



Title:	Obtaining Informed Consent from Research Subjects		
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## 1 Purpose

No investigator conducting research under the auspices of the University of North Carolina at Chapel Hill (UNC-Chapel Hill) may involve a human being as a subject in research without obtaining the legally effective informed consent of the subject or the subject's legally authorized representative unless a waiver of consent has been approved by the IRB in accordance with Section 2.9 of these procedures. Except as provided in Sections 2.10 and 2.11 of these procedures, informed consent must be documented by the use of a written consent form approved by the IRB.

The IRB will evaluate both the consent process and the procedures for documenting informed consent to ensure that adequate informed consent is obtained from participants.

The following procedures describe the requirements for obtaining consent from participants in research conducted under the auspices of the UNC-Chapel Hill.

## 2 Procedure

### 2.1 Basic Requirements

The requirement to obtain the legally effective informed consent of individuals before involving them in research is one of the central protections provided for by the Federal regulations and the UNC-Chapel Hill IRB. Investigators are required to obtain legally effective informed consent from a subject or the subject's Legally Authorized Representative unless the requirement has been waived by the IRB. When informed consent is required, it must be sought prospectively, and properly documented.

The informed consent process involves three key features: (1) disclosing to the prospective human subject information needed to make an informed decision; (2) facilitating the understanding of what has been disclosed; and (3) promoting the voluntariness of the decision about whether or not to participate in the Research.

Informed consent is more than just a signature on a form. It is a process of information exchange to include reading, discussion, receiving answers to any questions, and signing the consent document. The informed consent process is the critical communication link between the prospective Human Subject and an Investigator, beginning with the initial approach of an Investigator and continuing through the completion of the Research study. Investigators must have received the appropriate training and be knowledgeable about the study Protocol in order

that they may answer questions to help provide understanding to the study participant or potential study potential study participant. The exchange of information between the Investigator and study participant can occur via one or more of the following modes of communication, among others; face to face dialogue; mail; telephone; or fax; however, obtaining informed consent must allow for a dialogue so that the potential subject has the opportunity to ask questions and receive responses. Investigators must obtain consent prior to entering a subject into a study, gathering data about a subject, and/or conducting any procedures required by the research plan, unless consent is waived by the IRB.

If someone other than the investigator conducts the interview and obtains consent, the investigator needs to formally delegate this responsibility, and the person so delegated must have received appropriate training to perform this activity. The person so delegated must be knowledgeable about the research to be conducted and the consenting process, and must have the expertise be able to answer questions about the study including those regarding risks, procedures, and alternatives.

Sample or draft consent documents may be developed by a sponsor or cooperative study group. However, the IRB-of-record is the final authority on the content of the consent documents that is presented to the prospective study subjects.

These informed consent requirements are not intended to preempt any applicable federal, state, or local laws that require additional information to be disclosed for informed consent to be legally effective.

## **2.2 Informed Consent Process**

Informed consent must be obtained under the following circumstances:

1. Informed consent may only be obtained from subjects who have the legal and mental capacity to give consent. For subjects without that capacity, permission must be obtained from a legal guardian or a legally authorized representative. See Section 2.3 below.
2. The informed consent process provides the prospective subject (or legally authorized representative) with sufficient opportunity to read the consent document, when applicable.
3. The informed consent process shall be sought under circumstances that provide the subject (or legally authorized representative) with sufficient opportunity to consider whether or not to participate.
4. The informed consent process shall be sought under circumstances that minimize the possibility of coercion or undue influence.
5. The informed consent information must be presented in language that is understandable to the subject (or legally authorized representative). To the extent possible, the language should be understandable by a person who is educated to 8th grade level and layman's terms shall be used in the description of the research.
6. For subjects whose native language is not English, informed consent must be obtained in a language that is understandable to the subject (or the subject's legally authorized

representative). In accordance with this policy, the IRB requires that informed consent discussions include a reliable interpreter when the prospective subject does not understand the language of the person who is obtaining consent.

7. The informed consent process may not include any exculpatory language through which the subject is made to waive, or appear to waive any of the subject's legal rights or through which the investigator, the sponsor, the Organization or the UNC-Chapel Hill employees or agents are released from liability for negligence, or appear to be so released.

8. The investigator is responsible for ensuring that each prospective subject is adequately informed about all aspects of the research and understands the information provided.

### **2.3 Who can act as a legally authorized representative (LAR) for a decisionally impaired research subject in North Carolina?**

As is the case for most states, North Carolina does not have State legal statutes that specifically address research enrollment. In accordance with federal regulations and guidance from the OHRP, UNC-Chapel Hill has established that the informed consent laws applicable to clinical care in North Carolina (North Carolina General Statute 90-21.13) will be followed to determine who would be considered an acceptable LAR for purposes of providing surrogate consent for decisionally impaired subjects in studies conducted in North Carolina. Although the statute is specific to medical care, it may reasonably be applied to research participation as well.

In the case of an adult subject who lacks the capacity to consent, the LAR of the subject will be determined by taking the following individuals in this order of priority:

(1) **Court-appointed legal guardian** (except to the extent any appointed health care agent has authority, unless the health care agent's authority has been suspended by a court order) is a court appointed guardian granted "general" guardianship or "guardian of the person" may provide surrogate consent for all activities of the individual; therefore, this guardian may provide surrogate consent for research participation of the individual.

