Informed Consent Process		
VCU/VCUHS CLINICAL RESEARCH STANDARD OPERATING PROCEDURES		
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1. PURPOSE

The purpose of this Standard Operating Procedure is to reinforce the current policies of the Institutional Review Board (IRB) of record while elaborating on the specific policies of VCU and/or VCU Health System. It focuses on supporting the informed consent process for research participation and the authorization for the use and disclosure of Protected Health Information (PHI) in clinical research.

2. REQUIREMENTS

The ethical conduct of clinical research investigations is based upon the voluntary consent of a research participant who has been appropriately informed about a clinical research study's risks and benefits. The principal investigator (PI) will ensure that legally valid informed consent form (ICF) has been properly obtained from the participant or the participant's legally authorized representative. Documentation of the informed consent process is required to establish that the participant was accurately and adequately informed and that no study-related procedures were initiated prior to obtaining informed consent.

The only exceptions to this policy are limited circumstances in clinical research, where the requirement of consent has been waived, excepted, or altered by an Institutional Review Board (IRB) in accordance with at least one of the following:

- 45 CFR 46.116 and if applicable, FDA guidance "IRB Waiver or Alteration of Informed Consent for Clinical Investigations involving No More than Minimal Risk to Human Subjects" issued July 2017;
- 21 CFR 50.24
- The research is exempt from IRB review pursuant to 45 CFR 46.104.

3. DEFINITIONS

<u>Decisionally Impaired</u>

Impaired decision-making capacity is having a condition that affects mental processing or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished. The PI must make a specific determination as to decisional impairment on a case-by-case basis.

Health Insurance Portability and Accountability Act (HIPAA) Authorization

HIPAA authorization is an agreement between a participant and a researcher documenting a participant's agreement to permit the researcher to use or disclose the participant's PHI for the conduct of a research project. HIPAA authorization is part of the informed consent process and must be signed and dated by the participant at the time of initial consent, unless a waiver has been approved by the IRB.

Informed Consent Process

Informed consent is a general term for the communication process that is used by key research personnel to facilitate and obtain an individual's informed decision to enroll in a clinical research study. During this process a participant voluntarily confirms their willingness to take part in research, after having been informed of all aspects of the research that are relevant to the participant's decision to participate. Obtaining informed consent involves dynamic and continuing exchanges of information between the research team and the study participant throughout the life of the study. HIPAA may be combined with the ICF or as a standalone form. HIPPA authorization is required for VCUHealth.

Documentation of Informed Consent

The consenting process is documented by means of a written, signed and dated informed consent document that may be updated and/or revised as warranted during the conduct of the study. When consent signatures are waived by the IRB, a record of consent being given is documented in the researcher's records along with the date, the method by which consent was communicated, and for verbal processes, any witnesses and the name of the person conducting consent.

Legally Acceptable Representative (LAR)

An LAR is an individual, judicial, or other body authorized under applicable law to grant permission, and continue to remain engaged in the ongoing informed consent process, on behalf of a prospective participant for participation in research activities.

Protected Health Information (PHI)

Protected Health Information (individually identifiable health information), is defined as a subset (record or transmission) of health information, including demographic information, collected from an individual. It is created or received by a health care provider, health plan, employer, or health care clearinghouse. It relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual. In addition, the information identifies the individual or can be used to identify the individual.

Re-consenting

Re-consenting is the process of presenting new information about the research to

study participants that could affect their willingness to continue to participate in the research study. If the participant makes the decision to continue participating in the research study, a new informed consent will be obtained.

4. PROCESS

The informed consent process should be an active exchange of information between research personnel and the prospective participant/LAR. This sharing of information between the investigator/research staff and prospective participants is protocol-specific. Consent can be obtained by the method(s) approved by the IRB of record. Prospective participants (or LAR) should be given sufficient opportunity to review the consent, to ask questions and seek clarification from the investigator. The prospective participant/LAR should be in a position to freely decide whether to initially enroll in the research, to continue in the research study, or to withdraw from the study at any time.

