UNC SCHOOL OF MEDICINE	Standard Operating Procedure		
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501.1: Obtaining and Documenting Informed Consent

PURPOSE

This SOP describes the process for obtaining and documenting written informed consent from adult research participants or participants' legally authorized representatives.

SCOPE

This procedure applies to all SOM personnel responsible for obtaining written informed consent from adults participating in human subjects research studies.

BACKGROUND

The research participant or the participant's 'legally authorized representative' (LAR) must provide 'legally effective informed consent' prior to participating in human subjects research, unless the IRB has approved a waiver of informed consent as allowed by the federal regulations. The requirement for 'informed consent' (IC) is in place to protect the rights of participants by ensuring that participants or LARs are fully informed about the risks and benefits associated with study participation and are provided with all information needed to reach a decision on whether or not to participate in a research study. With varying degrees of 'consent capacity' and research risk, it is essential for investigators to carefully establish consent procedures and identify safeguards as applicable.

Informed consent is a process that begins with the recruitment and screening of a potential participant, includes signing of the IRB-approved 'informed consent form' (ICF), and continues throughout the participant's involvement in the research and often even beyond study termination. The participant or LAR must be provided with relevant information and be given the opportunity to provide ongoing voluntary consent during the study. Additionally, any modifications to study procedures or discovery of new information or findings that may affect participants' willingness to continue in the study or affect former participants must be communicated to the participants as part of the ongoing informed consent discussion, as determined by the IRB.

Notes:
Throughout the remainder of this SOP, any informed consent procedures referencing participants apply equally to the participant or the participant's LAR.
The development of the Informed Consent Form is described separately in SOM SOP 702.1, Developing the Informed Consent Form (currently in development).

PROCEDURE

1. Preparing for the informed consent discussion
    a. Study team members responsible for obtaining informed consent must review the ICF in detail to ensure all text is accurate and complete, as well as to ensure personal understanding of the study procedures and other information included in the ICF (each time a new version of the ICF is generated)

   b. Print or otherwise prepare one or more copies of the ICF(s), ensuring utilization of the currently IRB-approved version of the ICF. Do not cross out or add information or fields as it invalidates the IRB's approval of the ICF
2. Informed consent discussion and presentation of ICF
   a. Arrange to meet with the participant in a private location or area otherwise suitable for having a private discussion
   b. Introduce yourself to the participant, stating your role in the research team (as applicable)
   c. Briefly tell the participant the reason for your discussion, including a simple and high-level statement of the research study and ask the participant if they want to discuss the study with you in more detail
      i. If they are interested, continue to follow the procedure below
      ii. If they are not interested, thank them for their time and offer any appropriate assistance for continuing with their visit, as applicable (e.g., refer the participant back to the clinical care team)
   d. Provide the participant with a copy of the ICF so that they may follow along during the discussion
   e. Begin a concise and focused presentation of the 'key information', information that would be most important to individuals contemplating participation in a particular study, including the purpose of the research, the expected duration of participation, major requirements of the study, the risks and benefits, and appropriate alternative treatments that might be beneficial to the prospective subject (Common Rule, 2018 Requirements: 45 CFR 46.116(a)5(i))
   f. Proceed with a discussion of the required elements of legally effective informed consent, including, but not limited to: voluntary nature of the study, purpose of the study, eligibility criteria, details of participating, risks, benefits, alternative treatments (if applicable), costs, measures to ensure confidentiality, and whom to contact with any future questions or concerns (Common Rule, 2018 Requirements: 45 CFR 46.116; FDA: 21 CFR 50.25; ICH E6 Guideline for GCP, 4.8.10; UNC CRSO: Guidance and Tips, Required Elements of Informed Consent)
   g. Provide prospective participants with information that a "reasonable person" would want to have to make an informed decision to participate or not
      i. Present the information in a neutral manner without leading the participant to make a particular decision (ICH E6 Guideline for GCP, 4.8.3)
      ii. Do not include any exculpatory language through which the participant is made to waive or appear to waive any of his/her rights, or that releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence (ICH E6 Guideline for GCP, 4.8.4)
   h. Adapt the presentation of information to the participant's capabilities and the complexity of the research
      i. As needed, encourage the participant to repeat or rephrase key points and to ask questions throughout the discussion to aid in comprehension
      ii. As needed, assess comprehension by asking open-ended questions and using the teach-back method (i.e., asking the participant how they would explain the study to their family or friends)