(2) A **health care power of attorney (HCPOA)** is a health care agent pursuant to the execution of health care power of attorney document. A HCPOA document (to the extent of authority granted) grants the agent power to make health care decisions for the individual following a physician's determination that the individual lacks adequate capacity to make her/his own health care decisions. Therefore, if such a physician determination has been made, the agent under an HCPOA may provide surrogate consent for research participation; to the extent this does not contradict the written HCPOA.

(3) A **durable general power of attorney** grants the agent whatever authority is specified in the power of attorney document and is referred to as an attorney-in fact. Where the power of attorney includes a specific provision stating that it shall survive any period of incapacity or mental incompetence of the principal it is considered a "durable" power of attorney, and the person holding power of attorney may provide surrogate consent for

research participation unless the research participation includes an activity expressly excluded from the power of attorney. NOTE that a general power of attorney is only valid when registered with the register of deeds in either the county named in the power of attorney or the county in which the principal resides. Before relying on the decision of a person holding a general power of attorney, investigators should require proof that the power of attorney has been registered and should examine the document to ensure that it expressly survives any period of incapacity or mental incompetence of the principal. For assistance with these determinations, please contact the Office of University Counsel.

Where there is both a valid HCPOA and a valid general power of attorney, the person holding the HCPOA has priority over the person holding the general power of attorney in making decisions regarding participation in human subjects research.

(4) In the event that there is neither a court appointed guardian nor an agent under a durable general power of attorney or HCPOA, surrogate consent for research may be given, as long as there is no evidence to the contrary, by the **other individuals listed below**, in order of priority. When surrogate consent will be sought from one of these individuals, in the absence of a legal designation, their authority would be no broader (and may be more limited) than that of a duly appointed health care agent:

(4a) The subject's spouse;

(4b) A majority of the subject's reasonably available parents and adult children;

(4c) A majority of the subject's reasonably available adult siblings; or

(4d) Another individual with an established relationship with the subject who is acting in good faith on behalf of the subject and can reliably convey the subject's wishes.

To determine the authorized representative, refer to UNC Health Care System Policy ADMIN 0019, Authorized Representatives of Patients. If there is any doubt as to which individual is the legally appropriate authorized representative for the subject, the Office of University Counsel must be contacted.

NOTE: In the case of designations (1), (2) or (3) above, the investigator should obtain a copy of the court order, HCPOA, or durable power of attorney and should maintain the copy with the research records as documentation of the authority of the surrogate decision maker.

Beyond the categories described above, others may not give surrogate consent for research enrollment. Institutional custodians or caretakers are not legally authorized representatives in the absence of a specific court appointment granting them guardianship (see above).

## 2.4 Determining a potential adult subject's ability to consent to research

In the absence of a specific legal or medical finding to the contrary, the individual subject must be presumed to have decision making power for himself/herself and must give consent, informed to the best ability of the research team. If there is any doubt as to the subject's capacity to consent, the investigator and the IRB should consider the need for independent assessment of capacity (e.g., psychiatric consult). If the subject does not have decisional capacity and the IRB has approved enrollment via surrogate consent, consent should be obtained from the highest available surrogate representative as described below.

There is an important distinction between the legal meaning of the term "incompetent" and our broader use of the term "decisionally impaired." Decisionally impaired persons are those who, due to a psychiatric, organic, developmental or other disorder or situation that affects cognitive or emotional functions, are unable to exercise independent decision making. "Incompetence" is a finding of a court of law that results in the appointment of a legally authorized representative for the individual judged incompetent by the court (see "court appointed guardian" below). Persons who have been judged "incompetent" in a court of law are only a subset of the larger group of persons who may be decisionally impaired.

Decisional impairment in a human research subject may be determined by a court finding of incompetence, by a physician's determination, or by a reasonable determination by the investigator or an independent consultant that the surrounding circumstances indicate that the individual is not able to exercise competent judgment about her/his personal risks and benefits in research participation. If a determination of decisional impairment is not confirmed by a court or physician, but only suspected, then consent should be obtained from both the subject and the appropriate representative.

For the purpose of this policy, a subject has the capacity to consent to his or her own participation in a research activity if s/he demonstrates an appreciation:

1. That the activity is research
2. Of the risks and benefits of a study
3. Of the study procedures and requirements
4. Of the alternatives that are available if not participating
5. That, by choosing not to participate, this decision will be accepted without penalty

In reaching a decision about participation, it is essential for the potential subject to demonstrate an ability to use this information in a rational manner. Thus, in considering risks, benefits, and available alternatives, subjects must show they understand the aspects of these factors that are unique to them as individuals.

See SOP 1201.7 for further discussion regarding adults who cannot consent for themselves.

The decision-making capacity of a potential research subject should be evaluated when there are reasons to believe that the subject may not be capable of making voluntary and informed decisions about research participation.

The investigator and research staff must have adequate procedures in place for assessing and ensuring subjects' capacity, understanding, and informed consent or assent. The IRB will evaluate whether the proposed plan to assess capacity to consent is adequate including consideration of state and local law and organizational policy.

