**Guidance Resource – For Use as an Example only; Adapted from the MTN**

**[Site Name]**Standard Operating Procedure (SOP)

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**Title:** Informed consent: Research Involving Children
**Original Effective Date:** XX MMM YYYY **Revision Effective Date**: N/A

## Purpose

To define informed assent/permission/consent procedures for potential participants who are children.

## Scope

This procedure applies to all staff involved in obtaining informed assent, parental permission, and consent when children are research participants. *[Insert if applicable - Please refer to the Obtaining Informed Consent SOP for general information about obtaining consent.]*

## Introduction

Informed consent is an on-going process. The assent/permission/consent process begins at the initial contact with the potential participant and his/her parent(s)/legally autorized representative (LAR)/guardian and continues throughout the entire follow-up period of the study.

Children (minors) are considered a vulnerable research population and, as such, require additional protections when they are potential research participants. Subpart D of both 45 CFR 46 (DHHS) and 21 CFR 50 (FDA) require certain additional protections for children involved as participants in research. These regulations require that adequate provisions be made for soliciting the assent of all children involved in research, when the children are capable of providing assent, and obtaining parental/legally authorized representative/guardian’s permission, as applicable. In determining whether children are capable of assenting, the ages, maturity and psychological state of the children should be taken into account.

*Permitted Categories for Research with Children*

As per U.S. Federal regulations (45 CFR 46 and 21 CFR 50, Subpart D), permissible research involving children are limited to those activities that meet one of four categories, based on the level of risk and potential for benefit to the individual participant. These categories are:

1. Research not involving greater than minimal risk (§46.404 and §50.51);
2. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual participants (§46.405 and §50.52);
3. Research that involves more than minimal risk and presents the prospect of no direct benefit to individual participants, but generalizable knowledge (societal benefit) (§46.406 and §50.53); or
4. Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children (§46.407 and §50.54)

## Definiations (per §46.102/§46.402/§50.3)

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

*Children*: 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.

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*Guardian*: an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.

*Legally authorized representative (LAR)*: 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.

*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.

*Parent* means a child's biological or adoptive parent.

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

## Responsibilities

*[Research Nurses and/or Staff delegated by the Investigator of Record]* to obtain informed assent/permission/consent are responsible for:

* Understanding and following this SOP.
* Being adequately trained and qualified to obtain informed assent/permission/consent, as determined by the Investigator of Record (IoR), by education, training, experience, and knowledge of the trial.
* Conducting the informed assent/parental permission/consent process with the participant and his/her parent/LAR/guardian. He/she will inform the potential participant and his/her parent(s)/LAR/guardian that participating in the study is voluntarily, and that the potential participant and his/her parent(s)/guardian has a good understanding about the study procedures/study agents.
* Obtaining from each potential participant assent/informed consent (for children who can consent on their own behalf) as determined by the IRB/EC, and informed permission from the parent(s)/LAR/guardian prior to initiation of study procedures.
* Conducting the assent/permission/consent process in a private setting free of coercion and undue influence. The possible study benefits will not be overstated nor will the risks be understated. Extra time will be spent as necessary to ensure understanding of these issues.
* Delivering all required information in a manner that is understandable to a potential study participant and his/her parent(s)/LAR/guardian.
* Confirming that the participant and his/her parent(s)/LAR/guardian comprehends the information.
* Documenting the informed assent/permission/consent process, as applicable, including documenting the process in the chart notes.
* *[Insert site-specific procedures on how informed assent/permission/consent sessions will be structured. For example, if site staff will obtain permission from the parent(s)/LAR/guardian before obtaining assent from the participant*, *if sessions will be conducted simultaneously or separate, etc.]*

*Investigator of Record (IoR)* is responsibile for:

* Retaining overall responsibility for the conduct of a given trial at the site, including delegated tasks such as obtaining informed assent/permission/consent
* Ensuring staff delegated the task of obtaining informed assent/permission/consent are adequately trained and qualified by education, training, experience, and knowledge of the trial; training and qualifications are completed prior to the staff performing the delegated task.
* Ensuring that staff delegated the task of obtaining informed assent/permission/consent are listed on study-specific Delegation Logs prior to the staff performing the delegated task; Delegation Logs to be kept in the Regulatory binder.
* Having a detailed plan for the supervision and oversight for a given trial
* Ensuring that all applicable staff have received the appropriate training, follow this SOP, and are compliant with all applicable CFR regulations and ICH Guidelines.
* Supervising and training staff, including all procedures related to informed assent/permission/consent.
* Ensuring applicable SOPs are kept in the Regulatory binder

*Institutional Review Board (IRB)/Ethics Committee (EC)* is responsible for the following:

* Determining that adequate provisions are made for soliciting the assent of the children, as applicable.
* Reviewing and approving all the study-specific informed assent/permission/consent forms.
* Reviewing and approving all informed assent/permission/consent support materials that will be used during the informed assent/permission/consent process
* Classifying research involving children into one of four pediatric risk categories as per Subpart D of both 45 CFR 46 and 21 CFR 50, based on the degree of risk and benefit to individual participants, and document their discussions of the risks and benefits of the research study.

## Relevant Training for Staff Involved in the Informed Consent Process:

* Each staff member receives HSP/GCP training.
* Each staff member receives or has direct access to applicable SOPs.
* Each staff member obtaining informed assent/permission/consent reviews the applicable SOPs *[Insert frequency of review]*.
* All SOP training is documented and tracked *[Insert where the documentation is kept].*
* New staff are trained on applicable SOPs within *[Insert # of days]* days of employment.
* Staff members whose duties fall within this SOP scope are retrained within *[Insert # of days]* days of the approval of each SOP revision.

## General Procedures

*Child Assent*

The IRB/EC shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB/EC, the children are capable of providing assent, taking 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 for a given protocol, or for each child, as the IRB/EC deems appropriate. If the IRB/EC determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention(s) or procedure(s) 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/EC determines that the child participants are capable of assenting, the IRB/EC may still waive the assent requirement under circumstances as described in §46.408(c) and §50.55(d) of Subpart D.

When the IRB/EC determines that assent is required, it shall also determine whether and how assent will be documented. The use of modified and/or simplified language in a language understandable to the child is required and should cover the basic elements of consent as described in §46.116 and §50.25.

*Children Who Reach the Legal Age of Consent While Enrolled in a Study*

Informed consent is an ongoing process throughout the duration of a research study. When a child who was enrolled in research with parental/LAR/guardian permission reaches the legal age of consent, the participant’s participation no longer requires parental/LAR/guardian permission. Informed consent must then be obtained from the now-adult participant to continue research particpation, unless the IRB/EC determines that the requirements for obtaining informed consent can be waived.

*Consent Process for Minors Who Can Consent For Themselves*

Depending on the applicable law of the jurisdiction in which the research will be conducted, persons under the legal age of 18 *[or local legal age of consent]*, who because of their unique circumstances (e.g. emancipated minors, self-sufficient minors, etc.), may have the legal rights of adults, including the right to consent to treatments or procedures involved in research. Such individuals would not meet the definition of children as defined at §46.402 and §50.3.Hence, Subpart D would not apply to the research and parental/LAR/guardian permission (or waiver) is not required for these minors. Under these circumstances, minors may provide their own informed consent to participate in the research.

*Parental permission*

Sections §46.408 and §50.55 of Subpart D require that adequate provisions be made for soliciting the permission of parents/LAR/guardian of each child involved in a research study (unless the child is able to consent on his/her own behalf based on the applicable law of the jurisdiction in which the research will be conducted). All of the requirements concerning informed consent apply to obtaining parental/LAR/guardian permission and the appropriate elements of consent must be included in a written informed perission document. In addition to the information generally required in an adult consent form, the permission form should clearly describe aspects of the study that involve or affect the child. In some circumstances, it may be beneficial to discuss the level of parental involvement, and limitations on parental access to their child’s research data or responses.The IRB/EC may waive the requirement for obtaining parental permission as described in §46.408(c) for non-IND studies. FDA regulations (21 CFR 50) do not have a provision for waiver of parental/LAR/guardian permission).

