INFORMED CONSENT AND ITS DOCUMENTATION

8/4/2021

For every IRB approved protocol, the investigator must either use an IRB approved consent process to obtain prospective informed consent, or receive IRB approval for a waiver of consent. In some situations, the investigator may wish to request IRB approval for waiver of documentation of consent. Each of these consent provisions is discussed below.

It is also the policy of the DUHS IRB that a person may enter a research study involving the use or disclosure of individually identifiable health information (protected health information [PHI]) only with prior IRB approval of a valid HIPAA authorization document incorporated into the consent document, or with prior IRB approval of a waiver or alteration of authorization.

The consent and authorization document will be referred to below as the *consent document*.

Informed Consent

When required by the DUHS IRB, legally effective informed consent must be obtained for every subject on every research study according to 45 CFR 46.116 and/or 21 CFR 50.25. “Legally effective” means that the individual providing consent or permission would (1) have enough information to make a decision, (2) understand the consequences of a decision, (3) be able to make a decision, and (4) be able to communicate a decision. For example, legally effective informed consent to participate in a research study occurs when the potential research subject understands the difference between standard treatment and research activities, understands the risks and benefits of participating in a specific research study, appreciates the consequences of participating or not participating, and is able to make and communicate a decision about participation or non-participation.

This consent must be obtained from the adult subject unless he/she is incapable of informed decision making, in which case the investigator must describe the process used for evaluating the person’s capability to provide consent, and the process for identifying and obtaining consent from the subject’s legally authorized representative (LAR) (45 CFR 46.102(i) and/or 21 CFR 50.3) in accord with North Carolina law. Only with prior IRB approval may an investigator ask the subject’s legally authorized representative to act on behalf of the subject regarding consent for study participation. If the subject is a minor, the investigator must describe how permission for the child’s study participation will be obtained from the child’s parent(s)/guardian, and if appropriate, how assent will be obtained from the child (45 CFR 46.402 and 45 CFR 46.404-8).

Use of the Standard Consent Document

Legally effective informed consent must be sought from each potential subject or the subject's legally authorized representative, in accordance with, and to the extent required by, 45 CFR 46.116 and 21 CFR 50.25. Unless otherwise approved by the DUHS IRB, the consent document must include both the basic elements of informed consent, and as appropriate, additional elements of informed consent.

Additionally, the consent document begins with a concise and focused presentation ("concise summary") of the key information most likely to assist a prospective subject, parent, or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. Please note that instructions for writing the ***concise summary*** are found in the box at the top of the DUHS IRB Sample Consent Template, located on the IRB web site. Examples of a concise summary, written by the IRB, are also posted on the IRB web site and are meant to serve as a guide to researchers:
https://irb.duhs.duke.edu/forms/duhs-sample-consent

The basic elements of informed consent are:

- A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental; a description of any reasonably foreseeable risks or discomforts to the subject;
- A description of any benefits to the subject or to others which may reasonably be expected from the research;
- A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
- A statement describing the extent, if any, to which confidentiality of records identifying the subject must be maintained; for FDA-regulated studies, the possibility that the Food and Drug Administration may inspect the records must be included;
- For research involving more than minimal risk, an explanation as to the availability of medical treatment in the case of research-related injury, including who will pay for the treatment and whether other financial compensation is available;
- An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject;
- A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled;
- An explanation of whom to contact to voice concerns or complaints about the research;
- Contact information for the IRB to obtain answers to questions about the research; to voice concerns or complaints about the research; to obtain answers to questions about their rights as a research participant; in the event the research staff could not be reached; and in the event the subject wishes to talk to someone other than the research staff.
- 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.