It is often possible for investigators and others to enable persons with some decisional impairments to make voluntary and informed decisions to consent, assent, or refuse participation in research. Potential measures include repetitive teaching, group sessions, audiovisual presentations, and oral or written recall tests. Other measures might include follow-up questions to assess subject understanding, videotaping or audio-taping of consent interviews, second opinions, use of independent consent observers, allowing a waiting period before enrollment, or involvement of a trusted family member or friend in the disclosure and decision making process.

Both investigators and IRB members must be aware that for some subjects, their decision-making capacity may fluctuate. For subjects with fluctuating decision-making capacity or those with decreasing capacity to provide consent, periodic reevaluation of capacity and re-consent or consent for continuing participation by a legally authorized representative may be necessary.

In the event that research participants lose or become impaired in decision-making capacity after enrollment, and this is not anticipated in the research plan, the investigator is responsible for notifying the IRB. The investigator is responsible for developing a plan for the IRB's consideration which follows the guidelines outlined above for persons with fluctuating or diminishing capacity.

Whenever the participants have the capacity to give consent (as determined by qualified professionals), informed consent should be obtained and document in accordance with Section 2.2 above. When participants lack the capacity to give consent, investigators may obtain consent from the legally authorized representative of a subject as described in SOP 1201.7.

When assent is possible for some or all subjects, the investigator should provide the IRB with an assent plan that describes when and how assent will be obtained, provisions that will be taken to promote understanding and voluntariness, and how assent will be documented. Under no circumstances may subjects be forced or coerced to participate.

If the investigator plans to use audio or videotapes, computer video presentations, or written materials, to promote understanding, these materials must be provided to the IRB for review. If the investigator intends to use audio or video recordings to document assent, provisions to ensure the security of the recordings should be described to the IRB. If the investigator will use an assent form to document assent, this must be submitted to the IRB for review.

## **2.5 Basic Elements of Informed Consent**

To be valid, the consent process must provide the following basic elements of information to potential subjects:

1. 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;
2. A description of any reasonably foreseeable risks or discomforts to the subject;
3. A description of any benefits to the subject or to others which may reasonably be expected from the research;
4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
5. A statement describing the extent, if any, to which confidentiality of records identifying the subject must be maintained;
6. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;
7. 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;
8. 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;
9. For FDA-regulated studies, a statement that notes the possibility that the Food and Drug Administration may inspect the records;
10. For "applicable" FDA-regulated clinical trials, the following statement must be included verbatim:

"A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."

In general, "applicable" clinical trials mean controlled clinical investigations, other than Phase 1 clinical investigations, of a drug or biologic; and prospective clinical studies of health outcomes comparing an intervention with a device against a control (other than (i) small clinical trials to determine the feasibility of a device, (ii) a clinical trial to test prototype devices where the primary outcome measure relates to feasibility and not to health outcomes, or (iii) mandated pediatric postmarket surveillance activities)

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

1. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;

2. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
3. Any additional costs to the subject that may result from participation in the research;
4. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;
5. A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject;
6. The approximate number of subjects involved in the study.

## **2.6 Documentation of Informed Consent**

Except as provided in Section 2.10 of this document, informed consent must be documented by the use of a written consent form approved by the IRB.

1. Informed consent is documented by the use of a written consent form approved by the IRB and signed and dated by the subject or the subject's legally authorized representative at the time of consent. The person obtaining consent will also sign the consent form.
2. A copy of the signed and dated consent form must be given to the person signing the form. The investigator should retain the signed original in the research records.
3. The consent form may be either of the following:
  - a. A written consent document that embodies the basic and required additional elements of informed consent. The consent form may be read to the subject or the subject's legally authorized representative, but the subject or representative must be given adequate opportunity to read it before it is signed; or
  - b. A short form written consent document stating that the elements of informed consent have been presented orally to the subject or the subject's legally authorized representative.

A *short form* may be used when consenting non-English speakers or illiterate subjects. The short form should be used when you do not anticipate enrolling non-English speakers. If you anticipate enrolling non-English speakers, the consent form must be translated into the subject's native language. The short form is *not* to be used when a study team has simply failed to make provisions for translated versions of the consent document in commonly spoken languages in the recruitment area/population. If the potential subject is blind, the consent form may be read to the person or the use of an audio version of the consent form (audiotape, digital audio format (e.g., MP3) should be considered.

Federal regulations (21 CFR 50.27(b)(2) and 45 CFR 46.117(b)(2) permits oral presentation of informed consent information in conjunction with a *short form* written consent document (stating that the elements of consent have been presented orally) and a written summary of what is presented orally. A witness to the oral presentation is required and the subject must be given copies of both the short form document and the summary.



When this method of consent is used, there are additional regulatory requirements that must be followed. These include:

- The IRB must approve the full version of the consent form documents (or summary of information to be orally presented to the subject) including stored specimens and HIPAA authorization forms.
- The short forms available on the IRB website are considered IRB-approved documents. Several different languages are available. The short forms do not need to be submitted separately to the IRB for approval however *only* the study and contact information should be edited. The short form must be used in conjunction with the IRB-approved consent documents.
- A witness to the oral presentation must be present. The witness may be the interpreter, if one is used, or an independent third party. When consenting non-English speaking subjects, the witness must be bilingual in order to verify the exchange.
- Required signatures:
  - The short form must be signed by the subject (or subject's representative) and the witness/interpreter.
  - The full version of the consent documents must be signed by the witness/interpreter and the person obtaining consent.
- At IRB Renewal: Report to the IRB, the number of times you used the short form to enroll subjects.

