Chapter 11

Required Elements of Informed Consent

Investigators must obtain the legally effective, prospective informed consent of subjects before they can be included in research. Research investigators are responsible for obtaining and documenting informed consent in accordance with Federal regulations (45 CFR 46.116 and 46.117 ad 21 CFR 50.25 and 50.27) and Institutional specific policies.

Prospective participants must be given sufficient information about the research and its risks and potential benefits to reach an informed decision and clearly convey that participation is voluntary.

Effective informed consent includes both a clearly presented informed consent document and a structured process of presenting this information to the potential participant. DHHS regulations at 45 CFR 46.116(b), the Common Rule, and FDA regulations at 21 CFR 50,25(a) mandate the inclusion of nine basic informed consent elements. Nine additional elements may be required, depending on the nature of the research (45 CFR 46.116(c) and 21 CFR 50,25(b)).

The elements of informed consent as outlined in these regulations shall not preempt any other Federal, State, or local regulations which require additional information to be disclosed for informed consent to be legally effective. Also, nothing in the regulations is intended to limit the authority of a physician to provide emergency care to the extent the physician is permitted to do so under applicable Federal, State, or local law. Such emergency care may not be identified as research, except as required by FDA reporting requirements.

Prisma Health Informed Consent Templates are available in IRBNet under the Forms and Templates tab. The templates provide specific guidance on wording and order of the document information.

1. KEY INFORMATION (45 CFR 46.116(a)(5-6)

A. Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective participant 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.
B. Informed consent must present information in sufficient detail related 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 participant's or legally authorized representative's understanding of the reasons why one might or might not want to participate.
C. No informed consent may include any exculpatory language through which the participant or legally authorized representative is made to waive or appear to waive any of the participant's legal rights, or releases or language that appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.

2. BASIC ELEMENTS OF INFORMED CONSENT (45 CFR 46.116(b)(1-9)

A. Research Statement: Required Element #1

Informed consent information **must** specifically include **each** of the following**:**

i. A statement that the study involves research,
ii. An explanation of the purposes of the research,
iii. An explanation of the expected duration of subjects' participation,
iv. A description of what procedures will be followed, and
v. Identification of any procedures that are experimental.

B. Reasonably Foreseeable Risks or Discomforts: Required Element #2

The Informed Consent document must describe any reasonably foreseeable risks or discomforts associated with the research. All risks listed or described in the research protocol must be referenced in the informed consent document.

C. Reasonable Expected Benefits: Required Element #3

The Informed Consent document must describe any benefits to subjects or to others which may reasonably be expected from the research. However, benefits must not be overstated to create an undue influence on subjects.

D. Appropriate Alternatives: Required Element #4

The Informed Consent document must include a disclosure of any appropriate alternative procedures or courses of treatment that may be advantageous to the subject. Sufficient detail must be provided so that the subject can understand and appreciate the nature of any alternatives.

E. Extent of Confidentiality: Required Element #5

The Informed Consent document must describe the extent to which confidentiality or record identifying the subject will be maintained. Consent information should describe any procedures that the research team will use to protect subjects' private information or records.

Prisma Health HRPP requires that HIPAA authorization language be included in the context of the consent form when appropriate. When not included, as in some externally reviewed documents, a local HIPAA authorization document will be presented to the participant for review and signature.

Federal officials have the right to inspect research records, including consent forms and individual medical records, to ascertain compliance with the rules and standards of their programs. The FDA requires that information regarding this authority be included in the consent information for all research that it regulates. This required language is included in the Prisma Health template language.

F. Compensation or Treatment for Injury: Required Element #6

Informed consent information for research involving more than minimal risk must include explanation regarding:

- Whether any compensation is available if injury occurs,
- Whether any medical treatments are available if injury occurs and whether the participant is responsible for such medical treatment, and
- A description of any such compensation or treatments or information on where more information about them is available.

Prisma Health provides approved local context language for consent required language, available in the consent template documents within the Forms and Templates library in IRBNet.

G. Contact Information: Required Element #7

Informed Consent information must include details, including phone numbers and whom to contact for these specific situations:

- **Answers to questions about the research**. The principal investigator and other members of the research team are appropriate contacts for this information.
- **Answers to questions about subject rights**. The Office of Human Research Protection is an appropriate contact for information regarding subjects' rights.

- **Information in the event of a research-related injury.** The Principal Investigator should be the primary contact for reporting injuries. The Office of Human Research Protection or Legal Counsel may also be contacted if necessary for information and support in these situations.