Additional elements of informed consent to be applied, as appropriate:

- A statement that the particular treatment or procedure may involve risks to the subject that are currently unforeseeable. (Include this when the research involves an unapproved drug, device or biologic or procedure for which the risks to subjects are not well known.)
- A statement that if the subject is or becomes pregnant, the particular treatment or procedure may involve risks to the embryo or fetus that are currently unforeseeable. (Include this when the research involves pregnant women or women of childbearing potential, and the risks to a fetus of the study drug, device, biologic or procedures involved in the research are not well known.)
- Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent. (Include this when there are anticipated circumstances under which the investigator may terminate participation of a subject.)
- Any additional costs to the subject that may result from participation in the research. (Include this when it is anticipated that subjects may have additional costs.)
- The consequences of a subject's decision to withdraw from the research. (Include this when withdrawal from the research may be associated with risks that are more than minimal.)
- Procedures for orderly termination of participation by the subject. (Include this when the protocol describes such procedures.)
- A statement that significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to the subject. (Include this, for example, when the research will continue long enough that interim information is likely to be developed during the subject's participation in the research.)
- The approximate number of subjects involved in the study. (Include this, for example, when the research involves more than minimal risk.)
- The amount and schedule of all payments to subjects (Include if applicable).
- 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).

Informed Consent Process

The principal investigator must describe in the initial IRB submission and the submission for periodic continuing review the consent process that will utilize the consent document. It is the

policy of the DUHS IRB that only individuals listed as Key Personnel in the IRB submission materials may conduct the consent process.

The investigator's IRB submission materials must describe the circumstances under which consent will be obtained, including:

- Who (by title) will conduct the consent process;
- Where the process will take place;
- The process that will be followed;
- How much time will likely be allocated for conducting the consent process;
- How much time the potential subject (or the legally authorized representative) will have to consider whether or not to participate;
- How it will be determined that the subject or the subject's legally authorized representative understands the information presented.
- If some patients with cognitive impairment will be targeted for study accrual:
    - how the investigator will determine the extent of cognitive impairment in order to decide whether the potential subject can give legally effective informed consent:
        - will the individual have enough information to make an informed decision,
        - will the individual be able to make a decision,
        - will the individual understand the consequences of the decision, and
        - will the individual be able to communicate the decision;
    - whether the subject's legally authorized representative must be asked to act on behalf of the subject;
    - whether the subject's assent will be sought;
    - under what circumstances the subject's failure to assent can be overridden by the subject's legally authorized representative;
    - if a periodic reassessment of the subject's cognition will occur, when it will occur, and by whom; and
    - whether the subject will be asked to consent for continued study participation if the subject's decisional capacity improves, and if not, why not.

Waiver or Alteration of Consent

The IRB may waive or alter the requirement for the investigator to obtain a potential subject's consent for research participation. To approve such a waiver or alteration, the IRB must find:

- The research is not subject to FDA regulation;
- 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;
- The research could not practicably be conducted or carried out without access to and use of the protected health information.
- For research using biospecimens or identifiable information, the research could not practicably be carried out without access to and use of the protected health information.
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Research (clinical investigation) subject to FDA regulation may occur without prior consent of the subject in four circumstances:

- When the research involves planned research in life-threatening emergent situations

where obtaining prospective informed consent has been waived for some or all of the potential research subjects, as provided by 21 CFR 50.24. The research plan must be approved in advance by FDA and the IRB, and publicly disclosed to the community in which the research will be conducted. (See Policy on Planned Emergency Research)

- When the research involves an unplanned emergency use of an FDA regulated product for a single subject.

- When the research involves the use of an investigational in vitro diagnostic device to analyze leftover human specimens that are not individually identifiable. (See policy on In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable)

- When the research involves no more than minimal risk (as defined in 21 CFR 50.3(k) or 56.102(i)) to the subjects, and as per FDA Guidance titled IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects, July 2017

When subjects withdraw consent in research (clinical investigation) subject to FDA regulation

When a subject withdraws from an FDA-regulated clinical investigation:

- A researcher may ask a subject who is withdrawing whether the subject wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the subject distinguishes between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through non-invasive chart review, and the researcher addresses the maintenance of privacy and confidentiality of the subject's information.

- The researcher must obtain the subject’s consent for this limited participation in the study (assuming such a situation was not described in the original consent document). The IRB must approve the consent document.

- If a subject withdraws from the interventional portion of a study and does **not** consent to continued follow-up of associated clinical outcome information, the researcher must not access for purposes related to the study the subject's medical record or other confidential records requiring the subject's consent. However, a researcher may review study data related to the subject collected prior to the subject's withdrawal from the study, and may consult public records, such as those establishing survival status.

