

## STANDARD OPERATING PROCEDURE

### OBJECTIVE/SCOPE

To ensure that the human research subject is provided with the information necessary to understand the risks and benefits and their rights as a research subject participant.

Note: The current version of this document complies with 2018 Revised Common Rule Requirements effective January 21, 2019. Previous versions should be referenced for Pre-2018 Common Rule Requirements.

### MATERIALS

Not applicable

### SAFETY

Not applicable

### DEFINITIONS

1. **Assent:** A minor child's affirmative agreement to participate in research.
2. **Common Rule:** A Federal Policy for the Protection of Human Subjects codified in separate regulations by the Department of Health and Human Service (DHHS) and other Federal departments and agencies.
  - 2.1. **2018 Revised Common Rule Requirements:** Revised Federal Policy for the Protection of Human Subjects (Revised Common Rule) requirements effective on January 21, 2019.
  - 2.2. **Pre-2018 Common Rule Requirements:** Federal Policy for the Protection of Human Subjects (Common Rule) requirements originally published on June 18, 1991 and effective until January 21, 2019.
3. **Human subject (or human being as an experimental subject):** A living individual about whom an investigator (whether professional or student) conducting research:  
(i) obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens. A human subject may also be an individual who is or becomes a participant in research, either as a recipient of a test article or as a control, or an individual on whom or on whose specimen an investigational device is used. A human subject may or may not be a healthy individual.
4. **Informed consent:** A process of information exchange that may include subject recruitment materials, verbal instructions, and question/answer sessions in addition

to reading and signing the informed consent document. The process provides the research subject with the information necessary to assure the subject understands the potential risks and benefits and their rights as a research participant.

5. **IRB of record:** The IRB of record is the IRB responsible for conducting the IRB reviews of a study on behalf of a participating study site.
6. **Legally authorized representative:** 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.
7. **Minimal risk:** 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.

## **PROCEDURE**

### **1. Elements of informed consent**

- 1.1. Informed consent 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. This part of the informed consent must be organized and presented in a way that facilitates comprehension. Informed consent as a whole must present information 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.
  - 1.1.1. Generally, the following elements of consent should be considered to encompass key information:
    - 1.1.1.1. The fact that consent is being sought for research, and that participation is voluntary;
    - 1.1.1.2. The purposes of the research, the expected duration of the prospective subject's participation, and the procedures to be followed in the research;
    - 1.1.1.3. The reasonably foreseeable risks or discomforts to the prospective subject;
    - 1.1.1.4. The benefits to the prospective subject or to others that may reasonably be expected from the research;
    - 1.1.1.5. Appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the prospective subject.
  - 1.1.2. The elements of consent listed above may or may not be sufficient to satisfy the requirement for providing key information depending on the study. Other elements of consent, including additional information, may be required for a study if it would assist a prospective subject in

understanding the reasons why one might or might not want to participate in the research.

- 1.1.3. The concise and focused presentation of key information should be brief but comprehensive, leaving the detailed elaboration of the information for the body of the consent form.
- 1.1.4. For relatively simple research studies with limited risk, if all the information provided in the body of the consent satisfies the requirements for concise and focused presentation of key information and a description of any reasonably foreseeable risks or discomforts, the consent form does not need to begin with a summary of key information.
- 1.2. Basic elements of informed consent
  - 1.2.1. In seeking informed consent, the following basic elements of informed consent shall be provided to each subject or the legally authorized representative:
    - 1.2.1.1. 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.
    - 1.2.1.2. A description of any reasonably foreseeable risks or discomfort to the subject.
    - 1.2.1.3. A description of any benefits to the subject or to others which may reasonably be expected from the research.
    - 1.2.1.4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.
    - 1.2.1.5. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.
    - 1.2.1.6. For FDA-regulated research, a statement that notes the possibility that the Food and Drug Administration may inspect the records.
    - 1.2.1.7. For an applicable clinical trial regulated by the FDA, a statement noting that the results of the research will be posted on [clinicaltrials.gov](http://clinicaltrials.gov).
    - 1.2.1.8. 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.
    - 1.2.1.9. An explanation of whom to contact for answers to pertinent questions about the research, including concerns or complaints.
    - 1.2.1.10. An explanation of whom to contact for questions about the research subject's rights, and whom to contact in the event of a research-related injury to the subject.
    - 1.2.1.11. An explanation of whom to contact independent of the research team for problems, concerns, questions, information, or input.
    - 1.2.1.12. 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.

