CARILION CLINIC INSTITUTIONAL REVIEW BOARD
Standard Operating Guidelines

Title: 5.2: Informed Consent Process: COMPONENTS OF INFORMED CONSENT FORM, WAIVER OF CONSENT, WITNESS SIGNATURES, TELEPHONE CONSENT, PARENTAL PERMISSION, ASSENT PROCESS	
Original Date: April 2006	**Date of Last Revision:** 1-10, 8-23, 2-24, 12 - 25
Primary Sponsor: Human Research Protections Office	**Approved By:** Director of the Human Research Protections Office

Objective:

To describe the necessary requirements of a Carilion Clinic informed consent document and consent process, as outlined by Federal Regulations.

General Description:

All informed consent documents must include basic elements as required by 21 CFR 50.25(a) and 45 CFR 46.116. In addition, the Carilion Institutional Review Board (IRB) requires local additions to its consent forms.

Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject 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.

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 legally authorized representative's understanding of the reasons why one might or might not want to participate.

Procedure:

Elements of Informed Consent

Federal regulations prescribe some information as essential for understanding any research project. At a minimum, principal investigators must:

- Include a Concise Summary of the Study if the consent is greater than 4 pages.
- Include a statement that the study involves research
- Describe the purposes of the research
- Report the expected duration of the subject's participation
- Describe the procedures to be followed
- Identify any procedures or products that are experimental
- Describe any foreseeable risks or discomforts that the subject will bear
- Describe any benefits to the subject or to others that can reasonably be expected

- Disclose appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject
- Explain the extent to which confidentiality of any records that identify the subject will be maintained
- For research involving more than minimal risk, explain whether compensation or medical treatment will be available if the subject is injured and where to get further information about this
- Identify people who can answer questions about the research and the research subjects' rights, and whom to contact in the event of a research-related injury
- Explain that participation is voluntary; that refusal to participate will involve no penalty or decrease in benefits to which the subject is otherwise entitled; and that the subject may discontinue participation at any time without penalty or loss of benefits
- One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:

  (i) 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
  (ii) 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.

In addition to this essential information, other elements may be appropriate for the consent form, depending on the type of study and the level of risks to the subjects. The following elements may be necessary to address:

- Conditions under which the principal investigator can remove people from the study without regard to the subject's consent
- A statement that the research treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable
- Any additional costs that participating in the study might involve
- The consequences of a subject's decision to withdraw from the research and the procedures for orderly termination of participation
- A statement that significant new research findings during the course of the research could affect the subject's willingness to remain in the study will be provided to the subject
- The approximate number of people involved in the study
- 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
- A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions
- 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)

If the research is subject to FDA regulation, there must also be a statement that notes the possibility that the FDA may inspect study records (Research is FDA regulated if it involves the use of any drugs or medical devices other than the use of approved drugs and medical devices

in the course of medical practice, or if the data will be submitted to or held for inspection by the FDA.)

The Carilion IRB requires the following local elements be added to consent forms:

- Name of Principal Investigator, address, and contact info, phone number and/or email address at the top of the first page
- A statement describing the difference between the role of the physician as a researcher versus the role of physician as personal doctor, as appropriate
- A statement identifying the sponsor of the research
- A statement identifying the number of subjects to be enrolled locally
- A statement disclosing the financial interests of the principal investigator
- The pre-written paragraph regarding the IRB survey

These elements (both required and optional) are included in the Carilion IRB Consent template form(s). The researcher should include this standard text when drafting the informed consent as applicable to their study, and not duplicate items when preparing a consent form for IRB review.

Spelling, grammar, sentence structure, and page layout must be correct and promote ease of reading. Twelve-point font is required. An eighth grade reading level is recommended for all consent forms.

Obtaining Consent in Person

Consent for participation in research requires an informed consent process. This process involves an exchange of information and on-going communication that takes place between the investigator and the potential research participant. The consent process should be conducted in a private area. To obtain consent in person, the identity of the potential subject should be verified. The most current IRB-approved stamped version of the study specific consent form should be printed and used on the day of the visit. Provide a copy of the consent form to the potential participant to view during the consent process. If the approved consent process involves the use of a Legally Authorized Representative (LAR), then this person will be making the decision and providing consent. Whenever possible provide the consent form to the subject/LAR in advance of the consent discussion.

Explain the study to the potential subject verbally, providing all essential information, and allow the potential participant time to ask questions throughout the process. Each section of the consent document may be paraphrased. Expressly state that the research is voluntary and that the decision to participate or not participate will not affect the standard of care they may receive. Ask open ended questions and request the subject/LAR describe the study back to the person obtaining consent.

To achieve understanding, potential subjects should not be presented information all at once or only at the last minute. People need time to think about whether or not they want to participate. They may wish to discuss the decision with family, close friends, or religious advisors. They should not feel rushed or coerced. They need time, especially if the information is disturbing or particularly complex, to digest the information and come to terms with it.

Subjects should be approached when they are rested, lucid, and able to use eyeglasses or hearing devices if they need them.