Investigators should carefully consider the ethical/legal ramifications of enrolling subjects when a language barrier exists. If the subject does not clearly understand the information presented, the subject's consent will not truly be informed and may not be legally effective. In addition, interpreters must be available for studies in which there is ongoing contact with the subject in order to facilitate study procedures, reporting of problems, etc.

## **2.7 Special Consent Circumstances**

The IRB should include procedures to ensure that potential subjects are not excluded from potentially beneficial research due to barriers such as language and physical disabilities. At the same time, in order to ensure that subject welfare is protected throughout the participation, subjects should not be enrolled if they may not be able to communicate with the investigator on an ongoing basis.

### **2.7.1 Enrollment of persons with limited English-language proficiency**

1. Expected enrollment: In some studies, the investigator may be able to anticipate enrollment of persons who do not speak or read, or have limited proficiency in, oral or written English. When the target subject population includes such persons or the investigator and/or the IRB otherwise anticipates that consent will be conducted in a language other than English, the IRB requires a translated consent document, and other subject materials, to be prepared In

order to ensure that translated documents are accurate, the IRB may choose to require a certified translation, to have an independent back-translation or to have a review of the translated documents by an IRB member or other person who is fluent in that language. When non-English speaking subjects enroll, they and a witness sign the translated consent document. The subjects are given a copy of the signed translated consent document.

2. Unexpected enrollment: If a person who does not speak or read, or has limited proficiency in, English presents for possible enrollment, an IRB-approved translated version of the written consent may not be available for use. Investigators should carefully consider the ethical and legal ramifications of enrolling subjects when a language barrier exists. If the subject does not clearly understand the information presented during the consent process or in subsequent discussions, his/her consent may not be informed, and therefore, not effective.

If an investigator decides to enroll a subject into a study for which there is not an extant IRB-approved consent document in the prospective subject's language, the investigator must receive IRB approval to follow the procedures for a "short form" written consent in as described in Section 2.6.

3. Use of interpreters in the consent process: Unless the person obtaining consent is fluent in the prospective subject's language, an interpreter will be necessary to facilitate the consent discussion. Preferably someone who is independent of the subject (i.e., not a family member) should assist in presenting information and obtaining consent. Whenever possible, interpreters should be provided copies of the translated consent, or short form and the IRB-approved consent script (typically the English-language version of the consent document) well before (24 to 48 hours if possible) the consent discussion with the subject. If the interpreter also serves as the witness, she/he may sign the translated consent, or short form consent document and script, as the witness and should note "Interpreter" under the signature line. The person obtaining consent must document that the "short form" process was used in the subject's research record, including the name of the interpreter.

### **2.7.2 Braille consent**

For blind subjects who read Braille, the IRB may approve a consent document prepared in Braille. In order to assure itself that a Braille consent document is accurate, the IRB may require a transcription into print text or review of the document by an IRB member or other person who reads Braille. If possible, the subject will sign the Braille consent; otherwise oral consent will be obtained, witnessed and documented as described under "Oral Consent" (see Section 2.7.4).

### **2.7.3 Consenting in American Sign Language (ASL)**

For deaf subjects who are fluent in ASL, the IRB may approve a consent process using ASL and the IRB-approved written consent form. When this process is approved, the individual authorized to consent prospective subjects must use the UNC-Chapel Hill-certified interpreter fluent in ASL to conduct the consent process and the documentation of the consent process must conform to the requirements set forth in Section 2.6.

#### **2.7.4 Oral Consent**

When subjects are unable to read a written consent form (such as blind or illiterate subjects), the IRB may approve an oral consent process, provided the subject (1) retains the ability to understand the concepts of the study and evaluate the risk and benefit of being in the study when it is explained orally and (2) is able to indicate approval or disapproval to study entry.

For research that is no more than minimal risk, documentation of consent may be waived according to the criteria in Section 2.9.

For greater than minimal risk research, the consent form must be read to the subjects and the subjects must be given an opportunity to ask questions. An audiotape approved by the IRB may also be used. If capable of doing so, the subject signs, or marks an X to signify consent. If that is not possible, the subject will provide oral consent. The person obtaining consent and a witness will sign the written study consent form with a statement that documents that an oral process was used and, if necessary, that the subject gave oral consent. The consent process will also be documented in the subject's research record. Signed copies of the consent form are given to the subject and, whenever possible, these documents should be provided to the subject on audio or video-tape.

#### **2.8 Subject Withdrawal or Termination**

For a variety of reasons, a subject enrolled in a research study may decide to withdraw from the research, or an investigator may decide to terminate a subject's participation in research regardless of whether the subject wishes to continue participating. Investigators must plan for the possibility that subjects will withdraw from research and include a discussion of what withdrawal will mean and how it will be handled in their research protocols/research plans and consent documents.

When seeking informed consent from subjects, the following information regarding data retention and use must be included:

- For FDA-regulated clinical trials, when a subject withdraws from a study, the data collected on the subject to the point of withdrawal remain part of the study database and may not be removed. The consent document cannot give the subject the option of having data removed.
- For research not subject to FDA regulations, the investigator should inform subjects whether the investigator intends to either: (1) retain and analyze already collected data relating to the subject up to the time of subject withdrawal; or (2) honor a research subject's request that the investigator destroy the subject's data or that the investigator exclude the subject's data from any analysis.