- 1.2.1.13. One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens: (i) a statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility; or (ii) a statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

### 1.3. Additional elements of informed consent

- 1.3.1. When appropriate, additional elements of informed consent may be required. For example:

- 1.3.1.1. 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.
- 1.3.1.2. The approximate number of subjects involved in the study.
- 1.3.1.3. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.
- 1.3.1.4. Any additional costs to the subject that may result from participation in the research.
- 1.3.1.5. The consequences of a subject's decision to withdraw from the research.
- 1.3.1.6. Procedures for orderly termination of participation by the subject.
- 1.3.1.7. 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.
- 1.3.1.8. The amount and schedule of all payments to the subject.
- 1.3.1.9. 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.
- 1.3.1.10. A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions.
- 1.3.1.11. 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).

- 1.4. Per 2018 Revised Common Rule Requirements, broad consent is an alternative consent process for storage, maintenance, and secondary

research uses of identifiable private information and identifiable biospecimens. The NMDP has chosen not to use broad consent as an alternative consent process.

1.5. Consent language regarding Certificates of Confidentiality

1.5.1. For studies funded by the NIH that commenced or are ongoing on or after December 13, 2016, in which informed consent is sought, investigators must inform research participants of the protections and the limits to protections provided by a Certificate of Confidentiality. This language must be added to the consent form.

1.5.2. For any other studies that have been issued a Certificate of Confidentiality by a federal agency, language must be included in the consent form to inform research participants of the protections and the limits to protections provided by the Certificate of Confidentiality.

2. Documentation of informed consent

2.1. National Marrow Donor Program (NMDP) Institutional Review Board (IRB) consent form

2.1.1. Informed consent of the research subject shall be documented by the use of a written consent form approved by the NMDP IRB.

2.1.2. The IRB shall affix the approval date to all approved informed consent documents. Only these dated documents may be used for obtaining informed consent.

2.1.3. The consent document embodies the basic and appropriate additional elements of disclosure.

2.1.4. The subject or the subject's legally authorized representative will sign and date the consent document.

2.1.4.1. If consent is obtained from an individual who is unable to read and/or write but can otherwise communicate and is not cognitively impaired (e.g., blind, illiterate, physically unable to write), a witness must be present during the consent session and sign the consent document attesting to the research participant's consent to participate.

2.1.5. A copy of the consent document will be given to the person signing the consent document.

2.1.6. The investigator will give either the subject or the representative adequate opportunity to read the consent document before it is signed.

2.2. Short form and written summary

2.2.1. When the informed consent has been presented orally to the study subject (or their legally authorized representative), the short form may be used to document this process.

2.2.2. The short form, a written consent document in the subject's primary language, must state that the basic elements of informed consent and appropriate additional elements of disclosure, as required by the Code of Federal Regulations (21 CFR 50.27 and 45 CFR 46.116), have been

presented orally to the subject or the subject's legally authorized representative. When applicable, the key information required by §46.116(a)(5)(i) should be presented first to the subject, before other information, if any, was provided.

