Title: Informed Adult Consent, Minor Assent, and Parental/Guardian Permission
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12.1 Executive Summary

This document provides information regarding the informed consent process for research involving human subjects. This document contains information regarding NC State University's IRB policy, standard operating procedures, and terms and definitions. This document outlines the processes that researchers should follow when determining the most appropriate manner for implementing informed consent for the proposed study and any considerations that the IRB will make regarding communication of informed consent, continued consent, and waiver of consent.

12.2. Standard Operating Practice

When completing research with human subjects, all NC State University faculty, staff, students, or others acting on behalf of the University, must obtain informed consent in accordance with 45 CFR 46.116 (opens in a new window) and 45 CFR 45.117 (opens in a new window) from participant's or their legally authorized representative unless the IRB has granted a waiver of consent. This includes informed consent, parental permission, and minor assent documents. All procedures related to the informed consent process must be documented within the approved IRB protocol and supplemental approved documents. The IRB will evaluate all forms and processes for obtaining and documenting informed consent, parental permission, and minor assent.

12.3. Operational Procedures

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 NC State 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 begins when the participant first learns of the study through recruitment, continues through formally requesting consent to be in the study through written or verbal communication, and then continues through voluntary participation within a research environment promoting a culture of voluntariness, data destruction, and publication of findings.

12.3.a. Informed Consent Process

In accordance with 45 CFR 46.116 (opens in a new window) informed consent must be obtained under the following circumstances:

1. Informed consent is a process by which the interests and the concerns of the participant are centered in the information you give and the conversations that you have. The purpose of this consent process is to give the participant or representative all of the relevant information that will help them decide whether or not participating in the research is a good fit for them. Throughout the informed consent process, information must be presented in a manner that is consistent, organized, avoids jargon, is comprehensible to the individual, and provides some way for participants or their representatives to ask questions.

2. The informed consent process provides the prospective subject (or legally authorized representative) with sufficient opportunity to read the consent document, when applicable. This means that participants must have the time and resources to properly

consider the risks, benefits, and time required to be in the study.

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 investigator is responsible for ensuring that each prospective subject is adequately informed about all aspects of the research and understands the information provided. This responsibility starts with recruitment and ends when the study is complete.

12.3.b General Requirements for an Informed Consent Form

1. When using an informed consent form, 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.

2. The information on the informed consent form must present in sufficient detail relating to the research and must be organized and presented in a way that does not merely provide lists of isolated facts but rather facilitates the prospective subject's or legally authorized representative's understanding of the reasons why one might or might not want to participate.

3. The informed consent form must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research.

4. The information on the informed consent form 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 sixth-grade level and layman’s terms shall be used in the description of the research.

5. 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.

6. The informed consent form 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.

12.3.b.i Basic Elements of Informed Consent:

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 that 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 that 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 will 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. One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:

    a. A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility; or

    b. A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies

12.3.b.ii Additional Elements of Informed Consent, as Appropriate

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

2. Anticipated circumstances under which the participant’s participation may be terminated by the investigator without regard to the participant’s or the legally authorized representative's consent;

3. Any additional costs to the participant that may result from participation in the research;

4. The consequences of a participant's decision to withdraw from the research and procedures for orderly termination of participation by the participant;

5. 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;

6. The approximate number of participants involved in the study;

7. A statement that the participant's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;

8. A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to participants, and if so, under what conditions; and

9. 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).

12.3.c. Parent/Guardian Permission and Minor Assent

12.3.c.i. Definitions

1. Children are persons who have not attained the legal age for consent to treatments or procedures involved in the research under the applicable law of the jurisdiction in which the research will be conducted.

2. Assent is a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

3. Permission is the agreement of parent(s) or guardian(s) to the participation of their child or ward in research.

4. The parent is a child's biological or adoptive parent.

5. A guardian is an adult who is authorized under applicable state or local law to consent on behalf of a child to general medical care.

12.3.c.ii. Processes for Parent/Guardian Permission and Minor Assent

1. Minor Assent:

a. In accordance with 45 CFR 46.408 (opens in a new window) the IRB shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent.
b. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate.

c. If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research.

d. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived.

e. When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

f. Regarding inclusion of minors attending institutions of postsecondary higher education, please refer to the IRB unit standard on inclusion of minors enrolled in post-secondary institutions (Word document).