Where parental permission is to be obtained, the IRB/EC may find that the permission of one parent is sufficient for research as per §46.408 and §50.55 of Subpart D (for research determined by the IRB/EC to be pediatric risk categories §46.404/405 and §50.51/52).

For research determined by the IRB/EC to be pediatric risk categories §46.406/407 and §50.53/54, 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.

*Wards*

Children who are wards of the state or any other agency, institution, or entity can be included in research approved under §46.404/405 and §50.51/52 only if the research is:

(1) Related to their status as wards; or
(2) Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

If the research is approved under this section, the IRB/EC shall require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB/EC) with the research, the investigator(s), or the guardian organization.

*Documentation of Informed Assent/Permission/Consent*

The permission form must be signed and dated by the parent(s)/LAR/guardian prior to the child’s participating in any study-related activities, unless permission is waived by the IRB/EC for non-IND studies. The parent(s)/LAR/guradian must be offered a copy of the consent form. If the potential parent(s)/LAR/guardian does not want a copy of the permission form, this should be documented in the chart notes. The original signed assent/permission/consent form must be kept on file in a locked cabinet at the site for audit purposes.

When the IRB/EC determines that assent is required, it also determines how assent will be documented, taking into account the ages, maturity and psychological state of the children particpating in the research.

Specific Procedures for Obtaining Assent/Permission/Consent ***[revise as applicable, based on local local laws, regulations, and institutional policies, the ages, maturity and psychological state of the children, and the IRB’s/EC’s determination regarding obtaining assent]*:**

1. *[Insert site delegated role/person]* will meet with the potential participant in a private, quiet, coercion-free setting and explain all aspects of the research. Prior to initiating the informed assent process, staff will ascertain whether the potential participant is literate (able to read and write on his/her own) in English/relevant local language *[revise as applicable]*.
2. The informed assent form will be reviewed with the potential participant and each section will be addressed adequately and the main points will be highlighted. During the discussion, potential participants will be encouraged to ask questions or express any concerns he/she may have. Staff will answer all participant questions and discuss all participant concerns before moving on to the next section of the form.
3. After all informed assent materials have been reviewed, and all participant questions/concerns have been addressed, *[insert site delegated role/person]* will verify understanding of the study and informed assent process with the participant *[site to include site specific information here if using site specific comprehension assessment tools, etc., if applicable].*
	1. Staff will listen carefully to all questions and/or concerns expressed by the potential participant and take as much time as needed to discuss these thoroughly. If the potential participant does not seem to understand the study even after answering questions, or he/she seems hesitant, site staff will not proceed with signing the assent form. The potential participant will be thanked for his/her time and will be provided with the phone number and requested to call the study site clinic if he/she have further questions.
4. All questions asked during the informed assent process and all responses provided will be documented in chart notes and/or on the informed assent cover sheet *if applicable.*
5. After the potential participant demonstrates that he/she fully understands the material in the informed assent form, if he/she chooses to take part, he/she will be asked to sign (print his/her name) and date two separate informed assent forms (one to be offered to the participant and the other for the research records).
6. In addition to providing written informed assent for study participation, the potential participant must indicate his/her willingness [do agree/do not agree] to allow the storage and future testing of specimens and related health information.