When a subject's withdrawal request is limited to discontinuation of the primary interventional component of a research study, research activities involving other types of participation for which the subject previously gave consent may continue. Investigators should 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 would distinguish between study-related interventions and procedures and continued follow-up in person, by phone, or via records review, of data and address the maintenance of privacy and confidentiality of the subject's information.

If a subject withdraws from the interventional portion of the study, but agrees to continued follow-up as described in the previous paragraph, the investigator must obtain the subject's informed consent for this limited participation in the study (assuming such a situation was not described in the original consent document). IRB approval of consent documents for these purposes would be required.

If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up, the investigator must not access or gather private information about the subject for purposes related to the study. However, an investigator 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.

## **2.9 Waiver of Informed Consent**

An IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent; or waive the requirements to obtain informed consent, provided the IRB finds and documents that:

- (a) The research involves no more than minimal risk to the subjects;
- (b) The waiver or alteration will not adversely affect the rights and welfare of the subjects;
- (c) The research could not practicably be carried out without the waiver or alteration; and
- (d) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

In addition, an IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent; or waive the requirements to obtain informed consent, provided the IRB finds and documents that:

- (a) The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:
  - 1. Public benefit or service programs;
  - 2. Procedures for obtaining benefits or services under those programs;
  - 3. Possible changes in or alternatives to those programs or procedures; or
  - 4. Possible changes in methods or levels of payment for benefits or services under those programs; and,
- (b) The research could not practicably be carried out without the waiver or alteration.

FDA regulations do not provide for waivers of informed consent except in certain emergency situations. Additionally, waivers of consent are not permissible for federally-funded research using Newborn Blood Spots.

## **2.10 Waiver of Documentation of Informed Consent**

The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either that the:

1. 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;

Note 1: Subjects must be asked whether they want documentation linking them with the research, and their wishes must govern. (Example: domestic violence research where the primary risk is discovery by the abuser that the subject is talking to investigators.)

Note 2: In order to waive written documentation of consent where the only record linking the participant and the research would be the consent document, the IRB has to determine that the research was not FDA-regulated.

2. 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. Procedures such as non-sensitive surveys, questionnaires and interviews generally do not require written consent when conducted by non-investigators (e.g., marketing surveys, telemarketing). Note: The FDA does permit a waiver of documentation of consent if this condition is satisfied. This is most commonly applied in the context of minimal risk screening activities that are necessary to determine eligibility for enrollment in the full trial.

Unless the IRB has granted a full waiver of the requirement to obtain informed consent, investigators who seek and receive approval for a waiver of documentation of consent still must perform an adequate consent process.

In cases in which the documentation requirement is waived, the IRB requires the investigator to provide in the application materials a written summary of the information to be communicated to the subject, and the IRB will consider whether to require the investigator to provide subjects with a written statement regarding the research. The IRB documents its findings justifying the waiver or alteration.

## **2.11 Waiver of Informed Consent for Planned Emergency Research**

The conduct of planned research in life-threatening emergencies where the requirement to obtain prospective informed consent has been waived by the IRB is covered by 21 CFR §50.24 for FDA-regulated research and by the waiver articulated by DHHS at 61 FR 51531-33 for non-FDA-regulated research.

The FDA exception from informed consent requirements for emergency research under FDA regulations, 21 CFR 50.24, permits planned research in an emergency setting when human subjects who are in need of emergency medical intervention, cannot provide legally effective

informed consent themselves, and there is generally insufficient time and opportunity to locate and obtain consent from their legally authorized representatives (LARs).

The Secretary of Health and Human Services (DHHS) has implemented an Emergency Research Consent Waiver under 45 CFR 46.101(i) with provisions equivalent to those of the FDA with the exception of the requirements specified in Sections 2.11.2.1 and 2.11.2.2 below. The DHHS waiver is not applicable to research involving prisoners, pregnant women, fetuses, or in vitro fertilization.

### **2.11.1 Definitions**

**Planned Emergency Research.** It is research that involves subjects who, are in a life-threatening situation for which available therapies or diagnostics are unproven or unsatisfactory, and because of the subjects' medical condition and the unavailability of legally authorized representatives of the subjects, it is generally not possible to obtain legally effective informed consent.

**Family Member.** For this section means any one of the following adult and legally competent persons: spouses; parents; children (including adopted children); brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship.

### **2.11.2 Procedures**

The IRB may approve the planned emergency research without requiring informed consent of all research subjects prior to initiating the research intervention if the IRB finds and documents that the following conditions have been met:

(1) The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

(2) Obtaining informed consent is not feasible because:

(i) The subjects will not be able to give their informed consent as a result of their medical condition;

(ii) The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and

(iii) There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the research.

(3) Participation in the research holds out the prospect of direct benefit to the subjects because:

(i) Subjects are facing a life-threatening situation that necessitates intervention;

(ii) Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and

(iii) Risks associated with the research are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

(4) The research could not practicably be carried out without the waiver.

(5) The proposed research plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.

(6) The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with Sections 46.116 and 46.117 of 45 CFR 46 and Sections 50.20, 50.25 and 50.27 of 21 CFR 50. These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the research consistent with paragraph (7)(v) of this section.

