# INFORMED CONSENT AND ITS DOCUMENTATION

**2/7/2025**

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 valid HIPAA authorization 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 participant 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 participant 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 participant unless they are 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 participant’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 participant’s legally authorized representative to act on behalf of the participant regarding consent for study participation. If the participant 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 46.408).

**Use of the Standard Consent Document**

Legally effective informed consent must be sought from each potential participant or the participant'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 ("key information summary") of the information most likely to assist a prospective participant, 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/key information summary*** are found in the box at the top of the DUHS Sample Consent, 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.

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 person'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 participant;
- A description of any benefits to the participant 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 participant;
- A statement describing the extent, if any, to which confidentiality of records identifying the participant 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 participants' rights, and whom to contact in the event of a research-related injury to the participant;
- A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the individual is otherwise entitled, and the participant may discontinue participation at any time without penalty or loss of benefits to which they are 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 participant 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 participant or the legally authorized

representative, if this might be a possibility; **OR**
(ii) A statement that the participant'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 participant that are currently unforeseeable. (Include this when the research involves an unapproved drug, device or biologic or procedure for which the risks to participants are not well known.)
- A statement that if the participant 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 persons or people 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 individual's participation may be terminated by the investigator without regard to the participant's consent. (Include this when there are anticipated circumstances under which the investigator may terminate participation of an individual.)
- Any additional costs to the participant that may result from participation in the research. (Include this when it is anticipated that participants may have additional costs.)
- The consequences of a participant'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 individual. (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 participant's willingness to continue participation will be provided to the participant. (Include this, for example, when the research will continue long enough that interim information is likely to be developed during the person's participation in the research.)
- The approximate number of participants involved in the study. (Include this, for example, when the research involves more than minimal risk.)
- The amount and schedule of all payments to participants (Include if applicable).
- A statement that the participant's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the participant 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 participants, 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 the consent process in the IRB submission. . It is the policy of the DUHS IRB that only trained individuals listed as Key Personnel in the IRB submission 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 participant (or the legally authorized representative) will have to consider whether or not to participate;
- How it will be determined that the participant or the participant's legally authorized representative understands the information presented.
- If some individuals 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 participant 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 participant's legally authorized representative must be asked to act on behalf of the subject;
    - whether the participant's assent will be sought;
    - under what circumstances the participant's failure to assent can be overridden by the participant's legally authorized representative;
    - if a periodic reassessment of the participant's cognition will occur, when it will occur, and by whom; and
    - whether the participant will be asked to consent for continued study participation if the participant's decisional capacity improves, and if not, why not.
- How consent will be obtained if individuals speak a language other than English. This should include any translated consent(s), use of an interpreter, and requirement of a witness.
- If using electronic consent (eConsent):
    - describe if the consent will be obtained in person (i.e., using a tablet) or remote
    - identify what electronic platform will be utilized. For FDA-regulated research, confirm eConsent is Part 11 compliant (21 CFR 11)
    - indicate what mechanism will be used to verify identification, if remote consenting
    - describe how the consenting discussion will occur
    - explain how signature(s) will be obtained
    - and, indicate how participants will be provided with a signed copy of the eConsent. For example, when using REDCap, participants could get this copy via email.
- If consenting by mail:
    - describe the process of providing the consent document to the potential participant
    - provide a consenting script
    - describe how written consent will be obtained and returned to the study team
    - indicate that no research activities will occur until consent is fully executed

**Waiver or Alteration of Consent**

The IRB may waive or alter the requirement for the investigator to obtain a potential participant'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 participants;
- The waiver or alteration will not adversely affect the rights and welfare of the participants;
- 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 participants will be provided with additional pertinent information after participation.

**Research (clinical investigation) subject to FDA regulation may occur without prior consent of the participant 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 Research in an Emergency Setting)

- 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 Devices)

- 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 the Revised Common Rule.

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

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

- A researcher may ask a participant who is withdrawing whether the participant 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 participant 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 participant's information.

- The researcher must obtain the individual’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 participant 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 individual's medical record or other confidential records requiring the person's consent. However, a researcher may review

study data related to the participant collected prior to the individual'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 participant's agreement to participate in a research study is usually documented by the participant indicating their approval by signing and dating the consent document, which includes, where appropriate, the HIPAA authorization information. For research conducted within Duke University Health System or any other facility utilizing the Duke Electronic Medical Record system, the consent document must be printed on the Duke MO345 form so it will be suitable for inclusion in the subject's medical record by Health Information Management (HIM). See policy "Placement of a Research Consent form in the Participant'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 and include the time of signature.
Study teams are strongly encouraged to use the DUHS Sample Consent template, found on the IRB web site, when preparing consent documents.

When eConsent is used, electronic signature of the participant/parent(s)/LAR is required, just like with a paper consent form. Documentation by the person obtaining consent is still required, even if the consenting is done remotely, and can be done on a different form than the participant used to consent. A copy of the eConsent must be sent to HIM if the research activities are clinically relevant.

**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 their 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 participant include the required elements of consent, and additional elements, if applicable?
- Does the written description or script for presentation to the potential participant include the required elements of authorization?
- Does the written description or script include the requirement for the signature of the participant or their legally authorized representative?
- If the written description or script is to be signed and dated by the participant or their 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 participant?
- 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?

**Remote Consenting**

When a study is using an electronic consent (eConsent) in addition to a paper consent (M0345), only the paper consent form should be submitted to IRB, as the eConsent will be the same as the approved paper form. The consent process, as described earlier in this policy, should indicate

that eConsent will be a method and all the required specifics.

When a study is using only an eConsent, this should be submitted to the IRB as a Microsoft Word document uploaded in the iRIS system as an Informed Consent. If any videos or web-based information will be embedded in the eConsent, these will also need to be submitted and approved. This approval should be obtained prior to building in the electronic consent platform (i.e., REDCap). For those studies that are FDA-regulated, (and where waiver or alteration of consent is not allowed) confirmation of Part 11 compliance (21 CFR Part 11) will be required for the electronic consent.

When consenting by mail, the consent form, IRB-approved cover letter and return envelope is sent to the potential participant including a time when a remote consenting conversation will occur. Either a script or the full consent would be used to have the consenting process conversation remotely, allowing the participant time to ask questions and consider participation. The participant would then sign/date/time the consent form and return it to the study team. The consent process used must be documented in the source records. Research activities cannot ensue until the appropriately signed consent form is returned to the study team with the person obtaining consent signing/date/time the form.

**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. The use of a short form consent document is largely limited to a study that will enroll small numbers of participants (not more than 1-2 people) who do not speak English.

Further information can be found in the DUHS IRB policy *"Translation Requirements for Research".*

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 participant 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 participant (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 participant by (name of person doing the reading) on (date) because of participant's inability to read." 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 the consent form as well.

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

In the case of a blind participant or a participant 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 their 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 participant to do can be done safely by a blind person.

**Conducting the Consent Process with Persons with Limitations to Sign the Consent Form**

If the individual wishes to give consent, and the person is unable to sign their name, they can make another kind of mark (like an X) if needed to indicate consent. 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 participant wrote a mark or X instead of a signature.

**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.

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

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