*Participants may choose not to have their health information and specimens collected and stored for future research testing and still enroll in the study. For participants who do not consent to specimen storage and possible future research, specimens collected and stored on-site per protocol will be retained until the study is completed and all protocol-specified testing has been done. Thereafter, any remaining specimens collected from these participants will be destroyed.*

1. For participants who are not able to understand all the required information, a copy of the consent assent will be provided to take home and read. Another visit date will be scheduled for the potential participant to return to the clinic for further discussion or explanation. If, after all efforts [*sites to specify maximum number of attempts to be made*], he/she is unable to understand the required information, he/she is ineligible for the study *[revise as applicable]*.
2. After witnessing his/her signature, [*insert site delegated role/person*] who is conducting the informed assent discussion will print their name, date, and sign both informed assent forms. All signature and date blocks included on informed assent forms must be completed by the applicable signatory.
	1. Signatures and dates will be entered in ink, and date blocks will be completed by each signatory. Any errors made to the informed assent form must be corrected per GCP.
3. The [*insert site delegated role/person*] delivering the assent discussion should check the assent form for completeness and accuracy. It should be checked when the participant is still available. If any information needs to be changed, a single line should be drawn through the incorrect information, and the correct information should be written above it. The correction should be initialed and dated. If the reason for the change is not obvious, an explanation should be recorded, initialed, and dated on the assent form.
4. A copy of the assent form will be offered to the potential participant. If the potential participant does not want a copy of the assent form, this will be documented on the informed assent coversheet (if applicable), documented in the chart notes, and both copies will be filed in the [site to insert]. *Note: Because it contains confidential information it must remain in a secure location at all times, preferably in a locked file/cabinet, in a locked room.,*

## The steps outlined below will be followed when administering the parent(s)/LAR/guardian informed permission and consent for those minors who can consent on their own behalf:

1. *[Insert site delegated role/person]* will meet with the potential participant’s parent(s)/LAR/guardian in a private, quiet, coercion-free setting and explain all aspects of the study.
2. *[Sites to insert site-specific procedures for ascertaining and accommodating literacy level for the parent(s)/LAR/guardian. Including IRB/EC recommendations such advocates, local interpreters. Include site-specific forms as needed as appendices].*
3. The informed permission/consent form will be reviewed with the potential participant’s parent(s)/LAR/guardian and each section will be addressed adequately and the main points will be highlighted. During the discussion, the potential participant’s parent(s)/LAR/guardian will be encouraged to ask questions or express any concerns he/she may have.
4. After all informed permission/consent materials have been reviewed, and all questions/concerns have been addressed, *[insert site delegated role/person]* will verify understanding of the study and informed consent process with the potential participant’s parent(s)/LAR/guardian *[site to include site specific information here if using site specific comprehension assessment tools, etc., if applicable].*
5. All questions asked during the informed permission/consent process and all responses provided will be documented in chart notes and/or on the informed permission/consent cover sheet *if applicable*.
6. After the potential participant’s parent(s)/LAR/guardian demonstrates that he/she fully understands the material in the informed permission/consent form, if he/she allows his/her child/chooses to take part, he/she will be asked his/her to sign (print name) and the date two separate informed consent forms (one to be offered to the parent(s)/LAR/guardian and the other for the research records).
7. After witnessing his/her signature, [*insert site delegated role/person*] who is conducting the informed permission/consent discussion will print their name, date, and sign both informed consent forms. All signature and date blocks included on informed permission/consent forms must be completed by the applicable signatory.
	1. Signatures and dates will be entered in ink, and date blocks will be completed by each signatory. Any errors made to the informed permission/consent form must be corrected per GCP.
8. The [*insert site delegated role/person*] delivering the permission/consent discussion should check the permission/consent form for completeness and accuracy. It should be checked when the potential participant’s parent(s)/LAR/guardian is still available. If any information needs to be changed, a single line should be drawn through the incorrect information, and the correct information should be written above it. The correction should be initialed and dated. If the reason for the change is not obvious, an explanation should be recorded, initialed, and dated on the permission/consent form.
9. A copy of the permission/consent form will be offered to the potential participant’s parent(s)/LAR/guardian or participant, as applicable. If the potential participant’s parent(s)/LAR/guardian or participant does not want a copy of the permission/consent form, this will be documented on the informed consent coversheet (if applicable), and both copies will be filed in the [*site to insert*]. *Note: Because it contains confidential information it must remain in a secure location at all times, preferably in a locked file/cabinet, in a locked room.*