- 2.2.3. The NMDP IRB-approved consent document will serve as the "written summary" when consenting subjects using the short form.
  - 2.2.4. There will be a witness to the oral presentation.
    - 2.2.4.1. For subjects who do not speak English, the witness is conversant in both English and the language of the subject.
    - 2.2.4.2. The witness will sign both the short form and a copy of the summary (i.e., NMDP IRB-approved consent document).
  - 2.2.5. The subject (or their legally authorized representative) will sign and date the short form.
  - 2.2.6. The person actually obtaining consent will sign a copy of the summary.
  - 2.2.7. A copy of the short form and summary will be given to the subject or the representative.
  - 2.2.8. Circumstances of use
    - 2.2.8.1. A person speaks and understands English, but does not read and write English.
    - 2.2.8.2. A person who can understand and comprehend spoken English, but is physically unable to talk or write.
    - 2.2.8.3. A person is unexpectedly encountered that does not speak or understand English.
    - 2.2.8.4. A short form, or any other consent form, may not be used if the person does not retain the ability to understand the concepts of the study and evaluate risk and benefit of being in the study.
- 3. Requirements for permission by parents or guardians and for assent by children (per 45 CFR 46.408)**
- 3.1. 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. 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. 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. 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 in accord with [§45 CFR 46.116](#) of [Subpart A](#).

- 3.2. The IRB shall determine, in accordance with and to the extent that consent is required by [§45 CFR 46.116](#) of [Subpart A](#), that adequate provisions are made for soliciting the permission of each child's parents or guardian. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research to be conducted under [§46.404](#) or [§46.405](#). Where research is covered by [§46.406](#) and [46.407](#) 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.
- 3.3. In addition to the provisions for waiver contained in [§45 CFR 46.116](#) of [Subpart A](#), 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.
- 3.4. Permission by parents or guardians shall be documented in accordance with and to the extent required by [§45 CFR 46.117](#) of [Subpart A](#).
- 3.5. When the IRB determines that assent is required, it shall also determine whether assent must be documented and make recommendations for how assent must be documented (e.g., approval of template assent forms).
  - 3.5.1. Institutions relying on the NMDP IRB as their IRB of record for a study may follow their institutional requirements for how assent is documented.

#### 4. Translations

- 4.1. When the study subject population is anticipated to include non-English speaking people, the NMDP IRB should require that a translated informed consent document be prepared. The NMDP IRB must assure that the translation is accurate by, for example, requiring a certification of accuracy to accompany the translation.

#### 5. Process for informed consent interview

- 5.1. The NMDP IRB must review the informed consent document that will be administered to the research subject.
- 5.2. The NMDP IRB must review the process for conducting informed consent interviews (i.e., the circumstances under which informed consent will be obtained, who will obtain informed consent, etc.).

- 5.2.1. The process for obtaining consent must incorporate all of the following:
  - 5.2.1.1. The legally effective informed consent of the subject or the subject's legally authorized representative will be obtained.
  - 5.2.1.2. Consent will be sought only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate.
  - 5.2.1.3. Consent will be sought only under circumstances that minimize the possibility of coercion or undue influence.
  - 5.2.1.4. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative.
  - 5.2.1.5. The informed consent does not include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the participant's legal rights.
  - 5.2.1.6. The informed consent does not release or appear to release the investigator, the sponsor, the institution, or its agents from liability for negligence.

## 6. Waiver of informed consent

- 6.1. If the research is not FDA-regulated, the IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent or waives the requirements to obtain informed consent, provided that the IRB finds and documents that the criteria for waivers or alterations, found in 45 CFR 46.116 (f), are met.
- 6.2. If the research is FDA-regulated, the IRB may waive or alter the consent process if the regulatory criteria found in the FDA guidance, *IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects (July 2017)* are met.
- 6.3. If a broad consent procedure is used, the IRB may not omit or alter any of the required elements of consent, or when appropriate, any of the additional elements of consent.
- 6.4. The IRB may waive parental permission by determining that the criteria for waivers or alterations are met and documenting those findings.
- 6.5. If the study is funded by the Department of the Navy (DoN), and is research involving human beings as experimental subjects, the consent process may not be waived unless a waiver is obtained from the Assistant Secretary of Defense for Research and Engineering. However, if the research does not involve human beings as experimental subjects, the IRB may waive the consent process. (Refer to Department of Defense Instruction 3216.02, section 9 and Glossary)
  - 6.5.1. The Assistant Secretary for Defense for Research and Engineering may waive the requirements for consent when all of the following are met:
    - 6.5.1.1. The research is necessary to advance the development of a medical product for the Military Services.