i. Offer the participant sufficient time to read the ICF and further consider participation (sufficient time will vary depending on the nature of the study and the individual participants) (ICH E6 Guideline for GCP, 4.8.7)
j. Ask the participant if he/she has any questions related to the study or the decision to participate; if you are unable to answer questions sufficiently, consult with the investigator or other study team member(s) to obtain and offer sufficient explanation (ICH E6 Guideline for GCP, 4.8.7)

3. Documenting informed consent (Common Rule, 2018 Requirements: 45 CFR 46.117; FDA: 21 CFR 50.27)
   a. Written documentation of informed consent is required unless the IRB has granted a waiver
      i. If the participant chooses to participate, ask the participant to provide his/her name and signature, and enter the date on the ICF (Note: Only the participant should enter the date for his/her respective signature) (ICH E6 Guideline for GCP, 4.8.8)
      ii. Review the ICF to ensure the participant provided the requisite signature, printed name, correct date, and any additional signatures or initials (as applicable).
      iii. The person obtaining consent must also provide his/her name, signature, and date the ICF in real time (ICH E6 Guideline for GCP, 4.8.8)
      iv. Retain a signed copy of the ICF for the study record and provide the participant with a signed copy of the ICF (may be photocopied or may have two identical ICFs signed) (ICH E6 Guideline for GCP, 4.8.11)
   b. Document the informed consent process as well, to indicate who obtained the IC, when the IC was obtained, and how the IC was obtained. This documentation may be accomplished by
      i. completing a form for documentation of informed consent (Appendix A) and/or
      ii. including a contextual note in the research record or electronic medical record. (Appendix B & C)
   c. Once the IC process is complete, the study team should review the ICFs and other documentation for completeness prior to filing in the study record.
      i. Any discrepancies, missing or incomplete entries identified following informed consent must be documented, corrected, and if applicable, reported per IRB prompt reporting requirements.
   d. File a copy of the ICF in the participant's medical record if 1) the study is FDA-regulated, or 2) any of the study-related activities may have an effect, adverse or otherwise, on the clinical treatment of the participant. In all other cases, it is at the discretion of the investigator to place a copy of the ICF in the participant's medical record in accordance with the IRB-approved plan.
4. Maintaining informed consent
   a. Throughout the study, continue to verify the participant's understanding of key study information that may affect the decision to participate in research and make use of teachable moments during interactions with the participant.
      i. If a participant makes an incorrect statement about the study purpose or the risks/procedures of the research, take the opportunity to reeducate the participant.
      ii. If a participant expresses difficulty understanding a specific procedure or aspect of the study, consider providing supplemental consent materials.

iii. If a participant has concerns about ongoing participation, remind him/her that he/she has the right to withdraw at any time and that his/her clinical care will not be affected.