2. Parental/Guardian Permission

a. The IRB shall determine that adequate provisions are made for soliciting the permission of each child's parents or guardian.

b. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research to be conducted is minimal risk or has direct benefits to the minor.

c. Where research is more than minimal risk or otherwise not and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

d. If the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with federal, state or local law. The choice of an appropriate mechanism would depend upon

the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

e. Permission by parents or guardians shall be documented.

12.3.d. Translation of Forms and Interpreters for Non-English Speakers

12.3.d.i. Translation of Forms

1. When the investigator can anticipate enrollment of persons who do not speak or read, or have limited proficiency in oral or written English, or the investigator otherwise anticipates that consent will be conducted in a language other than English, the IRB requires a translated consent document and other appropriate materials to be prepared.

2. For studies reviewed at the expedited or convened full board level, a translation verification form must be submitted. In some cases, the NC State University IRB may request an additional translation certification.

12.3.d.ii. Interpreters

1. Unless the person obtaining consent is fluent in the prospective subject's language, an interpreter will be necessary to facilitate the consent discussion.

2. The NC State University IRB prefers that the translator be someone who is independent of the subject (i.e., not a family member) and should assist in presenting information and obtaining consent.

3. Whenever possible, interpreters should be provided copies of the IRB-approved consent materials (e.g., translated consent or short form consent, verbal script, etc.) well before (24 to 48 hours if possible) the consent discussion with the subject.

12.3.e. Consent Waivers, Alterations, Opt-Outs, Sampling Frames, and for Data Reuse

12.3.e.i Waivers of Consent

1. An IRB may waive the requirement to obtain informed consent for research provided the research protocol satisfies all five of the requirements noted below:

    a. The research involves no more than minimal risk to the subjects;

    b. The research could not practicably be carried out without the requested waiver;

    c. If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using them in an identifiable format;

    d. The waiver of consent will not adversely affect the rights and welfare of the subjects; and

e. Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.

2. If an individual was asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable (see section 12.3.g. below), and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.

12.3.e.ii. Waivers of Signed Consent

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

1. 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. 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.

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.

4. An electronic signature where a participant types their name onto the consent form is considered acceptable documentation for most research projects.

5. “Clicking yes/no” to consent requires a request to waive documentation of written consent.

12.3.e.iii. Alternations of Consent

An IRB may approve a consent procedure that omits some, or alters some or all, of the elements of informed consent provided the research protocol satisfies all five of the requirements below (*cf.* Appendix B for details):

1. The research involves no more than minimal risk to the subjects;

2. The research could not practicably be carried out without the requested waiver;

3. If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using them in an identifiable format;

4. The waiver of consent will not adversely affect the rights and welfare of the

subjects; and

5. Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.

12.3.e.iiv. Opt-Out Forms

1. An “opt-out” form is a letter sent to participants or their legally authorized representative that provides all relevant information about a study.

2. With opt-outs, the participants default to being in the research unless they (or their legally authorized representative) actively decline participation via an “opt-out” form.

3. The use of an “opt-out” form is acceptable when the study qualifies for a waiver of consent (*cf.* 12.3.e.i and Appendix B).

12.3.e.iiv. Sampling Frames and Consent

An IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject's legally authorized representative if either of the following conditions are met:

1. The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative, or

2. The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.

12.3.e.iiv. Reuse of Research Data and Consent

1. All anonymous and de-identified data can be reused for other research studies without additional consent from research subjects.

    a. Anonymous data is data about a living individual that was or is collected in a manner that identifiers were never associated with the information and that no one is able to identify the individual from whom the information was collected.

    b. De-identified data is data that the research team had access to in an identifiable or indirectly identifiable format but they have processed the data in such a way that the data no longer contains any personally identifying information of participants and no member of the research team can identify or re-identify respondents from the newly cleaned data set.

2. Re-identifiable and identifiable data cannot be reused for other research studies without explicit additional consent from participants.

    a. Re-identifiable data is that has direct identifiers (e.g., name, email, etc.) removed but retains indirect identifiers (e.g., demographics) in such a manner that a participant’s identity is readily ascertainable either because of the researcher’s positionality and expertise, the data content itself, the number of

participants, and/or data triangulation.

b. Identifiable data is data that directly links an individual participant's identity, such as a name, email, or full-face image so that the person is immediately known to anyone who views the material.