(7) Additional protections of the rights and welfare of the subjects will be provided, including, at least:

(i) Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the research will be conducted and from which the subjects will be drawn;

(ii) Public disclosure to the communities in which the research will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;

(iii) Public disclosure of sufficient information following completion of the research to apprise the community and investigators of the study, including the demographic characteristics of the research population, and its results;

(iv) Establishment of an independent data monitoring committee to exercise oversight of the research; and

(v) If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member who is not a legally authorized representative, and asking whether he or she objects to the subject's participation in the research. The investigator will summarize efforts made to contact

family members and make this information available to the IRB at the time of continuing review.

In addition, the IRB is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject's inclusion in the research, the details of the research and other information contained in the informed consent document. The IRB shall also ensure that there is a procedure to inform the subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If a legally authorized representative or family member is told about the research and the subject's condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into research with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the research is to be provided to the subject's legally authorized representative or family member, if feasible.

### **2.11.3 FDA-regulated Planned Emergency Research**

- 1) A licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation must concur that the conditions described in Section 2.11.2 are satisfied.
- 2) Studies involving an exception to the informed consent requirement under this section must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies that such studies may include subjects who are unable to consent. The submission of those studies in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists. Applications for investigations under this section may not be submitted as amendments under 312.30 or 812.35.
- 3) If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided in the regulations or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly (no longer than within 30 days) in writing to the clinical investigator and to the sponsor of the clinical investigation. The sponsor of the clinical investigation must promptly disclose this information to FDA and to the sponsor's clinical investigators who are participating or are asked to participate in this or a substantially equivalent clinical investigation of the sponsor, and to other IRB's that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor.
- 4) The IRB determinations and documentation required in Section 2.11.2 and paragraph 3 above are to be retained by the IRB for at least 3 years after completion of the clinical investigation, and the records shall be accessible for inspection and copying by FDA in accordance with 56.115(b).



#### **2.11.4 Planned Emergency Research Not Subject to FDA Regulations**

1) The IRB responsible for the review, approval, and continuing review of the research has approved both the research and a waiver of informed consent and has (i) found and documented that the research is not subject to regulations codified by the FDA at 21 CFR Part 50, and (ii) found and documented and reported to the OHRP that the conditions required Section 2.11.2 have been met relative to the research.

#### **2.12 Consent for use of stored samples and genetic testing**

In general, all anticipated uses of collected samples of human tissues, body fluids, or biological products should be carefully delineated in the *Procedures* section of the consent form. Issues to be addressed might include the specific information to be obtained, whether the information may be of value to the subject, whether and how that information will be disclosed or made available to the human subject and whether genetic counseling will be available at the subject's option.

If specimens are to be collected and stored for as yet unspecified purposes (genetic testing or otherwise), this should be addressed in the *Procedures* section of the consent form or in an addendum. The IRB will provide templates addressing these issues. Whether these templates must be included as an addendum to the consent form depends on the study. Generally, in cases where the primary purpose of the study is to store specimens or collection of specimens is not otherwise optional, then the addendum is unnecessary. Use of a separate addendum is generally preferred when storage of specimens is adjunct to the main purpose of the study and therefore optional.

The consent form and process for maintaining human specimens in a repository for future research uses must inform the subjects explicitly about the unspecified possible future use of the specimens and related personal information. The consent process should consider the following:

- The sample will be stored and possibly used in future research studies.
- A description of any personal information about the specimen source that will be maintained (this may or may not include identifiers).
- If no personal identifiers will be used for labeling the stored samples, i.e., if it is impossible for the sample to be linked with the subject, the consent form should so state.
- If personal identifiers are to be used that will allow future matching of the subject to the collected sample, the consent form should describe how they will be used, how privacy and confidentiality will be protected, and whether and under what circumstances identifying information would be disclosed.
- Future research using the samples will be reviewed by the IRB prior to additional use of the samples

- Whether and how researchers may contact individuals whose specimens are in the repository
- A statement about any potential commercialization and that there are no plans for subjects to share in financial proceeds that may accrue from products derived from the specimens.
- Whether, how, and under what circumstance results from research studies using the specimens would be communicated to the subjects and, where relevant, to their family members).
- If specimens are individually identifiable, how the specimens and associated data may be withdrawn from the repository. If the specimens are not individually identifiable, a statement that they may not be withdrawn for that reason. Specimens that have already been used and the data derived from their use cannot generally be withdrawn.

### **2.13 Consent for inclusion in research registry**

A research registry is a database of potential research subjects who have indicated their willingness to participate in research studies. Subjects must consent to inclusion in the registry. However, researchers may use a staged consent process in which preliminary consent is granted by subjects when they are included in the registry and additional consent is obtained when those subjects participate in a study.

### **2.14 Disposition of consent documents**

As noted above, participants or their Legally Authorized Representative (LAR) must sign and date the consent form prior to participating in the study, unless this documentation is waived by the IRB. A copy of the signed consent form (photocopy or duplicate signed original) shall be given to the person signing the form. An original signed consent form should be retained in the investigator's files.

#### **2.14.1 Research consent forms in health care records**

An informed consent document for research participation is not a health care document and ordinarily would not be included in a health care record. Similarly, other forms of information about research interventions that are not health care would not ordinarily be included in an individual's health care record.

