



INFORMED CONSENT AND ITS DOCUMENTATION

4/22/2008

It is the policy of the DUHS IRB that, with one exception, a person may participate in a research study or a clinical investigation as a research subject within DUHS only with prior IRB approval. The exception is in the setting of an emergency use of a test article (21 CFR 56.104(c)). This exemption from prior IRB review may not be used unless all of the conditions described in 21 CFR 56.102(d) exist. (See IRB Policy on Emergency Use).

In order to receive IRB approval of a research study, the investigator must submit an IRB protocol. For every IRB approved protocol, the investigator must either use an IRB approved consent process or have received 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 authorization document incorporated into the consent document, or with prior IRB approval of a waiver or alteration of authorization.

The consent and authorization document, or if no PHI is to be used or disclosed for research purposes, the consent 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(a) and (b) 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 treatment and research, 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 (45 CFR 46.102(c) and/or 21 CFR 50.3(l)) 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.

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.

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 biological 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.)

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; and
- 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 only three 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. The investigator is required to obtain informed consent of the subject or the subject's legally authorized representative as described in the Policy on Emergency Use of an Investigational Drug, Biologic or Device. Note that this policy includes a description of the narrow circumstances in which the investigational product may be used for research without prior consent of the 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)

Waiver or Alteration of 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. However, unless required by the research protocol and the nature of the research, the research subject is not required (21 CFR 312.62(b)) to indicate the time of signing the consent document. Guidance for the preparation of the consent document is found on the IRB website: <http://irb.mc.duke.edu/>.

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(c) and 21 CFR 56.109(c)(1)) 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(c)):

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 either:

- (1) That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or
- (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 the research context. In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

When the research involves an FDA-regulated product, the IRB may waive written consent only for research that meets item (2) above (21 CFR 56.109(c)(1) and 45 CFR 46.117(c)(2)).

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?

Use of the Short Form Consent Document

The federal regulations at 45 CFR 46.117(b)(2) and 21 CFR 50.27(b)(2) 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 form 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 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”.

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.

Consent Monitoring

The IRB has the authority under 45 CFR 46.109(e) and 21 CFR 56.109(f) 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, 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.