A. Planning - The informed consent process is governed by HRPP policies and guidance. In preparing an informed consent process and documents, the Principal Investigator, together with other members of the research team, should be familiar with ***ALL*** policies of the responsible IRB regarding informed consent, including (see active links within the Reference section of this SOP):

B. Preparing – The informed consent document, if applicable, should be prepared based upon the requisite template of the responsible IRB and the study protocol and investigator's brochure or a draft informed consent document provided by the sponsor. Steps to consider include:

- Designating who is responsible for ensuring the development of the informed consent process and document and oversight of any changes required over the life of the study.
- Ensuring that the sponsor, if applicable, reviews modifications to the informed consent document prior to submission for IRB approval. Division of Sponsored Programs subject injury language (SIL) review is mandatory for industry-sponsored studies.
- For studies utilizing the VCU IRB as the IRB of record: ICFs must be submitted to the VCU IRB
- For studies utilizing an external IRB as the IRB of record: ICFs must be submitted to the VCU HRPP for an internal compliance review and be reviewed by the VCU HRPP prior to being submitted to the external IRB of record for IRB approval.
- Consideration of logistics related to conducting the informed consent discussion with prospective participants.
- Upon notification of final IRB approval, the research team must ensure that the approved version of the informed consent document(s) is uploaded to the Clinical Research Management System (CRMS), see VCU/VCUHS SOP CR-AD-120 Clinical Research Management System.

C. Obtaining Informed Consent

- The participant and the person conducting the consent process must sign the consent prior to receiving any study-specific tests or procedures. The individual obtaining consent should sign the consent form only after the participant signs the consent. If an IRB-approved consent has a line for the PI to sign the consent in addition to the consenting staff, the Principal Investigator or equally qualified sub-/co-investigator will sign the consent as soon as practicable following review of the participant's signature. The PI or their designee will ensure that a copy of the signed informed consent document is uploaded in the VCUH electronic medical record if there are VCUHS clinical services performed in support of the study.
- The PI and/or designee will ensure that:
    - The most recent version of the IRB-approved informed consent document is used and that it is legible, clear, and complete.
    - The informed consent discussion occurs in a location that provides privacy, and that the informed consent document and its elements will be reviewed with the prospective research participant.
    - The prospective research participant must be provided with ample time to read the informed consent document and to ask questions.
    - The research participant has sufficient opportunity to consider whether to participate in the study.
    - If the prospective research participant is unable to give written informed consent, the participant's LAR will be provided the same information.
    - The assent of the research participant should also be obtained, as required by the IRB-approved protocol, and in such cases, the research participant's wishes will be honored.
- Consenting Minors
    - If the research is conducted outside of the Commonwealth of Virginia, ensure that state and local laws are understood for the consent of minors and their requirements for the assent of minors. (See HRP-013: SOP: Lars, Children, and Guardians)
    - If the prospective research participant is considered to be a legal minor, obtain consent from one or both parents or the legal guardian. The IRB may determine that only one or both parents/guardian(s) must sign the informed consent document. If two parent signatures are required by the IRB of record and two parent signatures are unable to be obtained, documentation describing the reason is needed within the participant's study notes and/or consent form. The following policies outline when it is allowable to not obtain two parent signatures in studies that are approved as requiring two parent signatures: HRP-090 - SOP - Informed consent process for research, §46.408, §50.55
    - Develop an assent form to be used by minors for their verbal or written

assent for their participation in the study. Multiple versions of this document may be prepared for minor's age ranges (e.g., 7-10 yrs; 11-14 yrs; 15-17 yrs), each describing the risks and benefits in age-appropriate language. The IRB must approve every version. Follow the IRB-approved protocol for guidance on when the assent version needs to be updated due to age. Documentation is needed if the minor is not able to assent (ex. due to cognitive impairment)

- When a child participant who was enrolled in research with parental/legal guardian permission reaches the age of majority, investigators must seek and obtain legally effective informed consent for their ongoing participation. This requirement to re- consent the now-adult participant applies both to research that involves ongoing interactions or interventions as well as to research that continues to meet the regulatory definition of "human subjects research" (for example, it involves the continued analysis of specimens or data for which the subject's identity is readily identifiable).

