Good clinical practice provides standards for the conduct of all aspects of a clinical investigation, including the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting. Clinical trials regulated by the U.S. Food and Drug Administration (FDA) are required to adhere to applicable FDA regulations, including those regulations that implicate good clinical practices, e.g. 21 CFR 11, 50, 54, 56, 58, 310, 312, 812, 814. The International Conference on Harmonization’s (ICH) Guidance for Industry E6 Good Clinical Practice (GCP): Consolidated Guidance provides a unified, international standard for the conduct of clinical trials involving human subjects. The FDA utilizes ICH-GCP as guidance for GCP. Clinical trials that follow ICH-GCP E6 guidance are conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and are consistent with GCP and applicable regulatory criteria.

A sponsor of a clinical investigation (e.g., multi-site clinical trials, international clinical trials) may require ICH-GCP (E6) compliance. In those instances, the Institutional Review Board (IRB) will make the determinations required by institutional policy and will also review the research plan submitted to identify aspects that may be inconsistent with ICH-GCP. If an investigator in the research contract agrees to conduct an investigation in full compliance with the investigator obligations under ICH-GCP, any compliance review conducted by the IRB will be done against the complete set of ICH-GCP requirements. The IRB will bring any issues of concern to the attention of the investigator, who may in turn ask for clarification from the sponsor.

The investigator, following ICH-GCP E6, shall:

1. Require and assure through appropriate oversight that research staff follows these requirements as appropriate to their role and involvement in the research study.

2. Provide a description of the manufacturing, handling, and storage in accordance with applicable good manufacturing practice (GMP).

3. Assign some or all duties for investigational articles accountability at the clinical trial sites to an appropriate pharmacist or another appropriate individual who is under the supervision of the investigator or Michigan State University (MSU) (where allowed or required). MSU or the IRB may require this as well.
4. Maintain records of the product's delivery to the clinical trial site, the inventory at the site, the use by each subject, and the return to the sponsor or alternative disposition of unused products. These records include dates, quantities, batch or serial numbers, and expiration dates (if applicable), and the unique code numbers assigned to the investigational products and trial subjects. If the investigator has assigned some or all of the duties for investigational articles to a pharmacist, or other designated individual, that individual is responsible for this requirement. However, the investigator should maintain appropriate oversight to assure proper records are being maintained.

5. Maintain records that document adequately that the subjects are provided the doses specified by the protocol and reconcile all investigational products received from the sponsor.

6. Report to the IRB:
   a. New information that may affect adversely the safety of the subjects or the conduct of the clinical trial, and / or
   b. Any changes significantly affecting the conduct of the clinical trial or increasing the risk to subjects.

7. Ensure that adequate medical care is provided to a subject for any adverse events, including clinically significant laboratory values, related to the clinical trial (during and following a subject's participation in a clinical trial).

8. Inform subjects when medical care is needed for other illnesses of which the investigator becomes aware.

9. Follow the clinical trial's randomization procedures, if any, and ensures that the code is broken only in accordance with the protocol.

10. Promptly document and explain to the sponsor any premature unblinding (if the clinical trial is blinded).

11. Inform the subject's primary physician about the subject's participation in the clinical trial if the subject has a primary physician and if the subject agrees to the primary physician being informed.

12. Make a reasonable effort to ascertain the reason for subject withdrawal, while fully respecting the subject's rights (a subject is not obliged to give his or her reasons for withdrawing prematurely from a clinical trial).

13. Provide all the disclosures and follow the requirements pertaining to consent covered by ICH-GCP.
14. Provide evidence of his or her qualifications through up-to-date curriculum vitae or other relevant documentation requested by the sponsor, the IRB, or the regulatory authority.

15. Familiar with the appropriate use of the investigational product, as described in the protocol, in the current investigator brochure, in the product information, and in other information sources provided by the sponsor.

16. Assure that the responsibility for all clinical trial-related medical (or dental) decisions is by a qualified physician (or dentist, when appropriate), who is an investigator or a co-investigator for the clinical trial.