H. Voluntary Participation Statement: Required Element #8

Informed consent information must contain clear statements of the following**:**

a) Participation in the research is "voluntary",
b) Refusal to participate will involve "no penalty or loss of benefits to which the subject is otherwise entitled",
c) The subject may discontinue participation at any time "without penalty or loss of benefits to which the subject is otherwise entitled", and
d) It is particularly important for subjects and prospective subjects to understand and have complete confidence that declining to participate in research will not jeopardize their care.

I. Collection of Identifiable Private Information or Biospecimens State: Required Element #9

One of the following statements must be included:

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 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

J. Additional Elements Where Appropriate (45 CFR 46.116(c)(1-9)

Where appropriate, the regulations require that one or more of the following elements be included in the informed consent document:

a. Unforeseeable Risks to Subjects

Some research involves particular procedures or interventions that may result in unforeseeable risks to subjects, to embryo, or the fetus (if a subject should become pregnant). For research of such a nature, the informed consent information must warn subject that there may be risks that are not known or not foreseeable.

b. Investigator-Initiated Termination of Participation

There may be instances that would require an investigator to terminate the participation of subject(s) e.g., subject non-compliance with the research requirements, subject not benefiting from research, or disease progressions. The informed consent information should specify these circumstances.

c. Additional Costs

If subjects must bear any additional costs, these must be disclosed in the informed consent document.

d. Early Withdrawal/Procedures for Termination

Subjects have the right to withdraw from the research. However, some studies may involve medications or procedures that would be dangerous for subjects to discontinue abruptly. For studies of this nature, the informed consent document must provide subjects with knowledge of the consequences affecting a decision to withdraw. In addition, if there are procedures regarding the safe withdrawal from the research, these must also be described.

e. Significant New Findings

Subjects will be informed of any new knowledge or findings about the medication or test article and/or condition under study that may affect the risks or benefits to subjects or subjects' willingness to continue in the research.

f. Approximate numbers of Subjects

For certain types of research, the informed consent document should disclose the approximate number of subjects to be enrolled.

g. Biospecimens and Commercial Profit

The Informed Consent document should contain 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 the commercial profit.

h. Disclosure of Research Results

The informed consent document should contain a statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions.

i. Whole Genome Sequencing

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

E. Broad Consent 45 CFR 46.116(d)(1-7)

Broad consent for storage maintenance, and secondary research use of identifiable private information or identifiable biospecimens collected for research studies other than the proposed research or non-research purpose is permitted as an alternative to the informed consent requirements as previously described.

NOTE: Prisma Health will not utilize "Regulatory Broad Consent" and research reviewed on, or after January 21,2019 will not be reviewed by the Prisma Health IRB as exempt under categories 7 or 8.

F. Requirement for Authorized Personnel to Obtain Consent

Informed consent may only be obtained by personnel authorized to do so by the IRB. The individual who conducts the informed consent conversation must be knowledgeable about the study and its requirements and able to answer questions that potential participants or their representatives may have.

Any individual that will be consenting study participants must have completed required and maintained current human subjects protection training. Individuals obtaining consent for any procedure must be credentialed to perform that procedure or treatment. The Prisma Health policies listed provide further detail on this process.

G. Waiver or Alteration of Informed Consent Requirements

DHHS regulations at 45 CFR 46.116(e)(3)(i) and the Common Rule permit an IRB to approve a consent procedure that eliminates or alters the required elements of informed consent, or to waive the requirement to obtain informed consent or to waive the requirement for consent in two specific situations. These situations are as follows:

State or Local Public Benefit Programs

DHHS regulations as sited above and the Common Rule permit the IRB to approve a consent procedure or waive consent if the IRB finds that the activity constitutes a research or demonstration project that 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:

- Public benefit or service programs,
- Procedures for obtaining benefits or services under those programs,
- Possible changes in or alterations to those programs or procedures,
- 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 of alteration of consent.***

These findings and their justifications will be clearly documented in IRB minutes when the IRB exercises this waiver provision. This waiver provision is not applicable to research governed by FDA regulations, and the IRB will not approve such alterations or waivers for FDA regulated research.

Minimal Risk Research

DHHS regulations at 45 CFR 46.116(e)(3)(i) and the Common Rule permit an IRB to approve a consent procedure that eliminates or alters the required elements of informed consent, or to waive the requirement to obtain informed consent, or to waive the requirement for consent. To approve such a waiver or alterations, the IRB must document that:

- The research involves no more than minimal risk to subjects,
- The waiver or alteration will not adversely affect the rights and welfare of the subject,
- 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, and
- Whenever appropriate, the subject will be provided with additional pertinent information after participation.

These findings and justifications will be clearly documented in IRB approval letter when the IRB exercises this waiver provision. This waiver provision is not applicable to research governed by FDA regulations, and the IRB will not approve such alterations or waivers for FDA-regulated research.