Once comprehension is confirmed and all questions are answered, documentation of consent must take place unless the IRB approved consent process does not require this step. Ask the subject/LAR to print their name, sign their name, and print the date that the consent is signed in the appropriate area. The person obtaining consent should verify that the required information has been entered by the subject/LAR and then print their name, sign their name, and print the date that the information was verified. The person obtaining consent should sign the form at the same time as the person consenting. All signatures on the consent form should be obtained on the same date prior to the conduct of research. Provide a copy of the signed and dated consent document to the subject/LAR. This may be accomplished either by making a photocopy or by having the above individuals sign and date two copies of the consent document. As outlined in the IRB Approved research plan, a note describing the consent process should be documented and a copy of the signed consent stored in a confidential manner.

Any new information that arises during the course of the study that may have an impact on the details of their participation or their decision about whether or not to continue participation in the study should be provided to participants. The IRB will determine the need for subjects to be re-consented when there are modifications and how that is to occur. The IRB approval letter will include instructions regarding the re-consent process.

Electronic Signature Consent Process

Please see HRP 804: Electronic Informed Consent.

Obtaining Consent Using the Telephone

Obtaining oral consent by phone from a subject or legally authorized representative to take part in research does not satisfy the requirement of documentation of informed consent as outlined in 21 CFR 50.27 (a) 45 CFR 46 117 (a). Unless the IRB has granted a waiver of documentation of informed consent, obtaining oral consent over the phone is not permitted. However, it is permissible to send the informed consent document to the subject/LAR prior to the discussion by fax, mail, secure email, or provide at the in-person visit, and conduct the consent discussion by telephone when the subject/LAR can read the consent as it is discussed. If the subject/LAR agrees, they must sign/date the consent and return the signed document to the investigator by fax, mail, in-person, or secure email. If secure email is used, the subject must have the ability to print the consent form, sign the consent form, and either scan the original signed document or return it via one of the other methods. The consent process must be described in the approved IRB application. There should be a detailed summary of the informed consent process documented in the research record with a statement regarding the differences in the dates of the signatures of the participant and the person obtaining consent. A copy of the completed consent should be provided to the participant.

Witness Signatures

There are specific situations where federal regulations require the use of a signature of a witness.

For subjects who understand English but cannot read, the IRB requires an impartial witness to be present during the entire informed consent discussion and sign and date the consent form. This practice is recommended by the International Conference on Harmonisation (ICH), a group

that sets standards on Good Clinical Practice in research. By signing the consent form, the witness attests that the subject's informed consent was freely given. The IRB considers an impartial witness to be anyone not connected with the study team. This can include relatives of the subject or employees of the institution not engaged in the conduct of the research. The IRB consent template contains a signature box for an impartial witness for subjects who understand English but cannot read.

Subjects who can understand spoken English but are physically unable to talk or write can be enrolled in a study if 1) they retain the ability to understand the concepts of the study and evaluate the risks and benefits of being in the study when it is explained verbally and 2) are able to indicate approval or disapproval to be in the study. In these cases, the consent form should document the method used to communicate with the prospective subject and the specific means by which the prospective subject communicated agreement to be in the study. An impartial witness should be present during the entire consent process and sign and date the consent document.

The sponsor of a study may have its own requirements for a signature of a witness. It is important for the principal investigator to understand the intent of the signature of a witness if the sponsor requires one. For instance, the sponsor may not allow the person obtaining consent to also serve as a witness to the signature. Also, the sponsor may want the witness to attest that the witness observed the entire consent process, not just the subject's signature. In these cases, the investigator should use a separate signature box with appropriate language explaining the purpose of the witness.

There are situations that require a witness signature when a subject does not understand English. For further information refer to IRB SOG 5.5.

Consenting Students or Employees of Carilion Clinic

The standard consent processes should be used to obtain consent from students and/or employees. Whenever possible, students and/or employees should not be consented by or approached by a person who holds an authoritative role over the potential subject. Students and/or employees must be assured that their relationship with the researchers and their grade, standing, employment, status, etc. are not dependent on and will not be otherwise affected by their decision to participate in a study and that participation is voluntary.

Parental Permission and Assent for Children

Written parental permission is required for studies involving children. If the research involves greater than minimal risk, signatures from both parents are required unless the second signature is not reasonably available. A single signature is sufficient if only one parent has legal responsibility for the care and custody of the child or if one parent is deceased, unknown, or incompetent. Parental permission is typically documented in a form similar to a subject consent form, inviting the parents' child to participate.

The child's agreement is documented with an "assent form," a child-friendly document that outlines the essential information about the research. All children 7 years through 17 years old should be given an opportunity to assent, since most children 7-years-old have the cognitive and emotional maturity to understand a research project and to decide whether they want to participate in it. It is important to note that failure to object to participate as a research subject cannot be construed as assent.

There are times when the IRB may determine that a waiver of assent is appropriate. If the capability of some or all of the children is so limited that they cannot reasonably be consulted, a waiver of assent may be granted. If the intervention or procedure involved in the research holds out a prospect of direct benefit to the children and is only available in the context of the research, the assent of the child may also be waived.