5. Provision of new information
   a. The PI and study team must recognize and identify any new information that should be communicated to current or former participants.
      i. New information may include changes in study procedures, the identification of new research-related risks, a clinically relevant increase in frequency of a known risk, an increase in severity of a previously known risk, unanticipated problem that exposes participants to new risks (e.g., a data breach), decrease in expected benefits to participation, availability of new alternative therapies, etc.
   b. If it is determined that new information needs to be communicated to participants, the study team must submit a notification to the IRB that details the plans for provision of information plan and an updated consent document if reconsent is warranted (ICH E6 Guideline for GCP, 4.8.2).
      i. Communication of new information may be accomplished through re-consent, verbal discussion, letter, or addenda, dependent on the type of information to be shared, the status of participants in the study and whether participants need to document that they wish to remain in the study. (SACHRPP Recommendations to HHS Secretary, Attachment A; Attachment A2)
      ii. Immediate verbal notification of new information may occur without prior IRB approval if necessary to eliminate apparent immediate hazards to participants; in this case, the IRB must subsequently be promptly notified.
6. Withdrawal of consent
   a. If a participant chooses to withdraw his/her consent, the details (including extent of withdrawal (e.g., partial or complete), time of withdrawal, reason for withdrawal (as communicated by the participant) must be documented in the study record.
7. Other circumstances
   a. Deviations to this procedure are allowed as explicitly approved by the IRB (e.g., remote consent, short form consent, verbal consent, emergency research, waivers of consent).
   b. Inclusion of vulnerable populations (i.e., anyone vulnerable to the possibility of coercion or undue influence) in research requires additional considerations and procedures. (UNC OHRE: SOP 1101; UNC OHRE: SOP 1201)
      i. If you plan to enroll individuals with impaired or fluctuating 'consent capacity,' develop and submit to the IRB a plan that describes the prospective participants that will be assessed for consent capacity, how consent capacity will be assessed and documented, procedures for obtaining surrogate consent (including designation of LAR (UNC OHRE: SOP 1101), procedures for initial and ongoing consent discussion) specific to participants whose capacity to consent can be affected by disorders with progressive or fluctuating courses, any enhancements to the consent process to enable participants with impaired consent capacity to participate in the consent process and as applicable provide legally effective informed consent, etc. (ICH E6 Guideline for GCP, 4.8.12)

ii. If you did not plan to enroll individuals with impaired consent capacity and encounter a prospective participant whose capacity to consent is questionable or an enrolled participant experiences a change in consent capacity, consult with the IRB.

c. The ICF should be prepared in the language understandable to the prospective participant. (ICH E6 Guideline for GCP, 4.8.6). Researchers should be fluent in the participant's language or an interpreter should be available during the consent process and throughout the participant's participation. For the occasional and unexpected prospective participant who does not speak English or has limited English-language proficiency, the short form method may be used. (UNC OHRE: SOP 1101)

d. A prospective participant who speaks and understands English, but does not read and write, may be enrolled using the short form method and 'marking their mark' on the short form to signify consent. (UNC OHRE: SOP 1101)

DEFINITIONS

- Consent capacity: An individual's ability to understand information relevant to making an informed, voluntary decision to participate in research. (NIH: Research Involving Individuals with Questionable Capacity to Consent: Points to Consider)
- Good Clinical Practice (GCP): International ethical and scientific quality standard for the design, conduct, performance, monitoring, auditing, recording, analyses and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial participants are protected. (ICH E6 Guideline for GCP, 1.24)
- Informed Consent (IC): Process by which a participant voluntarily confirms his or her willingness to participate in a study, after having been informed of all aspects of the study that are relevant to the participants' decision to participate (ICH E6 Guideline for GCP, 1.28). The active sharing of information between the researcher and the participant (or the participant's LAR/parent/guardian) begins with the first information exchange with the participant about the study to make an informed and voluntary decision about whether to participate (or not) and continues beyond study termination to ensure that the participant have information about the research to make an informed and voluntary decision about whether to continue participation in the study (or not). All interactions with study participants are opportunities for education and support the process of informed consent. In addition, any new information or findings about the study that may affect a subject's willingness to continue participation must be communicated to the participants, and former participants in some cases, as part of the ongoing informed consent discussion.
- Informed Consent Form (ICF): A written form with the required elements of informed consent approved by the IRB that when signed by the participant (or the participant's LAR/parent/guardian) documents the participants informed and voluntary consent to participate in the study.
- Legally Authorized Representative (LAR): An individual or juridical or other body authorized under applicable law to consent, on behalf of a prospective participant, to the participant's participation in the procedure(s) involved in the research. (Common Rule, 2018 Requirements: 46.102; FDA: 21 CFR 50.3)