3. If an opportunity arises to reuse data from the IRB-approved project for research activities not listed in the consent form and broad consent (see section 12.3.g. below) was not sought and obtained during initial data collection, the researcher must seek approval from the IRB to re-contact participants in order to get their consent to use their research data for purposes not outlined in the consent form that they agreed to. If recontacting participants is not possible, the IRB will determine whether the proposed new use of the data is within the spirit and scope of the study's purpose and use of the data that the participant agreed to.

12.3.g. Broad Consent

1. Broad consent is an additional consent process beyond the consent to research.

2. Broad consent cannot be required to participate in a research study.

3. Broad consent allows the research team to store, maintain, and reuse identifiable private information or identifiable biospecimens for future unspecified research projects beyond the initial research study that the participants agree to.

4. If a participant or their legally authorized representative is asked to provide broad consent, the following must be provided to them:

   a. A description of the identifiable private information or identifiable biospecimens that might be used in research, whether sharing of identifiable private information or identifiable biospecimens might occur, and the types of institutions or researchers that might conduct research with the identifiable private information or identifiable biospecimens.

   b. A general description of the types of research that may be conducted with the identifiable private information or identifiable biospecimens. This description must include sufficient information such that a reasonable person would expect that the broad consent would permit the types of research to be conducted.

   c. A description of the period of time that the identifiable private information or identifiable biospecimens may be stored and maintained (which period of time could be indefinite), and a description of the period of time that the identifiable private information or identifiable biospecimens may be used for research purposes (which period of time could be indefinite).

   d. Unless the subject or legally authorized representative will be provided details about specific research studies, a statement that they will not be informed of the details of any specific research studies that might be conducted using the subject's identifiable private information or identifiable biospecimens, including the purposes of the research, and that they might have chosen not to consent to some of those specific

research studies.

e. Unless it is known that clinically relevant research results, including individual research results, will be disclosed to the subject in all circumstances, a statement that such results may not be disclosed to the subject.

f. An explanation of whom to contact for answers to questions about the subject's rights and about storage and use of the subject's identifiable private information or identifiable biospecimens, and whom to contact in the event of research-related harm.

g. For broad consent that involves biospecimens:

    i. A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit

    ii. 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).

12.3.h. Research Environment

12.3.h.i. Undue Influence

1. Undue influence is an offer of an excessive or inappropriate reward or other overture to an individual in order to obtain compliance.

2. Undue influence can be subtle because it is contextual and depends on both the researcher’s and the participant’s positionality.

3. When considering the recruitment, consent, and data collection methods, researchers must design their research to manage any aspects of undue influence as a result of power dynamics.

12.3.h.ii. Coercion

Coercion occurs when an overt or implicit threat is intentionally presented by one person to another in order to obtain compliance.

12.3.h.iii. Encouraging a Culture of Voluntariness and Partnership

1. The researcher should implement a "general inquiry" into the motivations for a person's decision to enroll in a study. This practice builds relationships, trust, and it allows the researcher to pay attention to external and intentional influences that may impair voluntariness. Once this information is shared, the researchers can assess the legitimacy of the consent.

2. The researcher should continually assess the participant's verbal communication, body language, active participation, and demonstrated interest in being a part of the study.

3. Researchers should implement routine checkpoints to assess consensual

participation and provide reminders of voluntariness.

4. When completing immersive qualitative research, the researcher has an obligation to maintain boundaries - ensuring the participant knows the difference between what they are consenting to be used as data for research and what they are not.

12.3.i. Revocation of Consent

12.3.i.i. Timeline

A participant, their legally authorized representative, or their parent/guardian may revoke consent at any time during the study.

12.3.i.ii. Processes

1. Information about the revocation of consent and its limitations must be articulated in the informed consent form.

2. The method(s) to stop participation must be clearly articulated in the informed consent form.

3. A researcher's actions should reflect when a participant revokes their consent.

    a. When a participant revokes their consent during data collection, all procedures should be halted and their data destroyed unless destruction of the data is impossible or the participant requested that it not be destroyed.

    b. When a participant revokes their consent after data collection is completed, their data should be destroyed unless destruction of data is impossible or the participant has requested that it not be destroyed.

    c. If the participant revokes their consent once the data is published, the researcher should destroy the participant's data unless the participant has requested it not be destroyed. It should be clear in the initial consent process that revocation of consent is always possible but/and once the study is completed and published, redaction of data is not always possible.