## Procedures for Informed Assent/Permission/Consent Form Revisions

1. If any of the informed assent/permission/consent forms originally approved by the IRB/EC for use in a given study must be revised *[Insert procedures for revising and approving revised form(s)].*
2. The *[insert site delegated role/person]* will prepare the revised assent/permission/consent form(s), in consultation with community representatives, and other staff as needed *[revise as applicable]*. The *[insert site delegated role/person]* will forward the revised forms to the IRB/EC for review and approval prior to use.
3. The revised assent/permission/consent form(s) will be assigned a revision number and date. (For example, version 1.2 Feb 20, 2017)
4. IRB/EC approval of the revised assent/permission/consent form(s) must be obtained from responsible IRBs/ECs *prior to* its use with study participants. Consult with IRB/EC to determine if participants must be re-assented/re-permissioned/re-consented.
5. If the revision is minor and not associated with a protocol amendment, for example, if the contact information for the investigator needs to be updated, the new assent/permission/consent form(s) can be used as soon as all responsible IRBs/ECs any other applicable regulatory entity’s approval is obtained.
6. If the revisions to the assent/permission/consent form(s) are associated with a protocol amendment, the new assent/permission/consent form(s) may only be used after the IRB/EC approvals of the amendment are obtained.
7. When a new version of the assent/permission/consent form(s) is/are ready to be used, the *[insert site delegated role/person]* will:
* Inform all applicable staff of the revised version and the implementation date.
* Archive the prior master version of the previous forms.
* Destroy all blank copies of the prior version of the forms.
* Re-stock the storage locations with copies of the revised forms, along with coversheets. *[Indicate here if new colors will be used, or other mechanism for distinguishing between versions]*.
* Work with the [*insert site delegated role/person]* to develop and implement QC/QA activities to ensure proper transition to use of the new form(s).

## Attachments

*Attachment x: Comprehension Tool if applicable*

*[Insert additional as applicable]*

References **– This may not be a complete list of references**

1. (HHS) TITLE 45, PUBLIC WELFARE, DEPARTMENT OF HEALTH AND HUMAN SERVICES, PART 46, PROTECTION OF HUMAN SUBJECTS

<https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html>

1. (FDA) TITLE 21--FOOD AND DRUGS, CHAPTER I--FOOD AND DRUG ADMINISTRATION DEPARTMENT OF HEALTH AND HUMAN SERVICES SUBCHAPTER A—GENERAL, PART 50, PROTECTION OF HUMAN SUBJECTS

<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=50>

1. *[List applicable local laws, regulations, and institutional policies]*
2. ICH E6 R2

<http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2__Step_4.pdf>

1. Documentation of Informed Consent

<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.117>

1. General Requirements for Informed Consent (45 CFR 46.116)

<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.116>

1. FDA requirements for Informed Consent

<http://www.fda.gov/regulatoryinformation/guidances/ucm126420.htm#Informed%20Consent%20Process>

1. FDA Informed Consent content requirements

<http://www.fda.gov/regulatoryinformation/guidances/ucm126420.htm#Informed%20Consent%20Document%20Content>

1. Required Elements of Informed Consent

<http://answers.hhs.gov/ohrp/questions/7247>

1. Research with Children (Subpart D)

<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartd>

*[Insert additional references as applicable]*

## History

| **Version** | **Effective Date** | **Supersedes** | **Review Date** | Change |
| --- | --- | --- | --- | --- |
| XXX-XXX | DD MMM YYYY | NA | DD MMM YYYY | Initial Release |

## Approval

Author, Author’s Title Date

Reviewer, Reviewer’s Title Date