Waiver or Alteration of HIPAA Authorization

In order for the IRB to waive or alter authorization, the Privacy Rule (45 CFR 164.512(i)(2)(ii)) requires that the IRB find that:

- Disclosure of the PHI involves no more than minimal risk.
- The waiver will not adversely affect the privacy rights or welfare of the subject.
- The research could not practicably be carried out without the waiver.
- The research could not practicably be carried out without access to the PHI.
- The privacy risks are reasonable in relation to the information to be gained.

- There is an adequate plan to protect the identifiers from improper use and disclosure.
- There is an adequate plan to destroy the identifiers at the earliest opportunity.
- There is written assurance that the PHI will not be further disclosed, with a few exceptions specified in 45 CFR 164.512(i)(2)(ii)(A)(3).

Consent Documentation

A potential research subject's agreement to participate in a research study is usually documented by the subject indicating his/her approval by signing and dating the consent document which includes, where appropriate, the HIPAA authorization information. For research conducted within Duke University Medical Center or any other facility utilizing the Duke Hospital Medical Record system, the consent document must be printed on the Duke MO 345 form so it will be suitable for inclusion in the subject's medical record.

When the consent document is approved by the IRB for the use by a legally authorized representative, or in the case of a minor, by one or both parents or the guardian, signature lines for each must be provided on the signature page. If the subject is capable of written assent but not consent, a signature line for the subject must also be included. In addition, a signature line for the person conducting the consent process (referred to as the person obtaining consent) must be provided. Whoever signs the consent document must also date it at that time. Study teams are strongly encouraged to use the DUHS Sample Consent Template, found on the IRB web site, when preparing consent documents.

Waiver of Documentation of Consent/Authorization

For certain types of research, the investigator may request IRB approval for a waiver of documentation of consent (45 CFR 46.117 and 21 CFR 56.109) and HIPAA authorization (45 CFR 164.512(i)(2)). Whenever the IRB approves a consent process involving waiver of documentation of consent/authorization, the IRB ordinarily would need to approve a written description of the study that also contains all of the elements of consent/authorization. This written description may be in the form of a script for verbal use, such as during a telephone conversation. However, the IRB may approve an alteration of consent/authorization if some elements are omitted. The IRB must always approve a waiver of documentation of consent and, where appropriate, an alteration of authorization if the investigator will not obtain a consent document signed and dated by the research participant or his/her legally authorized representative.

Under certain circumstances the Common Rule allows the IRB to waive written consent (documentation of consent) (45 CFR 46.117):

An IRB may waive the requirement for the investigator to obtain a signed and dated consent document for some or all subjects, if it finds any of the following:

(1) That the only record linking the subject and the research would be the informed consent form and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject (or legally authorized representative) will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern;

(2) 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 of the research context; or

(3) 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 research involves an FDA-regulated product, the IRB may waive written consent only for research that meets item (2) above.

The DUHS IRB considers the following points when assessing whether to approve waiver of documentation of consent:

- Does the written description or script for presentation to the potential subject include the required elements of consent, and additional elements, if applicable?
- Does the written description or script for presentation to the potential subject include the required elements of authorization?
- Does the written description or script include the requirement for the signature of the subject or his/her legally authorized representative?
- If the written description or script is to be signed and dated by the subject or his/her legally authorized representative, and the consent process occurs by telephone, does the written description or script include the requirement for signature by a witness to confirm the identity of the subject?
- Does the research involve no more than minimal risk, and would written consent be required for the study procedures if they were not part of a research study?

Further information can be found in the DUHS IRB policy regarding *"Waiver of Documentation of Consent".*

Use of the Short Form Consent Document

The federal regulations at 45 CFR 46.117 and 21 CFR50.27 permit the use of a short form consent document stating that the required elements of informed consent have been presented to the subject or the subject's legally authorized representative orally, with a witness present. Within DUHS use of a short form consent document is largely limited to two situations:

- when English is not understandable to a potential research subject who is considering whether to participate in a research study, and the investigator does not have an IRB-approved consent document translated into a language understandable to the potential subject. In such cases, the investigator must follow the DUHS IRB Policy on Research Involving Non-English Speaking Subjects found on the IRB web site.
- in the very unusual situation when the window of opportunity for a subject to benefit from research participation is brief, and the IRB finds that by use of the short form consent document the subject or the subject's legally authorized representative will have sufficient opportunity to comprehend the nature of the study and the associated risks and benefits associated with the study to make an informed decision about study participation.