D. Documentation of Initial Informed Consent
   - When obtaining consent by fax, mail, email, or electronic signature platforms, research teams should adhere to the process outlined within the IRB-approved protocol or seek amendment to the protocol prior to deviating from the IRB approved method(s) of obtaining informed consent. Deviations to the informed consent process must be reported to the IRB.
   - Consent documents may be emailed, mailed or faxed to potential participants prior to enrollment as per the IRB-approved plan. In the case of faxed or emailed consents, an original signed consent and HIPAA Authorization must be secured for records as soon as practicable.
   - Waiver of documentation of informed consent (e.g. consent is given verbally or by some other means instead of being signed) is a specific process which must be approved by the IRB under limited circumstances described within HRP-091: Written Documentation of Consent. The IRB cannot waive documentation of informed consent under 45 CFR 46.117(c)(1)(i or iii) for FDA-regulated research.

E. Persons Conducting the Informed Consent Discussion
   Individuals other than the investigator may obtain consent. However, they must have completed all the required research training (per VCU/VCUHS SOP CR-ST-230 General Research Staff Training & Essential Documents), be trained on the protocol (per VCU/VCUHS SOP CR-ST-240 Study-specific Staff Education & Training), and they must be delegated the task of consenting as documented on the study-specific delegation of authority log (per VCU/VCUHS SOP CR-CO-525 Delegation of Authority). It is the responsibility of the PI to oversee the consenting of the study participants, ensure that all individuals obtaining consent are delegated the authority and trained, and must monitor all individuals who obtain consent.

F. Authorization for Use/Disclosure of Protected Health Information
   - In addition to the IRB approved informed consent the PI or their designee will

explain and have the participant sign the Authorization for Use/Disclosure of Protected Health Information form.

- The original, signed informed consent and the "Authorization for Use/Disclosure of Protected Health Information" (if not combined with the informed consent document) should be retained on file in the participant's research record maintained by the PI or their designee. A copy should be placed in the participant's health system electronic medical record (scanned and uploaded). In the case of studies involving genetic information, the consent and all study-specific genetic results may NOT be placed in the health system electronic medical record. In these cases, the informed consent document and study-specific results for research involving genetic testing would only be recorded in the participant's research record.

G. Revisions to the Informed Consent Process or Document
   - The Informed Consent Form (ICF) cannot be modified or annotated and then presented to the participant without prior approval from the IRB.
   - When a consent is revised, and after approval by an IRB, a participant enrolled in a study must sign the revised consent to continue in the protocol if changes might relate to the participant's willingness to continue their participation in the study (21 CFR 50.25(b). The decision to re-consent participants on a research study may be made and communicated to the PI and key research personnel by the IRB via an approval letter.
   - Re-consenting of participants should take place as soon as possible post IRB approval. The re-consenting process should take place in person whenever possible. When in-person re-consenting is not an option, consent may be obtained by fax, mail, or email following the process as previously outlined. Initial contact for re-consent must be in-person conversation or by telephone and documented in the participants medical record or research record. Receipt of a signed consent by fax, email, or mail is acceptable documentation of re-consent. A follow-up phone call should be placed to the participant to ensure comprehension of the consent changes. All other applicable conditions for documentation of informed consent must be met.
   - If a participant is consented to participate in a protocol between the date a revised consent is approved by an IRB and receipt of the IRB letter approving the consent, the participant will be re-consented utilizing the revised consent. Re-consent of the participant should be conducted as previously outlined.