However, some clinical research includes health care. Additionally, information about some research interventions, whether or not treatment-related, may be relevant to a health care provider's diagnosis and treatment decisions about the individual. For example, it may be important for a health care provider not associated with the research study to know that a patient is receiving drugs or interventions as part of a research protocol. In these circumstances it may be appropriate for the consent form to be included in the health care record.

At the time of the review, the IRB, in consultation with the PI, should make a determination as to the appropriateness of including the consent form in the health care record. Conversely, there may be circumstances where it is inappropriate to include the consent form in a subject's

health care record, and specific mechanisms should be in place to exclude research information from the health care record (e.g., when research participation is not relevant to ongoing health care but might disclose sensitive personal information such as sexual preferences). If the decision is made to include the consent form in the health care record, then the informed consent and HIPAA authorization for the study should state that this information will be placed in the health care record.

In determining whether research participation records will be placed in the health care record, IRBs and investigators should consider several points. Although protection of the subject's health and safety by providing research participation information to a health care provider is an appropriate concern, there are also other human subjects welfare issues to be considered, particularly privacy and confidentiality. Some human subjects will not want information about their research participation to be shared with their healthcare provider for a variety of reasons including personal privacy or the concern that the information may be transmitted to a health insurer or employer. These are the very privacy and confidentiality concerns that underlie the HIPAA regulations giving patients the right to know what is in their health care record and to control disclosure of their PHI from the health care record.

## **2.15 Record retention of informed consent forms**

As with all protocol related materials, a copy of the approved consent documents (not the signed consent forms themselves) should be retained by the IRB for a minimum of three (3) years following the end of the study. For more information on storage of records, see IRB records requirements.

## **2.16 Collection of Social Security Numbers for Research Purposes**

### **2.16.1 Introduction**

There are occasions within the research setting when an investigator either needs to or is required to collect the social security number (SSN) or individual taxpayer identification number (ITIN) of a subject. Most often, the SSN (or ITIN) is collected as required by law, to comply with Internal Revenue Service (IRS) reporting requirements. Less often, the SSN (or ITIN) may be collected as a unique identifier to help match research datasets.

The North Carolina Identity Theft Protection Act imposes restrictions on the collection and disclosure of SSNs and other personal identifying information (PII). They also require segregation of SSNs and other security measures to protect PII.

### **2.16.2 Conditions for use of SSN in research**

SSNs (or ITINs) collected for research must be relevant to the purpose for which they are collected, and shall not be collected until and unless the need for the SSN (or ITIN) has been clearly documented and approved by the IRB. When collecting the SSN (or ITIN), the investigator is required to provide a statement of the purpose or purposes for which the SSN

(or ITIN) is being collected and used. The SSN (or ITIN) may not be used for any purpose other than the purpose stated.

A subject must not be required to submit his or her SSN (or ITIN) over the Internet unless the connection is secure or the SSN (or ITIN) is encrypted. In addition, a subject's SSN (or ITIN) must not be printed on materials that are mailed to him or her unless state or federal law requires that the SSN (or ITIN) be on the document(s) mailed.

### **2.16.3 IRB responsibilities**

Review and Approval of Proposed Use:

The IRB has been designated to serve in lieu of the Social Security Number Management and Advisory Committee to review and approve collection of SSNs (or ITINs) and/or PII when required within the context of a research project.

The IRB may approve such collection for the following purposes:

1. Tax identification and other purposes mandated by federal or State laws. Per University policy, investigators are required to collect and report SSN and related information (as described below) when total payment(s) to an individual research subject will exceed \$200 per calendar year.
2. Use as a unique identifier for a national registry or database where there is potential for duplicate registration and no other means of unique identification exists.
3. Matching existing records or specimens to those contained in another data set (SSNs or ITINs should be destroyed prior to data analysis).
4. Payment of medical expenses by a sponsor on behalf of a research subject.

Collection of the SSN (or ITIN) **may NOT** be approved for:

1. Use as an identifier when other means of unique identification would suffice.
2. Labeling of stored biological specimens.
3. Convenience.
4. An identifier to facilitate future contact with subjects.

### IRB Documentation

The IRB will document the justification for collection of the SSN (or ITIN) and whether disclosure of the SSN (or ITIN) is voluntary or required for participation in the research.

### **2.16.4 Investigator responsibilities**

#### Mechanisms for Processing Payments to Subjects

Researchers should be aware that the method used to compensate subjects may have an impact on the need to collect an SSN (or ITIN).

- Amounts that will total less than \$400 per calendar year, investigators are not required to collect an SSN (or ITIN) if payments are made using a cash advance approach (e.g., gift cards or “petty cash” accounts).
- SSNs (or ITINs) must be collected for checks of any amount issued through the Accounts Payable system, even if that amount does not reach the \$400 threshold because the University system requires the SSN (or ITIN) in order to “cut checks.”
- Investigators are also reminded that the IRS requires an SSN (or ITIN) to be collected and reported for payments of any amount to research subjects who are University employees.

