11.5 ADDITIONAL REQUIREMENTS DOCUMENTATION OF THE INFORMED CONSENT PROCESS

Documentation of the consent process should include the following:

- Confirmation that informed consent was obtained prior to a participant's participation in the trial (i.e., prior to any study related procedures).
- l, the written consent document should be signed and personally dated by the participant or by the participant's legally acceptable representative.
    - Prior to a participant's participation in the trial, the written consent document should be signed and personally dated by the person who conducted the informed consent discussion.
    - If a participant is unable to read or if a legally acceptable representative is unable to read, an impartial witness should be present during the entire informed consent discussion.
        - e the written consent document and any other written information to be provided to participants is read and explained to the participant or the participant's legally acceptable representative, and after the participant or the participant's legally acceptable representative has orally consented to the participant's participation in the trial and, if capable of doing so, has signed and personally dated the consent document, the witness should sign and personally date the consent document.
        - By signing the consent document, the witness attests that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the participant or the participant's legally acceptable representative, and that consent was freely given by the participant or the participant's legally acceptable representative.
        - Prior to participation in the trial, the participant or the participant's legally acceptable representative should receive a copy of the signed and dated written consent document and any other written information provided to the participants.

A. Waivers of Consent Requirements

At 45 CFR 46.116(e) the regulations identify when IRBs may waive or approve an alteration of informed consent/assent. The investigator may request this waiver in the research plan for research that meets four specified criteria:

i. The research involves no more than minimal risk to the subjects (this includes the minimal risk studies as defined in 21 CFR 50.3(k) or 56.102(i))

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

iii. 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;

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

v. Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.

If an investigator feels that his or her research qualifies for an alteration of the required elements of informed consent or a waiver of the requirement to obtain informed consent, he or she must indicate this as part of the IRB application. An investigator must provide a protocol-specific justification that documents how the research meets all of the above-referenced criteria. The IRB will evaluate the investigator's explanation against the relevant federal regulations and will decide to support or deny the investigator's request for a waiver or alteration. When considering the issue of "practicability," the IRB must arrive at the determination that a requirement for informed consent would mean that the research would not be practicably carried out without the waiver.

B. Waiver of the Requirement for Documented (Signed) Informed Consent

Federal regulations generally require not only that informed consent be obtained from subjects of research, but also, that consent be documented via a signature on a study consent form.

However, federal regulations include a provision that allows the IRB to approve an informed consent process that does not require "documentation." In such instances, the IRB may determine that subjects' informed consent can be obtained without collecting signatures on a written consent document. The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects in research if it finds that:

i. For non-FDA regulated research, the only record linking the subject and the research would be the consent document, and the principal risk of study participation would be potential harm resulting from a breach of confidentiality. In such a case, each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or

ii. The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context; or

iii. 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.

When the requirement for the investigator to obtain a signed consent form is waived by the IRB under category ii above, ORIC routinely requires that the investigator provide subjects with written information about the research – usually, an information sheet containing the basic elements of informed consent. If the waiver is obtained under category (i) above, an informed consent document is required to be prepared by the investigator, as each subject must be presented with the decision to sign the consent form.

When a waiver is granted, investigators are still responsible for fulfilling all the basic principles of informed consent (above). Investigators who receive this waiver are still required to conduct a comprehensive oral consent process to obtain voluntary participation of subjects.

C. Waivers of Informed Consent when working with a state or local public benefit or service program

To obtain a waiver or alteration of informed consent under this provision, 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 alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs; and the research could not practicably be carried out without the waiver or alteration.

Note that only public benefit or service program research activities that are under state or local authority meet this criterion; similar research conducted under federal authority would not qualify here and is treated elsewhere in the regulations. Research conducted by or subject to the approval of only a private entity also would not qualify for this exception to the informed consent requirement.

D. Waiver of Parental Permission

In accordance with the federal regulations (45 CFR 46.408(c)), the IRB may waive the requirement for parental permission if it determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children) provided that an appropriate mechanism is in place to protect the children, provided that the research is not FDA-regulated, and provided that the waiver is not inconsistent with federal, state, or local law, or other Institutional policy. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

If an investigator feels that his or her research qualifies for a waiver of parental permission, he or she must indicate this as part of the IRB application. An investigator must provide a protocol-specific justification that documents how the research meets the above-referenced criteria. The IRB will evaluate the investigator's explanation against the relevant federal regulations and will decide to support or deny the investigator's request for a waiver.

E. Waiver of Child Assent

In accordance with the federal regulations, the IRB may waive the requirement for assent under the following two circumstances (45 CFR 46.408(a) and 21 CFR 50.55(c)):

- The capability of some or all of the children is so limited that they cannot reasonably be consulted; or
- The interventions or procedures involved in the research hold out a prospect of direct benefit that is important to the health or well-being of the children and is available *only* in the context of the research.