- Legally Effective Informed Consent: Informed consent obtained from the participant or the participant's legally authorized representative and documented in a manner that is consistent with federal human subjects regulations and with applicable laws of the jurisdiction in which the research is conducted. In general terms, the regulations stipulate that an investigator should seek consent only under circumstances that provide the prospective subject or the legally authorized representative sufficient opportunity to consider whether to participate and that minimize the possibility of coercion or undue influence. The information provided should be in language that is understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language. It is important to note that the informed consent requirements in the regulations are not intended to preempt any applicable federal, state, or local laws that require additional information to be disclosed for consent to be legally effective (OHRP: Informed Consent FAQs)
- Key information: A concise explanation at the beginning of the 'informed consent form' of information that would be most important to individuals contemplating participation in a particular study, including the purpose of the research, the expected duration of participation, major requirements of the study, the risks and benefits, and appropriate alternative treatments that might be beneficial to the prospective subject. Key information is described in the Concise Summary section of the UNC IRB's template ICFs. The template includes model summary statements. (Common Rule, 2018 Requirements: 45 CFR 46.116(a)5(i))
- Written: Writing on a tangible medium (for example, paper) or in an electronic format.

ASSOCIATED POLICIES, REGULATIONS, GUIDELINES

- Common Rule, 2018 Requirements: 46.102, Definitions for the Purposes of this Policy
- Common Rule, 2018 Requirements: 45 CFR 46.116, General Requirements for Informed consent
- Common Rule, 2018 Requirements: 45 CFR 46.117, Documentation of Informed Consent
- FDA: 21 CFR 50.3, Definitions
- FDA: 21 CFR 50, Subpart B, Informed consent of Human Subjects
- FDA: 21 CFR 50.25, Elements of Informed Consent
- FDA: 21 CFR 50.27, Documentation of Informed Consent
- FDA: Information Sheet, A Guide to Informed Consent, Guidance for Institutional Review Boards and Clinical Investigators
- FDA: Draft Guidance, Informed Consent Information Sheet, Guidance for IRBs, Clinical Investigators, and Sponsors
- ICH GCP E6 Guideline for Good Clinical Practice (GCP)
- OHRP: Informed Consent FAQs
- Secretary's Advisory Committee on Human Research Protections (SACHRP) recommendations to the HHS Secretary and Office of Human Research Protections (OHRP)(April 7, 2020):
    - Attachment A – New Information Provided to Previously Enrolled Research Subjects
    - Attachment A2 – Reconsent Appendix 2, Additional Information Scenarios and Suggested Options

- NIH: Research Involving Individuals with Questionable Capacity to Consent: Points to Consider
- UNC CRSO: Guidance and Tips, Required Elements of Informed Consent
- UNC OHRE: SOP 1101, Obtaining Informed Consent from Research Subjects
- UNC OHRE: SOP 1201, Vulnerable Subjects in Research

Additional requirements specific to applicable clinical trials:

- FDA: 21 CFR 50.25(c), Statement of disclosure specific to trial information included on clinicaltrials.gov
- FDA: Guidance for Sponsors, Investigators and Institutional Review Boards, Questions and Answers on Informed Consent Elements, 21 CFR § 50.25(c)
- Common Rule, 2018 Requirements: 45 CFR 46.116(h), Requirements for posting clinical trial consent forms for FDA-supported trials
    - OHRP: Guidance, Clinical Trial Informed Consent Form Posting

Revision History		
Version	**Effective Date**	**Change Summary**
501.1	TBD	First approved version

Appendix A: Template checklist for documenting the informed consent discussion

IRB Study #: _____ Participant Initials: _____ Study ID: _____

Please initial next to "Yes" or "No" by each line as appropriate. If "No," an explanation must be provided in the notes section below.

_____Yes	_____No	A concise and focused presentation of the key information was provided.
_____Yes	_____No	The details of this research study were discussed, including an explanation of the required elements of the ICF.
_____Yes	_____No	It was emphasized that study participation is voluntary, that the participant's clinical care would not be affected if study participation is declined, and that the participant may withdraw consent at any time.
_____Yes	_____No	The ICF was provided in the preferred language.
_____Yes	_____No	Ample time was provided for reading the consent document and questions were encouraged.
_____Yes	_____No	All questions and concerns were addressed to the satisfaction of the participant (or LAR).
_____Yes	_____No	The PI or Co-I was available for questions.
_____Yes	_____No	The participant (or LAR) reviewed the current IRB approved consent document(s) and agreed to participate. Specify ICF version and date/time signed below.
_____Yes	_____No	A copy of the signed consent document was provided to the participant and/or LAR.
_____Yes	_____No	No procedures specifically related to the study were performed prior to the participant signing the consent document.
_____Yes	_____No	A copy of the signed consent document was placed in the participant's research file. If a copy was also placed in the medical record, specify in Notes.