Appendix A

Legally Authorized Representative

Federal regulations that govern research involving human subjects define a legally authorized representative (LAR) as an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

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
2. A health care power of attorney (HCPOA)
3. A durable general power of attorney
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 by the other individuals listed below, in order of priority.
    a. The subject’s spouse;
    b. A majority of the subject’s reasonably available parents and adult children;
    c. A majority of the subject’s reasonably available adult siblings; or
    d. 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.

Appendix B

Details Regarding the Criteria of a Waiver of Consent

The research involves no more than minimal risk to the subjects

Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests, which is that the study:

- defines a threshold of anticipated harm or discomfort associated with the research that is "acceptably low" or "low enough";
- harms' and discomforts' are considered within the nature of the study procedures, other study characteristics, subject characteristics, and steps taken to minimize risk;
- considers subjects' characteristics, including an evaluation of subject susceptibility, vulnerability, resilience, and experience in relation to the anticipated harms and discomforts of research involvement;
- estimates that the anticipated harms and discomforts of the research for the proposed study population is not greater than an estimate of "the harms and discomforts ordinarily encountered in daily life or during the performance of routine medical and psychological examinations or tests"
    - An ethically meaningful notion of "harms and discomforts ordinarily encountered" should reflect "background risks" that are familiar and part of the routine experience of life for "the average person" in the "general population." It should not solely be based on those ordinarily encountered in the daily lives of the proposed subjects of the research or any specific population.
- applies minimal risk in a manner that recognizes that risks are procedure-specific and population-dependent and that the notion of acceptably low risk is fixed. When the harms and discomforts of the proposed research as they are anticipated to impact the study participants are judged to fall below this acceptably low risk threshold, the research is said to be "minimal risk."

The research could not practicably be carried out without the requested waiver or alteration

The commonly accepted definitions of the term "practicable" are:

- feasible;
- capable of being effected, done, or put into practice; and
- that may be practiced or performed; capable of being done or accomplished with available means or resources.

It should be noted that this criterion states that the research could not practicably be carried out without the waiver or alteration. Put another way, it would not be practicable to perform the research (as it has been defined in the protocol by its specific aims and objectives) if consent were required. <u>The emphasis being that it is impracticable to perform the research, and not just impracticable to obtain consent.</u> The justification must provide a reasonable rationale for why the research would not be possible without the waiver.

The following concepts may help an IRB determine whether the research could not be practicably carried out without the waiver of consent:

- Scientific validity would be compromised if consent were required.
- Ethical, legal, or risk-related concerns would be raised if consent were required.

- There is a scientifically and ethically justifiable rationale for why the research could not be conducted with a population from whom consent can be obtained.
- Practicability should not be determined solely by considerations of convenience, cost, or efficiency.

If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using them in an identifiable format

- A justification is required as to why identifiers are required to be directly on the data or linked to the data via a master list.
- Examples of scientific rationales include sharing results with participants and longitudinal studies.

The waiver or alteration will not adversely affect the rights and welfare of the subjects

- Whether there are other federal, state, or local laws that provide rights to potential subjects to require informed consent. IRBs should seek advice from their legal counsel when appropriate to help the IRB with these determinations. This would be especially important for state-specific regulations.
- Whether the subject population, in general, would object if they knew of the waiver and its intent in facilitating research.
- Whether the subject population, in general, would consider that the waiver has the potential to cause adverse consequences for their welfare or general well-being.

Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation

- This criterion is intended to refer to the need to consider debriefing after research is conducted. In these situations, it may be ethically required or determined to be respectful to provide the subject with pertinent information after the research is complete. IRBs may want to consider this mechanism when subjects are included in "deception research," in which some aspects of the study are not fully disclosed upfront so that subject responses are not biased.
- Under most circumstances, this criterion does not apply to retrospective research conducted under a waiver (e.g., review of existing records).