Waivers of assent must be obtained prior to conducting any protocol-related procedures. If a waiver of assent is subsequently needed after initial IRB approval for an individual subject,

the IRB Chair, Vice Chair or designee may grant a waiver if the above criteria are met. The request for the waiver is to be emailed to the IRB with the following documentation: study title, IRB number, and name of PI; the reason the child is not capable of assenting (e.g., cognitive delay due to disease); and confirmation that parental permission will be/has been obtained. An email documenting the waiver of assent will be returned to the PI and saved in the study file in Cayuse IRB. If the cognitive capability of the child to assent is temporary, and changes during study participation in such that he/she is able to provide assent (verbal or written) later, assent from the child should be obtained at that time.

F. Waiver or Alteration of Written HIPAA Authorization

The Privacy Rule contains criteria for waiver or alterations of HIPAA Authorizations by an IRB or another review body called a Privacy Board. The IRB serves as the Institution's Privacy Board for Research. The IRB may waive or approve and alteration of HIPAA Authorization provided that the research meets the criteria outlined in 45 CFR 164.512(i)(2)(ii):

i. The use or disclosure of protected health information (PHI) involves no more than a minimal risk to the privacy of individuals, based on, at least, the presence of the following elements:

    1. an adequate plan to protect the identifiers from improper use and disclosure;
    2. an adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and
    3. adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of protected health information would be permitted by this subpart;

ii. The research could not practicably be conducted without the waiver or alteration; and

iii. The research could not practicably be conducted without access to and use of the protected health information.

The IRB may also issue a *partial* waiver of HIPAA Authorization (45 CFR164.512(i)(1)(i)). A partial waiver of the Authorization requirements may be requested, for instance, to allow a researcher to obtain PHI as necessary to recruit individuals into a study.

A waiver or alteration of written HIPAA Authorization may not apply if the investigator is releasing any of the following sensitive identifiable information outside the covered entity:

- HIV/AIDS related health information and/or records (a participant 12 or over must authorize this release)

- Behavioral or mental health information and/or records (release must be witnessed and the participant 12 or over must authorize this release)
- Information about sexually transmitted disease (a participant 12 or over must authorize this release)
- Pregnancy (a participant 12 or over must authorize this release)
- Birth control (a participant 12 or over must authorize this release)
- Drug/alcohol diagnosis, treatment, and/or referral information (a participant 12 or over must authorize this release)
- Genetic testing information and/or records
- Information about sexual assault/abuse
- Information about child abuse and neglect
- Domestic abuse of an adult with a disability

For more information, refer to the Administrative Policy and Procedure Manual "Release of Information" (only accessible via The Portal).

G. Waiver of Informed Consent for Planned Research Conducted in Emergency Settings

There are some types of prospective research that involve emergency medical interventions in which informed consent cannot be obtained. Under 21 CFR 40.24, the IRB may approve an exception to the informed consent requirement for human subjects research if the study involves the use of an intervention (drug, biologic or device regulated by the FDA) to treat a life-threatening condition for which available treatments are unproven or unsatisfactory and where it is not possible to obtain informed consent. The IRB must find and document that the study meets the following requirements:

- The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.
- Obtaining informed consent is not feasible because:
    - The subjects will not be able to give their informed consent as a result of their medical condition;
    - The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and
    - There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.
- Participation in the research holds out the prospect of direct benefit to the subjects because:
    - Subjects are facing a life-threatening situation that necessitates intervention;

- Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and
- Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

- The clinical investigation could not practicably be carried out without the waiver.
- The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent.
- The investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.
- There are informed consent procedures and an informed consent document consistent with 21 CFR 50.25. These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible.
- Additional protections of the rights and welfare of the subjects will be provided, including, at least:
  - Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn;
  - Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;
  - Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results;
  - Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and
  - If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member who is not a legally authorized representative and asking whether he or she objects to the subject's participation in the clinical

investigation. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

This clinical investigation must be carried out under a separate IND or IDE, and the application to the FDA must clearly identify that the protocol includes subjects who are unable to consent.

If the IRB determines that the investigation cannot be approved due to the above criteria not being met or due to an ethical concern with the study, the decision will be documented and returned in writing to the investigator.

For research not subject to the FDA regulations, the Secretary of DHHS issued a notice in the Federal Register that waived the general requirements for waiver under §46.101(i). Consistent with this waiver, the IRB may waive the requirement for informed consent for planned emergency research provided the IRB reviews and approves both the activity and a waiver of informed consent and must:

(i) find and document that the research is not subject to 21 CFR 50 regulations, and

(ii) find, document, and report to the OHRP that the conditions listed above have been met relative to the research.

Because of special regulatory limitations relating to research involving fetuses, pregnant women, and human in vitro fertilization, and research involving prisoners, this waiver is inapplicable to these categories of research.