- 6.5.1.2. The research may directly benefit the individual experimental subject.
- 6.5.1.3. The research is conducted in compliance with all other applicable laws and regulations.
- 6.5.1.4. The research is not considered classified.
- 6.6. If an individual was asked to provide broad consent for the storage maintenance, and secondary research use of identifiable private information or identifiable biospecimens 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.

## 7. Waiver of documentation of informed consent

- 7.1. If the research is not FDA-regulated, the IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects in accordance with 45 CFR 46.117(c)(1) if it finds any of the following:
  - 7.1.1. That the only record linking the subject and the research would be the informed consent form and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject (or legally authorized representative) will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern;
  - 7.1.2. That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context; or
  - 7.1.3. 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.
- 7.2. If the research is FDA-regulated, the IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects in accordance with 21 CFR 56.109(c) if it finds:
  - 7.2.1. That the research presents no more than minimal risk of harm to subjects; and
  - 7.2.2. The research involves no procedures for which written consent is normally required outside the research context
- 7.3. The IRB must document its findings justifying the waiver of documentation of informed consent.
- 7.4. When the IRB considers waiving the requirement to obtain written documentation of the consent process, the IRB must review a written description of the information that will be provided to subjects.
  - 7.4.1. If the IRB grants a waiver of the requirement to obtain written documentation of the consent process, the IRB should consider requiring

the Researcher to provide subjects with a written statement regarding the research.

## 8. When participants withdraw from a FDA-regulated clinical trial

- 8.1. When a participant withdraws from a study, the data collected on the participant to the point of withdrawal remains part of the study database and may not be removed. The consent document cannot give the participant the option of having data removed.
- 8.2. A researcher may ask a participant who is withdrawing whether the participant wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the participant distinguishes between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through non-invasive chart review, and addresses the maintenance of privacy and confidentiality of the participant's information.
  - 8.2.1. The researcher must obtain the participant's consent for this limited participation in the study (assuming such a situation was not described in the original consent document). The IRB must approve the consent document.
- 8.3. If a participant withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the researcher must not access for purposes related to the study the participant's medical record or other confidential records requiring the participant's consent. However, a researcher may review study data related to the participant collected prior to the participant's withdrawal from the study, and may consult public records, such as those establishing survival status.

## 9. Remote Consent Sessions and Electronic Consent Signatures

- 9.1. Remote consent sessions are acceptable to the NMDP IRB, provided:
  - 9.1.1. The study protocol does not specify that the consent session must be done in person.
  - 9.1.2. Phone or videoconference consent sessions are not prohibited by the participating research site's Standard Operating Procedures.
  - 9.1.3. The research participant has the consent form in front of him/her (in either paper or electronic format) when the consent session is being discussed.
  - 9.1.4. The research participant feels he/she is in a private space and is comfortable to discuss the study and ask questions.
  - 9.1.5. The research participant is given the opportunity to ask questions.
  - 9.1.6. No research procedures may begin until the study site has the signed consent document back from the research participant.

- 9.2. Additionally, when obtaining consent remotely, researchers must:
- 9.2.1. Document in the research chart the conversation that took place, name of the study team member who provided the information, date and time.
  - 9.2.2. Document how the informed consent document was transmitted to the research participant (e.g., email, fax, mail, etc.).
  - 9.2.3 Document how the research participant's signature was obtained. For example:
    - 9.2.3.1 Electronic signature
    - 9.2.3.2 Scanned and emailed, faxed, or mailed back to the study team
    - 9.2.3.3 Photograph of signature/signature page sent back to the study team
  - 9.2.3. NOTE: For FDA-regulated research, the electronic signature program used by the site must be compliant with 21 CFR 11 regulations.