17. Ensure that adequate medical care is provided to a subject for any adverse events, including clinically significant laboratory values, related to the clinical trial (during and following a subject’s participation in a clinical trial).

18. Ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor.

19. Maintain a list of appropriately qualified persons to whom they have delegated significant clinical trial-related duties.

20. Report all serious adverse events (SAEs) to the sponsor except for those SAEs that the protocol or other document (e.g., investigator’s brochure) identifies as not needing immediate reporting.

21. Follow regulatory requirements related to the reporting of unexpected serious adverse drug reactions to the regulatory authority and the IRB.

22. Report adverse events or laboratory abnormalities identified in the protocol as critical to safety evaluations to the sponsor according to the reporting requirements and within the time periods specified by the sponsor in the protocol.

23. Supply the sponsor and the IRB with any additional requested information (e.g., autopsy reports and terminal medical reports) for reported deaths.

24. Provide written reports to the sponsor, the IRB, and, where applicable, MSU, on any changes significantly affecting the conduct of the clinical trial or increasing the risk to subjects.

25. Inform MSU, sponsor, and the IRB if the investigator terminates or suspends a clinical trial without prior agreement of the sponsor.

26. Promptly notify the sponsor if the IRB terminates or suspends approval of the clinical trial.
27. Inform MSU or the IRB upon completion of the clinical trial with a summary of the trial’s outcome and provide the regulatory authority with any required reports.

The IRB, following ICH-GCP E6, shall:

1. Evaluate the adequacy of the available nonclinical and clinical information on an investigational product to determine if it is adequate to support the proposed clinical trial.

2. Assess the information provided by the investigator regarding resources necessary to protect subject to confirm an adequate number of research staff and facilities.

3. Determine that the following consent disclosures are included:
   a. The alternative procedures or treatment that might be available to the subject, and their important potential benefits and risks.
   b. That the monitor, the auditor, the IRB, and the regulatory authority will be granted direct access to the subject’s original medical records for verification of clinical trial procedures or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written consent form, the subject or the subject’s legally acceptable representative is authorizing such access.
   c. The approval of the IRB.

4. Determine that the consent process will include, prior to a subject’s participation in the trial, that the written informed consent form should be signed and personally dated by the:
   a. Subject or by the subject’s legally acceptable representative.
   b. Person who conducted the informed consent discussion.

5. Determine that if a subject is unable to read or if a legally acceptable representative is unable to read, an impartial witness should be present during the entire informed consent discussion and:
   a. After the written informed consent form and any other written information to be provided to subjects, is read and explained to the subject or the subject’s legally acceptable representative, and after the subject or the subject’s legally acceptable representative has orally consented to the subject’s participation in the trial and, if capable of doing so, has signed and personally dated the informed consent form, the witness should sign and personally date the consent form.
   b. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject or the subject’s legally acceptable representative, and that informed consent was freely given by the subject or the subject’s legally acceptable representative.
6. Determine that prior to participation in the trial, the subject or the subject's legally acceptable representative should receive a copy of the signed and dated written informed consent form and any other written information provided to the subject.

7. Determine when adults are unable to consent:
   a. A non-therapeutic clinical trial (i.e. a trial in which there is no anticipated direct clinical benefit to the subject) should be conducted in subjects who personally give consent and who sign and date the written consent document.
   b. Non-therapeutic clinical trials may be conducted in subjects with consent of a legally acceptable representative provided the following conditions are fulfilled:
      i. The objectives of the clinical trial cannot be met by means of a trial in subjects who can give consent personally.
      ii. The foreseeable risks to the subjects are low.
      iii. The negative impact on the subject's wellbeing is minimized and low.
      iv. The clinical trial is not prohibited by law.
      v. The opinion of the IRB is expressly sought on the inclusion of such subjects, and the written opinion covers this aspect.
      vi. Such trials, unless an exception is justified, should be conducted in patients having a disease or condition for which the investigational product is intended. Subjects in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.

8. Determine that in cases of planned emergency research, the subject or the subject's legally authorized representative is informed about the clinical trial as soon as possible and provides consent if the subject wishes to continue.