H. Considerations Regarding Vulnerability
   - If a potential participant is cognitively impaired and unable to provide informed consent, the LAR may provide informed consent on the patient's behalf if specified in the studies protocol. The IRB must approve the use of LAR in the study's specific protocol.
   - If an adult is unable to provide consent for themselves, for guidance on how to proceed refer to VCU IRB policy or IRB policy of the responsible IRB.
   - If it is determined that a potential participant is unable to read the informed

consent but is cognitively competent, the consent process should be conducted as follows:
    - The informed consent should be read to the participant by a member of the study team.
    - The participant should be provided ample time and opportunity to consider the information and to ask questions
    - The entire process of consent must be conducted in the presence of a witness
    - If able, the participant should affix a signature to or make an 'X' or "make their mark" on the consent
    - The witness is to sign and date the informed consent document.
    - Per standard procedure, the individual conducting the consent must document that the process took place and the participant voluntarily provided consent to participate in the study.
    - A progress note in the subject's case history in the research files should indicate the reason for the lack of a signature.
- If a subject previously determined to lack capability to consent regains capacity during the study, the investigator must obtain the consent of the individual for the remaining part of the study.
- Enrollment of non-English speaking participants should follow VCU IRB Policy referenced within this SOP, or the policy of the responsible IRB.
- For guidance on consenting requirements for other vulnerable populations, refer to VCU IRB Policy referenced within this SOP, or the policy of the responsible IRB.

5. REFERENCES

A. Code of Federal Regulations

- 21 CFR 50 – Protection of Human Subjects (entirety)
- 21 CFR 56.109 – IRB Review of Research
- 21 CFR 56.111 – Criteria for IRB Approval of Research
- 21 CFR 312.60 – General Responsibilities of Investigators
- 21 CFR 312.62– Investigator Recordkeeping and Record Retention
- 21 CFR 812.100 – General Responsibilities of Investigators
- 21 CFR 812.110(a) – Awaiting Approval
- 21 CFR 812.140(a)(3)(i) – Documents Evidencing Informed Consent
- 45 CFR 46 – Protection of Human Subjects

B. FDA

- Information Sheets for IRBs, Clinical Investigators, and Sponsors

C. Good Clinical Practice

- ICH Harmonised Guideline Guideline For Good Clinical Practice E6(R3)

- Section 2.4 - Communication with IRB/IEC
- Section 2.5 - Compliance with Protocol
- Section 2.8 - Informed Consent of Trial Subjects
- Glossary: Legally Acceptable Representative

D. VCU

- VCU/VCUHS Clinical Research Standard Operating Procedures (SOPs)
  - CR-AD-120 Clinical Research Management System
  - CR-ST-230 General Research Staff Training & Essential Documents
  - CR-ST-240 Study-specific Staff Education & Training
  - CR-CO-525 Delegation of Authority
- VCU HRPP Policies and Guidance
  - HRP-013: SOP: Lars, Children, and Guardians
  - HRP-090: Informed Consent Process for Research
  - HRP-091: Written Documentation of Consent

E. Office for Human Research Protections (OHRP), US Department of Health and Human Services

Guidance Document: Informed Consent, Legally Effective and Prospectively Obtained (OPRR Reports 93-3)

F. VCUHS Policies Related to Clinical Research

- Documentation - Entries in the Medical Record

Review/Revision History CR-RE-315

Version No.	Effective Date	Description
CR-RE-315.3a	03/14/2025	• Updated to ICH E6(R3)
CR-RE-315.3		• Formatting edits • Updated purpose verbiage to specify that this document expounds upon current IRB of record Policies • Clarified when PI signature is required for the ICF • Clarified when to obtain a new assent • Updated references to align with HRPP policies • Clarified HIPPA use • Clarified how/ when consent can be obtained • Updated preparing ICF for external IRB • Clarified consenting minors- documentation of the reason one parent can not sign is mandatory • Updated links

CR-RE-315.2a	07-01-2020	● Links updated
CR-RE-315.2	07-01-2020	● Biennial review performed ● Minor formatting edits ● Reference links added and updated
CR-RE-315.1	11-20-2017	● Original