**10. Re-consent at Age of Majority (per OHRP Guidance *Research with Children FAQs*)**

- 10.1. The Office for Human Research Protections (OHRP) notes that informed consent should be viewed as an ongoing process throughout the duration of a research project. When a child who was enrolled in research with parental or guardian permission subsequently reaches the legal age of consent to the procedures involved in ongoing research, the subject's participation in the research is no longer regulated by the requirements of [45 CFR part 46.408](#) regarding parental or guardian permission and subject assent.
- 10.2. Unless the Institutional Review Board (IRB) determines that the requirements for obtaining informed consent can be waived, the investigators should seek and obtain the legally effective informed consent, as described in [45 CFR 46.116](#), for the now-adult subject for any ongoing interactions or interventions with the subjects. This is because the prior parental permission and child assent are not equivalent to legally effective informed consent for the now-adult subject. However, the IRB could approve a waiver of informed consent under [45 CFR 46.116\(d\)](#), if the IRB finds and documents that the required conditions are met.
- 10.3. Similarly, if the research does not involve any ongoing interactions or interventions with the subjects, but continues to meet the regulatory definition of "human subjects research" (for example, it involves the continued analysis of specimens or data for which the subject's identity is readily identifiable to the investigator(s)), then it would be necessary for the investigator(s) to seek and obtain the legally effective informed consent of the now-adult subjects. The IRB may consider, if appropriate, a waiver under [45 CFR 46.116\(d\)](#) of the requirements for obtaining informed consent in order for the subjects to continue their participation in the research.

**REFERENCES**

1. 21 CFR 50
2. 21 CFR 56
3. 45 CFR 46 Subpart A
4. 45 CFR 46 Subpart D
5. AAHRPP Standards (Association for the Accreditation of Human Research Protection Programs)
6. Department of Defense Instruction (DoDI) 3216.02
7. FDA Guidance: IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects
8. OHRP Guidance: Research with Children FAQs

**Revision History**

Revision	Brief Description of Revision
S00045 08/17/2001	New SOP
S00045 version 2.0	Annual Review: added Section 2.1.2
S00045 version 3.0	Added Section 1.2.1.2. Updated Sections 2.1, 2.2.2, and 2.2.3.1. Formatting changes.
S00045 rev. 4	Put into new SOP format. Clarifications in Section 1.1.1 and added Section 1.1.1.10. Added Sections 1.2.1.3 through 1.2.1.8. Added Sections 2.1.3 through 2.1.6. Clarifications in Section 2.2.1 and 2.2.2. and added Sections 2.2.3 through 2.2.7. Added Section 4.2.1 and Section 6.
S00045 rev. 5	Added definition of Human subject. Added 5.2 – 5.4, 6.1.1, 6.2, and 6.2.1. Clarification made to 5.1.
S00045 rev. 6	Added 1.1.1.7 posting on clinicaltrials.gov. Clarifications made to 5.4 and added 5.4.1. Added DoDI reference doc.
S00045 rev. 7	Added section 7 about participants withdrawing from a FDA-regulated clinical trial
S00045 rev. 8	Added note about Common Rule Requirements to objective/scope. Added definitions. Updated definition of “Human Subject.” Added 2018 requirements under the elements of informed consent in section 1, documentation of informed consent in section 2, and waiver of informed consent in section 6. Added CoC requirements in section 1.5. Added section 3 regarding parental permission and minor assent. Added

	References.
S00045 rev. 9	Added sect 2.1.4.1. Added criteria for waiver of documentation of consent in sect 7. Added sect 9 on Remote Consent Sessions and Electronic Consent Signatures and sect 10 on Re-consent at Age of Majority.
S00045 rev. 10	Added 1.1.1, 1.1.2, and 1.1.3 regarding Key Information section of consent forms. Added 6.2 and 6.3. Added 7.2 and its subparts.

**ADDENDA**

Not applicable