When proposing to use a short form consent document, the investigator must prepare:

- A written summary of what is to be said to the subject or the subject's legally authorized representative following the standard consent template. This summary may be written in English.

- A short form consent document prepared in a language understandable to the subject stating that the elements of informed consent required by regulations have been presented orally to the subject or the subject's legally authorized representative.

The IRB must approve both the written summary and the short form consent document.

For the oral presentation to the potential subject or his/her legally authorized representative:

- There must be a witness to the presentation. For potential subjects for whom English is not understandable, the witness must be fluent in both English and the language understandable by the potential subject or the subject's legally authorized representative.
- The subject or the subject's legally authorized representative must sign and date the short form consent document.
- The witness must sign and date both the short from consent document and the summary.
- The person obtaining consent must sign and date the summary.
- The person obtaining consent must give to the subject or the subject's legally authorized representative:
    - A copy of the summary.
    - A copy of the signed and dated short form consent document.

The use of a "short form" also requires an alteration of HIPAA authorization unless all elements of a valid authorization are included in the "short form".

Further information can be found in the DUHS IRB policy regarding "*Short Form Consent".*

When the IRB waives or alters the requirement for written documentation of consent/authorization, the findings will be documented in the Minutes or supporting documents, or if through the expedited review procedure, in the review form completed by the authorized IRB reviewer or supporting documents submitted by the investigator.

Conducting the Consent Process with Persons Not Able to Read Because of Illiteracy or Because of Blindness

In the case of a subject who is unable to read because of illiteracy or because of blindness, the person conducting the consent process reads the consent form aloud to the potential research subject (verbatim) and the person conducting the consent process writes a note on the consent form at the bottom that: "the consent form was read aloud to the subject by (name of person doing the reading) on (date) because of subject's inability to read." If the individual wishes to give consent, the person signs the form as usual or if the person is unable to sign his or her name, he/she can make another kind of mark (like an X) if needed to indicate consent. Again if an X or mark is used instead of a signature, the person conducting the consent process needs to make a notation on the consent form that the subject wrote a mark or X instead of a signature. There also needs to be a witness to this entire process -- the witness is a third person, and can be a family member. The witness should not be a member of Key Personnel on the study. The witness needs to sign and date as well.

The need for a legally authorized representative or guardian only applies when the subject does not have the cognitive capacity to give consent.

In the case of a blind subject or a subject with visual disability, the PI and study team must use extra care to evaluate whether the person's blindness will introduce additional risk while on the study. The PI must decide if the person can safely participate in the study, given the condition of his/her blindness. For example, does the study require that the person is able to see signs and symptoms related to drug effects and adverse events? Does the study require that the person see to be able to take certain dosages at certain times? What accommodations can be made so that the blind person can safely participate in the study? The study team must consider all of these factors before attempting to enroll a blind person, and ensure that all the things the protocol will require the subject to do can be done safely by a blind person.

Consent Monitoring

The IRB has the authority under 45 CFR 46.109 and 21 CFR 56.109 to observe or have a third party observe the consent process and the research. In order to ensure that the consent process is appropriate and the approved process is being followed, the IRB may determine that special monitoring of the process must occur.

Such monitoring may be particularly needed for the IRB to meet its responsibilities to ensure human subject protections for research that:

- Involves a vulnerable population
- Involves use of a highly risky and innovative procedure
- Is conducted by an inexperienced investigator and/or research team
- Is research about which the IRB has concerns that the consent process is not being conducted properly.

In reviewing the adequacy of proposed informed consent procedures, the IRB will determine on a protocol-by-protocol basis as a part of the initial and continuing review process those protocols that require third party observation/monitoring of the consent procedures. The person(s) authorized to conduct the monitoring will be identified by the IRB Chair or IRB Executive Director, and the meeting minutes will document these plans. The monitoring results will be reported to the IRB that requested the monitoring and reflected in the minutes, and the monitoring report will be included in the protocol file. If the initial determination requiring third party observation/monitoring of the consent procedures was open-ended, when the IRB determines that the monitoring is no longer required, the minutes will record that determination.

Further information can be found in the DUHS IRB policy regarding "*Consent Monitoring*".

Previous Version Date(s): 4/22/2008, 2/1/2016