1 PURPOSE
This procedure describes the preparation, review, and approval of the informed consent/assent form (ICF), and documentation of the informed consent process by persons delegated and appropriately trained to obtain informed consent from human research subjects.

2 GENERAL INSTRUCTIONS AND RESPONSIBILITIES
   a) The Investigator or designee is responsible for retaining copies of the IRB approval letter and the IRB approved informed consent form in the appropriate section of the Trial/Regulatory Master File (TMF).

   b) The Investigator or designee is responsible for preparing an informed consent form that meets all federal, state, local, and institutional (IRB) requirements.

   c) The Investigator is responsible for ensuring that:
      • The informed consent form contains the required elements of informed consent as defined in 21 CFR 50.25 and ICH 4.8.10, and as applicable to the study. The informed consent must include both sponsor and local IRB language to capture the full scope of the study and the required institutional HIPAA language (if not provided in a separate document).
      • The informed consent (for persons 18 years and older)/assent (for children 7-17 years old) form is submitted to the IRB with the appropriate IRB Submission Form during the initial review of the study.
      • The IRB approves the informed consent/assent form and the IRB approval letter and approved informed consent/assent form are in the site’s TMF.
      • Each potential subject is properly informed regarding study procedures, risks/benefits, and other information detailed the informed consent prior to any study related procedures being performed.
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- An informed consent form is personally signed and dated by each subject or legally authorized representative, the person obtaining consent and where required by the IRB/Sponsor, the accruing Investigator (if not the person obtaining consent).

- Subjects are given a copy of the signed and dated informed consent form, and the process recorded in the source document that the subject was provided with a copy. The original, signed ICF is retained in the Regulatory Master File (or other designated binder) and an additional copy is placed in the subject’s Medical and/or clinic record (source document), unless otherwise directed by the protocol or IRB.

- The Investigator or designee will establish adequate documentation in the source documents that informed consent and/or assent was obtained before protocol-related procedures were performed.

- The person who obtains consent is personally signing and dating the informed consent/assent form at the same time as the subject or their legally authorized representative, unless otherwise specified by the IRB. The Investigator may or may not be required to sign and date the informed consent form as well, as specified by the IRB of record.

3 SPECIFIC PROCEDURES

3.1 Informed Consent Development, Review and Approval

The Sponsor should:

a) Provide an informed consent draft (at a 6th - 8th grade level) including all applicable elements of 21 CFR 50.25 and ICH 4.8.10 and relevant protocol procedures for consideration by the investigative site for obtaining informed consent from subjects (Attachment A, Informed Consent Template).

b) Provide an assent draft (were appropriate for the population) that is age-appropriate for the protocol when consenting children.

c) Instruct participating Investigators to review the informed consent form to ensure it meets state, local, and institutional requirements, and to add any elements required by these authorities prior to submitting to the IRB for approval. IRB approval must be received before the document can be used to consent research subjects.

The Sponsor will ensure that:

a) Investigators submit the informed consent/assent form to obtain approval by their site’s IRB of record before use (601 Attachment B, IRB Submission Checklist).

b) The IRB approved informed consent/assent was given an approval stamp and date to ensure the correct version is used.

c) Investigators forward a copy of the IRB approved informed consent/assent form and approval letter to the Sponsor.

d) The Sponsor and Investigator should note the IRB approval date on the form to ensure that no lapse in IRB approval occurs during the conduct of the study.

3.2 Informed Consent Process

For the purposes of this SOP, reference to the subject includes legally authorized representative, as applicable.
The Investigator will ensure that the subject or their legally authorized representative goes through the full informed consent process before any protocol-related procedures are conducted on the subject. The most recent IRB approved informed consent/assent form (identified by the version number and/or date in the footer) will be used to obtain informed consent/assent from potential research subjects.

Elements of the informed consent process are noted below:

a) Only those persons qualified, properly trained on the protocol and proper informed consent procedures, and designated by the Investigator on the Delegation Log should obtain consent/assent from potential research subjects.

b) The Investigator or designee should discuss the elements of the informed consent/assent form with the potential subject or legally authorized representative, and take all reasonable measures to ensure that the potential subject or legally authorized representative understands the content and meaning of the informed consent/assent form. Points discussed should include (but are not limited to):
   - An explanation of what clinical research is, and why they are being approached
   - An explanation of what they can expect if they choose to participate in the clinical study
   - Possible risks, outcomes, and alternatives to participating in the clinical study
   - What rights they would have as a subject

c) After the potential study subject or legally authorized representative reads and reviews the informed consent/assent form (with the IRB stamped approval date), the subject and/or legally authorized representative must personally sign and date the form prior to the initiation of any protocol-related procedures, unless exceptions are noted in the protocol. Potential subjects or legally authorized representatives will be given sufficient time to read and/or listen to the informed consent/assent form being read to them, and ask any questions relevant to their participation. Questions should be answered to their satisfaction before proceeding.

d) The Investigator or designee who conducts the informed consent/assent process must sign and date the form at the same time as the subject or legally authorized representative to acknowledge that the potential subject or legally authorized representative verbalized understanding of the research and research-related procedures.

e) The Investigator or designee will ensure the original of each signed informed consent/assent form is filed in the subject's research study file (and/or TMF) and a copy of the informed consent/assent form is given to the subject or legally authorized representative. Where applicable, a copy should also be placed in the subject's medical records/source documents.

f) The Investigator or designee will ensure that:
   - Each informed consent/assent form was signed and dated prior to any protocol-related procedures
   - A notation is made in the source document that the subject or legally authorized representative signed the form before any protocol-related procedures were performed and the date of the signature
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- Each subject or legally authorized representative received a copy of his/her signed, IRB-approved informed consent/assent form.

