ratio which directly affects what the participant is being asked to do. For example:

1. The study originally was going to last for 6 weeks, but now the participants are going to be followed for 5 years.
2. Blood originally stored for future analysis of unknown biomarkers will now be used for genetic testing.
3. A certain study procedure/intervention will be added or changed.

Written documentation of re-consent may be obtained by having the participant sign an IRB approved updated version of the consent form or an addendum to the original consent form.

Written documentation of re-consent should also be obtained from (a) participants who were enrolled in research studies when they were minors but who have turned 21 years old while still participating actively in the study; and (b) participants who were enrolled in research studies by a legally authorized representative when they were cognitively impaired but who have regained competency while still participating actively in the study.

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 participant, but not written informed re-consent, as determined by the IRB.

The IRB reserves the right to approve the information provided to research participants and the method used for conveying that information.

Notification may be conveyed verbally or in writing, with the Protocol PI's documenting in the research file that he or she has done so. The notification, however, should reiterate to the participant or legally authorized representative that the participant is free to withdraw/be withdrawn from the research study at any time without penalty or loss of benefits to which the participant is otherwise entitled.

11. Oral Informed Consent

Oral consent is the process of obtaining consent without the use of a written document.[2]

10.1. The IRB may approve the use of oral consent where the participant is (1) blind, (2) illiterate, or (3) unable to write his or her name.

10.2. Oral consent must be documented.

1. The Protocol PI should provide to the IRB for review and approval the following documentation: (a) a written summary or script from the Protocol PI of what is to be said to the participant or his or her legally authorized representative, and (b) an information sheet documenting that the elements of informed consent required by federal regulations and the IRB have been presented orally to the participant or the participant's legally authorized representative. The information sheet 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 information sheet shall be provided to the participant or the representative, when possible.

2. The IRB may also decide that oral consent be documented, instead or additionally, by another method such as audio or video-recording.

11. Obtaining Informed Consent from Non-English or Spanish-Speaking Participants

The concept of "informed consent" requires that it be obtained in a language that the participant understands. The research study and all other elements of informed consent must be explained fully to participants in a language they understand by either a member of the research team qualified to obtain consent or a translator who speaks both English or Spanish and a language in which the participant is fluent.

There are two possible situations involving non-English or Spanish-speaking participants — (1) the Protocol PI knows in advance of submitting the protocol application that he or she may be enrolling one or more participants who do not speak English or Spanish; or (2) the Protocol PI identifies after IRB approval of the protocol application one or more potential participants who do not speak English or Spanish. The requirements for each situation differ slightly.

11.1. <u>Translation Processes</u>

[2] Oral informed consent is technically termed oral assent, as the concept of consent includes written documentation. However, to clearly distinguish the concept of oral assent from the assent of a child or cognitively impaired person, the term "oral consent" is used in this policy. [*Note: The IRB will discuss whether it prefers the term "oral assent."*]

If the protocol and the English versions have been approved already by the convened IRB, translation(s) may be reviewed and approved by the Chair of the IRB or the Chair's designee. However, if an additional risk for the non-English/Spanish-speaking participant is identified, the translation(s) should be referred to the convened IRB for review and approval.

Witness: The witness can be related to or closely associated with the participant or representative if that is acceptable to them. The witness may serve as the person obtaining consent, *but* may not then serve as the translator. The witness certifies that an oral presentation was made to the participant or representative in a language understandable to them and described accurately the content of the English/Spanish or Spanish-version consent form. As appropriate, the witness signs (a) both the English/Spanish consent form and the translated form or (b) the consent short form, which should state that the witness observed that the translator's presentation of the English/Spanish consent form details to the participant or representative was complete and understandable to them.

Person Obtaining Consent: The person obtaining consent *may not* be related to or closely associated with the participant or legally authorized representative. The function of the person obtaining consent is to supervise the consent process and to be able to answer any questions about the study posed by the participant or representative. The person obtaining consent may serve as the translator or witness, but not both. As appropriate, the person obtaining consent signs (a) both the English/Spanish consent form and the translated form or (b) the consent short form. As appropriate, the research participant signs and receives a copy of the consent form or the short form.

12. Procedures for IRB Review and Approval of Informed Consent

12.1. The Protocol PI must provide in the protocol application a detailed description of the consent process, including precautions to reduce undue influence. Documents relating to informed consent should be included as part of the application, including but not limited to appropriately translated consent documents if there is the potential or actual inclusion of non-Spanish speaking participants. Translated consent documents must be accompanied by a letter from the translator attesting to the thoroughness and accuracy of the translations or a back translation so that a comparison can be made of the accuracy of the translation.

12.2. Submitted protocol applications are reviewed in accordance with SOP 3: Initial and Continuing Review by the IRB: Requirements for Submission of Applications, Approval Criteria, and Expedited and Convened Committee Review Procedures.

12.3. Where the protocol application is subject to the Expedited Review process, the Expedited Reviewer or the IRB Chair will review the consent documents for content and form and either approve them or recommend changes. The Expedited Reviewer is responsible for determining whether waivers of informed consent or documentation of informed consent are applicable and appropriate. In the case of Convened Committee Review, the IRB members at the convened

meeting will review the consent process (or request for waiver of consent) and the content and form of the consent documents. The IRB will either approve the consent documents or recommend changes to their content or to some other aspect of the consent process. In the event the consent process/documents are in a language other than Spanish, the IRB must receive appropriately translated documents and assess their accuracy before approving their use.

12.4. The IRB Coordinator or other member will document clearly in the minutes the outcome of any IRB discussion relating to the consent process or documents, including but not limited to:

1. Use of non-Spanish documents
2. Use of a translator
3. Use of consent from a legally authorized representative
4. Consent requirements relating to participants from vulnerable populations
5. Waiver of consent
6. Waiver of documentation of consent

12.5 When IRB-requested changes are returned by the Protocol PI, IRB will confirm that all the changes have been made and will, as applicable, present them to the Expedited Reviewer or IRB Chair for review and approval or place them on the agenda of the next available meeting of the convened IRB.

12.6 Once consent documents are approved by the IRB, will issue an approval and expiration date established for the protocol by the IRB. These IRB-approved versions must be used during the consent process, as they are the only versions considered valid. The protocol approval period expires at midnight on the date of expiration and therefore, the consent form expires then as well. The dates of approval and expiration are also provided to the Protocol PI on all approval memoranda.