H. Research Involving Deception

Deception research involves social science research in which the subject is not told or is misled about the true purpose of the research. These studies may, for example, include studies of group processes or contextual influences. The IRB reviewing research involving incomplete disclosure or outright deception must apply logical consideration, sensitivity to the protection of the human subjects that will be engaged in the process, the integrity of the presented research plan and the value of the information and general objectives of the research, particularly to the group of subjects that will be involved.

The IRB must be satisfied that the deception is necessary and that, when appropriate, the subjects will be debriefed. The IRB should also make sure that the proposed subject population is suitable and that the debriefing activity itself would not present an unreasonable risk of harm without a countervailing benefit.

Deception can only be permitted where the IRB documents that waiver of the usual informed consent requirements is justified under the criteria present at 45 CFR 46.116(f).

The IRB determination to approve the use of deception considers and documents each criterion and how the proposed research meets those criteria.

Note that the regulations make no provisions for the use of deception in research that poses greater than minimal risks to subjects.

I. Waiver of Documentation of Consent

DHHS regulations at 45 CFR 46.117(c) and the Common Rule permit an IRB to waive the requirement to obtain written documentation of informed consent. To approve such a waiver, the IRB must find and document one or more of the following conditions:

- The only record linking the subject and the research would be the consent document and the principal risk would be the potential harm resulting from a breach of confidentiality. In this case, each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern.

- The research presents no more than minimal risk of harm to subjects and involved procedures or activities for which written consent is not normally required outside of the research context. In cases where the documentation is waived, the IRB may require the Principal Investigator to provide subjects with a written statement regarding the research. This waiver provision is applicable to research governed by the FDA regulations as set forth at 21 CFR 5.109.

- If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, and the research presents no more than minimal risk of harm to subjects, provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.

The IRB must also find, in addition to determining one of the above conditions, and document that the waiver or alteration will not adversely affect the rights and welfare of the participants, and whenever appropriate:

- the participants will be provided with addition pertinent information after participation, and

- the IRB must review a review a written description of the information to be orally provided to participants and any written information sheet or letter which includes all elements of consent, which will be provided to participants.

These findings and their justification will be clearly documented in IRB review records or minutes when the IRB approves the waiver provision.

J. Participation of Non-English Speakers in Research

a) Federal regulations at 45 CFR46.116(a)(3) and 21 CFR 50.20 require that informed consent be obtained in language that is understandable to the subject or the subject's legally authorized representative.
b) These regulations also require that informed consent discussion must include a certified interpreter when the prospective subject does not understand the language of the person obtaining the consent.
c) Investigators may document informed consent in either of two ways:
    i. A full-length informed consent document written in a language understandable to the subject, or
    ii. A "short-form" consent document in the language of the subject that states the general elements of informed consent.

NOTE: Any translated consent document must be certified as translated by an appropriate translation service. Prisma Health Language is available for any translation or interpreter services required for facilitation of these processes.
https://connect.prismahealth.org/team-member-resources/tools-and-resources/interpreter-request-form

d) If a "short form" is utilized to document informed consent, the subject most be provided with:
    i. The full-length consent form document in English, and
    ii. An interpreter who will take part in the oral informed consent discussion to ensure the subject's understanding and who may also serve as the witness.
e) In addition:
    i. The "short form" consent document written in the subject's language must be signed by the subject, or the subject's legally authorized representative and the interpreter.
    ii. The full-length English consent document must be signed by the interpreter and the person obtaining the consent.
    iii. The subject must be given copies of both the "short-form" consent document and the English consent document.
    iv. Non-English-speaking subjects should not be excluded from research without a sound scientific or ethical reason. The IRB should consider the requirement for equitable subject selection. Elements that should be considered in the determination should consider the purposes of the research and the setting in which the research will be conducted.
    v. The IRB should also consider and be particularly cognizant of the special issues related to research involving vulnerable populations such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons (45 CFR 46.116(a)(3) and 21 CFR 56.111(a)(s)).

f) Considerations when it might be permissible for a research protocol to exclude non-English speaking subjects include:
    i. A sound scientific reason for exclusion of non-English speaking subjects might be that the inclusion of this population would not promote the aims of the study,
    ii. A sound ethical reason for exclusion of non-English speaking people might be to protect them from harm or exploitation,
    iii. There are insufficient resources to include non-English speaking people,
    iv. Inclusion of non-English speaking people would not reflect the distribution of the population in the study area.

Investigators are advised to carefully consider the ethical/legal ramifications and risk/benefit of enrolling subjects when a language barrier exists.