#### SSN Collection Forms

- Investigators use the appropriate University-approved form to collect and store SSNs (or ITINs).
- The form states the purpose of collection and the planned use(s) of the SSN (or ITIN).
- The form also clarifies whether disclosure of the SSN (or ITIN) is voluntary or required for participation in the research; and/or required for payment of a medical claim by a sponsor on the subject’s behalf.
- If the SSN (or ITIN) is required solely for tax identification, the subject must be informed that (s)he has the right to renounce any research payment and consequently would not be required to disclose the SSN (or ITIN) in order to participate in the research study.
- If the SSN (or ITIN) is required for payment of a medical claim by a sponsor on the subject’s behalf, the subject must be informed that (s)he may refuse to provide the SSN (or ITIN) and decline the payment.
- The SSNs (and ITINs) authorization form must be segregated from the consent form. There are separate templates when the SSN (or ITIN) is collected for tax identification purposes, when the SSN (or ITIN) is used as a unique identifier to match datasets or when the SSN (or ITIN) is used for payment of a medical claim by a sponsor on a subject’s behalf. These templates may not be revised without the approval of the Office of University Counsel.
- Submit for IRB Approval:
  - If investigators know they will be required to collect an SSN or ITIN (e.g., because payments to subjects will exceed the stated threshold amounts) they should address this in the IRB application.
  - The IRB will review the justification for collecting the SSN (or ITIN).
  - It may also happen that the IRB identifies a previously-unrecognized need for collecting the SSN (or ITIN) while reviewing the study, in which case the investigator will be instructed accordingly.
  - Submissions that occur after the initial review should be submitted as a Modification, as with any change to an approved protocol.
- Storage and Disposition of Forms after SSN (or ITIN) Collection:
  - Investigators are expected to collect and store the signed SSN forms using appropriate security measures to protect the information.

- If total payments to a participant do not exceed \$400 by the end of the calendar year, the SSN forms should be destroyed (e.g., shredded), unless payments will continue and might reach that amount in subsequent years.
- At the end of each calendar year, SSN forms for study participants who have been paid a total of more than \$400.00 during the calendar year, should submit the completed SSN forms along with a separate list that includes the dollar amount paid to each subject, to [Disbursement Services](#) .
- The SSN forms should be hand-delivered to the attention of the Director, Disbursement Services (located at 104 Airport Road, Suite 3500). If hand-delivery is not possible, the forms should be sent via campus mail or faxed (least preferred).
- *No study-related information* is required by Disbursement Services, which should alleviate concerns about identities being linked to potentially-sensitive research topics by others outside the research team.
- Disbursement Services will file necessary tax forms with the IRS and the individual (i.e., 1099-Misc).
- Note: Researchers may elect to submit completed W-9 forms to Disbursement Services in lieu of SSN forms, in which case, the SSN forms should be destroyed. Regardless of which form is submitted to Disbursement Services, study participants must sign the appropriate SSN form.
- Confidentiality:
 

SSNs and other PII must be maintained utilizing proper security measures to protect the information. Proper security measures include, for example, locked file cabinets in locked offices, password-protected electronic files, and encryption. An investigator or any other member of the research team may not intentionally communicate or otherwise make available to the general public a person's SSN or other PII.
- Breach of Confidentiality:
 

In the event of a security breach, as defined by the University's "Data Security Breach Protocol," (<http://policies.unc.edu/policies/breach-protocol/>) the matter must be reported immediately to the Information Technology Resources Center at 919-962-HELP or Campus Police at 919-962-8100, as specified in the Protocol.
- Statement of Contractor Compliance:
 

When the IRB approves collection and disclosure of an SSN to an outside entity (e.g., research sponsors or database administrators), the outside receiving party must complete a [Statement of Contractor Compliance with the North Carolina Identity Theft Protection Act of 2005](#). This signed form should be kept with the investigator's study records.

### **2.16.5 DEFINITIONS:**

Social Security Number (SSN) – SSN refers to the unique nine-digit number assigned by the United States government to individuals. For the purposes of this SOP, this also applies to the use of 4 or more digits of the SSN when accompanied by place and date of birth. This SOP also applies to circumstances where an individual subject (e.g., a worker who is not a US resident) has an Individual Tax Identification Number (ITIN) in lieu of an SSN.

Personal Identifying Information (PII) consists of:

1. SSN, ITIN or Employer Taxpayer Identification Numbers (EIN)
2. Driver's license (unless appearing in a law enforcement record), State identification card, or passport numbers.
3. Checking account numbers.
4. Savings account numbers.
5. Credit card numbers.
6. Debit card numbers.
7. Personal Identification (PIN) codes, which are numeric and/or alphabetical codes assigned to the cardholder of a financial transaction card (FTC) by the issuer to permit authorized electronic use of that FTC.
8. Digital signatures.
9. Any other numbers or information that can be used to access a person's financial resources.
10. Biometric data
11. Fingerprints
12. Passwords

Legally Authorized Representative A legally authorized representative is an individual or body authorized under applicable law to provide permission on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. For the purposes of this policy, a legally authorized representative includes.

Legal guardian. A person appointed by a court of appropriate jurisdiction.

### **3 References:**

UNC Material & Disbursement Services: [http://www.unc.edu/mds/ds/help\\_hint.htm](http://www.unc.edu/mds/ds/help_hint.htm)

NC Identity Theft Protection Act of 2005: <http://www.unc.edu/depts/legal/ssn>  
NCGS §14-309.15 Raffles