- Any changes to the protocol that are not minor or the acquisition of significant new information that affects subject safety may result in the need to revise the informed consent form. The Investigator or designee should make those revisions when necessary, and submit revisions to the IRB for approval.

- The Sponsor and/or IRB may require subjects or their legally authorized representative to be re-consented using the revised IRB approved consent form.

3.3 Consenting Non-English Reading Subjects

- If the Investigator intends on enrolling Non-English reading subjects, the Investigator or designee will be responsible for submitting certified translations of the most recently approved informed consent/assent form, as well as any other translated tools that will be used during the course of the study (i.e. Quality of Life Assessments, Patient Diaries etc.) to the IRB for approval prior to use.

- The investigator must provide the qualifications of the individual or the service that was used to translate the informed consent documents (For e.g. credentials, certifications, education). All non-English consent/assent forms must be translated by someone not associated with the study. In other words, an outside party who is appropriately trained/certified should translate the English IRB approved document into the desired language. Ad hoc translation of the document from English to another language by MHS staff is not allowed.

- The Investigator and/or designee, if not fluent in the subject’s language, will use a certified translator (a list of certified translators are available through MHS Intranet) to assist in the discussion of the informed consent process. When a translator is used, it should be noted on the documentation of consent process form (name of the translator and their translator number).

3.4 Assent of Children and Other Vulnerable Groups

- Consent of minors (7-17) aka "assent" is subject to the guidelines of and approved by the IRB. The IRB should be contacted by the Investigator or designee for consultation and specific procedures prior to proceeding.

- For other vulnerable groups (e.g. pregnant women, fetuses, subjects of genetic research, the cognitively impaired or mentally disabled, terminally ill patients, employees, etc.), the Investigator should contact the IRB for consultation and specific procedures prior to proceeding.

3.5 Waivers and Exceptions

- An IRB may, for some or all study subjects, waive the requirement that the subject sign a written informed consent form in certain circumstances. The Investigator should contact the IRB for consultation and specific procedures prior to proceeding.

- When the waiver is in effect, the IRB may require the Investigator to provide subjects with a written statement regarding the research.
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c) Regarding the use of an investigational product in an emergency situation, obtaining informed consent shall be deemed feasible except in certain emergency situations where the investigator and a physician who is not otherwise participating in the clinical care of the patient certify in writing all of the following:

- The subject was confronted by a life-threatening situation necessitating the use of the investigational product
- Informed consent could not be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject
- Time was not sufficient to obtain consent from the subject's legally authorized representative
- There was no available alternative method of approved or generally recognized therapy that provided an equal or greater likelihood of saving the life of the subject

d) If immediate use of the investigational product was, in the Investigator's opinion, required to preserve the life of the subject and time was not sufficient to obtain the independent determination required above in advance, the determinations of the investigator must be reviewed in writing within 5 working days after the use of the investigational product by a physician who is not otherwise participating in the clinical care of the patient.

e) The Investigator must submit documentation to the IRB for review within five (5) working days after emergency use of the investigational product.

f) The Investigator should maintain the aforementioned documentation in the appropriate section of the Regulatory Master File.

g) For any other unique situation (e.g. treatment use of an investigational drug/biologic/medical device, compassionate or humanitarian use), the Investigator should contact the IRB for consultation and specific procedures before proceeding.

4 REFERENCES TO OTHER APPLICABLE SOPS

- 201 Contacts and Submissions for FDA
- 301 Clinical Protocol Development, Implementation, and Compliance
- 402 Initiation Visit and Site Training
- 503 Documentation and Records Retention
- 504 Routine Monitoring Visits

5 ATTACHMENTS

A. Informed Consent Template
B. IRB Submission Checklist
C. Documentation of the Consenting Process Template

6 APPLICABLE REGULATIONS AND GUIDELINES

- Protection of Human Subjects (21 CFR 50)
- Informed Consent of Human Subjects (21 CFR 50.20 – 50.55)
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- Institutional Review Boards (21 CFR 56)
- Requirements for an IND (21 CFR 312.20)
- Treatment Use of an Investigational New Drug (21 CFR 312.24)
- Emergency Research Under 50.24 of This Chapter (21 CFR 312.54)
- Assurance or IRB Review (21 CFR 312.66)
- Drugs Intended to Treat Life-Threatening and Severely-debilitating Illnesses (21 CFR 312 Subpart E)
- Availability for Public Disclosure of Data and Information in an IND (21 CFR 312.130)
- Treatment Use of an Investigational Device
- Confidentiality of Data and Information (21 CFR 812.38)
- FDA and IRB Approval (21 CFR 812.42)
- Emergency Research Under 50.24 of This Chapter (21 CFR 812.47)
- IRB Review and Approval (21 CFR 812 Subpart D)
- The Principles of ICH GCP (ICH E6, Sections 2.1, 2.2, 2.3, 2.6 and 2.9)
- Institutional Review Board/Independent Ethics Committee (ICH E6, Section 3.0)
- Medical Care of Trial Subjects (ICH E6, Section 4.3)
- Communication with IRB/IEC (ICH E6, Section 4.4)
- Informed Consent of Trial Subjects (ICH E6, Section 4.8)
- Compensation to Subjects and Investigators (ICH E6, Section 5.8)
- Confirmation of Review by IRB/IEC (ICH E6, Section 5.11)