Some children under the age of 7 may also be capable of granting and withholding assent, and the IRB asks researchers to be sensitive to the needs of these children on an individual basis. Researchers should try to draft a form that is age-appropriate and study-specific, taking into account the typical child's experience and level of understanding, and composing a document that treats the child respectfully and conveys the essential information about the study.

In situations where an independent witness may not be available, a patient information document (i.e., "consent" form), written in language appropriate to the subject's school level and signed by the minor and the Principal Investigator/Delegate, may be used instead of the assent certification. This form must be reviewed and approved by the IRB before being used.

Below are the assessments from 21 CFR 50.50 through 21 CFR 50.55 and 45 CFR 46.404 through 45 CFR 46.407 to assist in determining what level of risk, and, therefore, what type of parental permission/assent is necessary:

- **No Greater Than Minimal Risk --** Research that presents no greater than minimal risk [defined as the probability that magnitude of harm or discomfort are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological tests] requires the assent of the child and permission of a parent/guardian.
- **Greater Than Minimal Risk But Presenting The Prospect Of Direct Benefit --** This type of research may be performed if 1) the anticipated benefit justifies the risk and 2) the anticipated benefit is at least as favorable as that of alternative approaches and requires the assent of the child and permission of a parent/guardian.
- **Greater Than Minimal Risk And No Prospect Of Direct Benefit --** This type of research may be performed if 1) there is only a minor increase over minimal risk, 2) the research is likely to yield generalizable knowledge about the child's disorder or condition that is of vital importance for the understanding or amelioration of the disorder or condition, and 3) the intervention or procedure presents experiences to the child that are reasonably commensurate with those in the child's actual or expected medical, dental, psychological, social, or educational situations and requires the assent of the child and permission of both parents/guardian(s).
- **Any Other Research --** Any research that does not fit into the above categories may be performed if 1) the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children or 2) the Commissioner of Food and Drugs, after consultation with a panel of experts in pertinent disciplines (e.g., science, medicine, education, ethics, law) and following publication in the Federal Register and public comment and requires the assent of the child and permission of both parents/guardian(s).

Under very special circumstances the IRB may waive the requirement for parental consent. Waivers can only be granted for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (e.g. neglected or abused children), if an appropriate mechanism for protecting the child is provided, and if the waiver is not inconsistent with federal, state, or local law.

Once children meet the Age of Majority, defined by Virginia state law as 18, they should be presented with the option to continue participation or withdraw from the study. This may be done with an IRB Approved, modified consent document or by using the full study consent document. This discussion should also be documented in the research record or medical record.

Biospecimen Repository Consent

When biospecimens will be stored for research purposes, there are several important points to include in the consent:

- What tissue samples will be collected, and how they will be collected
- What type of research will, or may, be conducted using the tissue sample, including whether genetic analysis will be performed
- Potential risks of disclosure of personal information
- The potential benefits, including whether any results will be provided to the subject
- What types of processes are in place to protect confidentiality and privacy
- With whom the sample may be shared, if known
- Whether the sample will eventually be anonymized, and if so, how and when
- Whether there will be any commercial applications of the research
- Whether the subject can have the sample destroyed if he or she decides to withdraw from the research
- How long the samples will be kept

For further guidance see IRB SOG 3.7 and the Consent To Take Part In A Biorepository Research Study template.

Waiver of Informed Consent

The IRB may approve a consent procedure that does not include, or that alters some or all of the elements of informed consent, or waive the requirements to obtain informed consent in accordance with 45 CFR 46.116 and 21 CFR 50.22, provided the IRB finds and documents that:

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

For FDA regulated studies that do not meet the above requirements, in accordance with 21 CFR 50.23, obtaining informed consent is required unless both the investigator and a physician who is not otherwise participating in the investigation certify in writing all of the following:

- The human subject is confronted by a life-threatening situation necessitating the use of the test article
- Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from the subject
- Time is not sufficient to obtain consent from the subject's legal representative

- No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the life of the subject

If the investigator decides immediate use of the test article is required to preserve the life of the subject, and time is not sufficient to obtain the independent determination as stated above, the determination of the investigator shall be made. Within five working days after use of the article, the determination must be reviewed and evaluated in writing by a physician who is not participating in the clinical investigation. Additionally, this documentation shall be submitted to the IRB within five working days after the use of the test article. (See IRB SOGs for Emergency and Treatment Use of Investigational Drug and Significant/Non-Significant Risk Devices, Humanitarian Use Devices, Emergency Use, Compassionate Use for more information.)

Nothing in this guidance is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state or local law.

Waiver of Documentation of Informed Consent

For research not falling under the jurisdiction of the Food and Drug Administration (FDA), the IRB may waive the requirements for the investigator to obtain a signed consent form for some or all subjects in accordance with 45 CFR 46.117 if it finds either:

- That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or
- That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context.
- If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.

For FDA regulated studies, in accordance with 21 CFR 56.109(c), the requirement for documentation of informed consent may be waived if the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context, or if the conditions for emergency research are met.

In cases where the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.