☐ Main Study ICF, Version/Date: _____

☐ Other ICF, Specify: _____Version/Date: _____Time: _____

☐ Other ICF, Specify: _____Version/Date: _____Time: _____

Additional Notes:

Additional Notes may include,

- *People who were present during the consent discussion, such as the participant, an LAR, the person obtaining consent, relative(s), PI, study coordinator, interpreter, witness, etc.)*
- *any questions or concerns raised during the consent discussion*
- *use of a verbal consent process, LAR or the short form method*

_____ _____ _____

Signature of Person Completing the Note **Date** **Time**

Appendix B: Template contextual note for documenting the IC discussion in the study record

IRB Study #: _____ Participant Initials: _____ Study ID: _____

A concise and focused presentation of the key information was provided. The details of this research study were discussed with the participant, including an explanation of all of the elements of the ICF. It was emphasized that study participation is voluntary, that the participant's clinical care would not be affected if study participation is declined, and that the participant may withdraw consent at any time. The participant was given opportunity to read the informed consent form in the participant's preferred language and to ask questions.

All questions and concerns were addressed to the satisfaction of the participant. The participant verbalized understanding of the information and agreed to participate prior to any study-related procedures. The participant signed and dated the currently approved main ICF [version/date]; other ICF(s) [version(s)/date(s)] and the HIPAA Authorization form [version/date], as applicable, on [date and time of the discussion] prior to any study procedures being conducted and received a copy of the signed forms.

Additional Notes:
Additional Notes may include,

- *People who were present during the consent discussion, such as the participant, an LAR, the person obtaining consent, relative(s), PI, study coordinator, translator, witness, etc.)*
- *any questions or concerns raised during the consent discussion*
- *use of a verbal consent process, LAR or the short form method*

_____	_____	_____
Signature of Person Completing the Note	**Date**	**Time**

Appendix C: Template contextual note for documenting the IC discussion in the EMR

Initial Consent Discussion:

Dr. _____ and I met with participant _____to discuss consent for _____. The protocol was reviewed, including discussion of risks & benefits, that the treatment involves research, review of charges covered / not covered by study, medications/treatments used, procedures involved including optional procedures, confidentiality, time commitments involved, study contact list, the option to withdraw at any time, and required use of birth control (as applicable).
Alternatives to study participation were discussed and the participant was given reasonable time to consider participation in the study, in the absence of coercion or undue influence. The participant was offered an opportunity to ask questions and these questions were answered. The participant verbalized understanding of information presented.

The participant has signed the main informed consent form (ICF), _____ [version/date]; other ICF(s) _____ [version(s)/date(s)] and the HIPAA Authorization Form [version/date], as applicable, in my presence, prior to any study procedures being conducted. Copies of the informed consent form(s) and HIPAA Authorization Form were given to the participant.

The ICF(s) and HIPAA Authorization Form were submitted to UNC Health Information Management for upload into the participant's electronic medical record. The signed and dated ICF(s) and HIPAA Authorization Form will be kept in _____. Every effort to maintain confidentiality will be employed.

Date: _____Time: _____
Other ICF(s), HIPAA Form Signature: Same date, time and signature as above

Reconsent:

Dr. _____ and I met with participant _____ to discuss reconsent for _____. Changes to the study, including any changes in risk, procedures, treatments, and time commitments were reviewed. The participant was reminded of the option to withdraw at any time. Alternatives to study participation were discussed again. The participant given reasonable time to consider continued participation in the study in the absence of coercion or undue influence. The participant was offered an opportunity to ask questions and all questions were answered. The participant verbalized understanding of the new information presented and indicated his/her wishes to continue the study.

The participant has signed the ICF in the presence of the researcher obtaining informed consent. A copy of the consent form was given to the participant. A copy was submitted to UNC Health Information Management for upload into the participant's electronic medical record. The signed and dated ICF will be kept in _____. Every effort to maintain confidentiality will be employed.

Date: _____Time: _____