1.13 Compliance with ICH-GCP Guidelines

1.0 Purpose

The purpose of this policy and procedure is to describe the Organization's requirements for compliance with the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) E6 Guidelines.

2.0 Policy

- **2.1.** It is the policy of the Organization that, in addition to all applicable HRPP policies, the Organization will apply ICH-GCP E6 guidelines to IRB review and the conduct of clinical research when the sponsored agreement specifies adherence to ICH GCP.
- **2.2.** It is the policy of the Organization that clinical trials subject to ICH-GCP will be conducted in accordance with the ethical principles that have the origin in the Declaration of Helsinki and that are consistent with good clinical practice and the applicable regulatory requirements.

3.0 Procedures

- **3.1.** Contract Specialists notify the IRB via IRBORA whether the trial is subject to ICH-GCP Guidelines. The assigned IRB administrator reviews the submission for compliance with ICH-GCP.
- **3.2.** When the protocol requires ICH GCP compliance, the IRB Administrator will ensure that the submission includes all necessary information in section 4.0.
- **3.3.** When the full IRB reviews research that requires ICH GCP compliance, the IRB will ensure that all requirements are met prior to final approval.

4.0 ICH GCP Requirements

- **4.1.** New research and substantive scientific modifications to approved research shall undergo scientific review (including review by outside experts as needed) and that the review is considered by the IRB in accordance with HRPP policy 1.10 (Scientific and Other Committee Review of Research).

- **4.2.** In order to satisfy the ICH-GCP requirements, the IRB must be assured of the following:
  - **4.2.1.** The PI is qualified by education, training, and experience to assume responsibility for the proper conduct of the trial and should meet all the qualifications specified by the applicable regulatory requirement(s). (ICH-GCP 4.1.1)
    Note: The IRB relies upon the Organization's credentialing process and the peer review certification. However, when any questions arise concerning qualifications the IRB may request an up-to-date Curriculum Vitae (CV) and additional documentation.
  - **4.2.2.** A qualified physician (or dentist, when appropriate), who is an investigator or a sub-investigator for the trial, will provide the medical (or dental) care given to, and medical (or dental) decisions made on behalf of, subjects (ICH-GCP 4.3.1)
  - **4.2.3.** The available nonclinical and clinical information of an investigational product is adequate to support the proposed clinical trial. For purposes of this requirement, "investigational product" means a pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use (ICH-GCP 1.33 and 2.4), and
  - **4.2.4.** The clinical trials is scientifically sound; adequately designed to answer the research question, and described in a clear, detailed protocol (ICH GCP 2.5).
  - **4.2.5.** In addition to the elements described in HRPP policy 5.1 (Obtaining Informed Consent from Research Subjects), consent form disclosures provide the following additional elements of information to potential subjects:
    - **4.2.5.1.** The approval by the IRB.
    - **4.2.5.2.** The probability for random assignment to each treatment.
    - **4.2.5.3.** The participant's responsibilities.
    - **4.2.5.4.** When applicable, the reasonably foreseeable risks or inconveniences to an embryo, fetus, or nursing infant.
    - **4.2.5.5. For alternative procedures or treatment that may be available to the subject, include the important potential benefits and risks of alternative procedures or treatments that may be available to the subject. (ICH-GCP 4.8.10(i)).
    - **4.2.5.6.** The subject should be made aware if there is no intended clinical benefit to the subject.
    - **4.2.5.7.** 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 applicable laws and regulations and that, by signing a written consent form, the subject or the subject's legally authorized representative is authorizing such access. (ICH GCP 4.8.10(n))
    - **4.2.5.8.** The subject's identity will remain confidential if the trial results are published.
  - **4.2.6.** Except as described in section 4.2.7 below, non-therapeutic clinical trials (trials in which there is no anticipated direct benefit to the subject), should be conducted in subjects who personally give consent and who sign and date the written informed consent form (ICH-GCP 4.8.13).
  - **4.2.7.** Non-therapeutic clinical trials conducted in subjects with consent of a legally authorized representative (LAR) fulfill the following additional requirements (ICH-

GCP 4.8.14):
    - **4.2.7.1.** The objectives of the clinical trial cannot be met by means of a trial in subjects who can give consent personally.
    - **4.2.7.2.** The foreseeable risks to the subjects are low.
    - **4.2.7.3.** The negative impact on the subject's well-being is minimized and low.
    - **4.2.7.4.** The clinical trial is not prohibited by law.
    - **4.2.7.5.** The opinion of the IRBs is expressly sought on the inclusion of such subjects and the written opinion covers this aspect.
    - **4.2.7.6.** Such trials, unless an exception is justified, should be conducted inpatients 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.
  - **4.2.8.** In those situations where there is an exception for the requirements for informed consent for planned emergency research, the subject, or LAR, will be informed about the clinical trial as soon as possible and provide informed consent if the subject wishes to continue in the clinical trial.
    Note: Currently there is no planned emergency research conducted within the Organization.
- **4.3.** In order to satisfy the ICH-GCP requirements, the PI must assure the following:
  - **4.3.1.** The PI must provide evidence of such qualifications through an up-to-date CV or other relevant documentation requested by the sponsor, the IRB, or the regulatory authority. (ICH GCP 8.2.10)
  - **4.3.2.** The PI must be thoroughly familiar with the appropriate use of the investigational products, as described in the protocol, in the current Investigator's Brochure (IB), in the product information, and in other information sources provided by the sponsor. (ICH-GCP 4.1.2)
  - **4.3.3.** During and following a subject's participation in a trial, the PI must ensure that adequate medical care is provided to a subject for any adverse events, including clinically significant laboratory values, related to the clinical trial. (ICH-GCP 4.3.2)
  - **4.3.4.** The PI must inform a subject when medical care is needed for other illnesses of which the investigator becomes aware. (ICH-GCP 4.3.2)
  - **4.3.5.** The PI must follow the trial's randomization procedures, if any, and ensure that the code is broken only in accordance with the Protocol. If the trial is blinded, the PI will promptly document and explain to the sponsor any premature unblinding. (ICH-GCP 4.7)
  - **4.3.6.** When appropriate, the PI must 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. (ICH-GCP 4.3.2)
  - **4.3.7.** Although a subject is not obliged to give his or her reasons for withdrawing prematurely from the clinical trial, the PI must make a reasonable effort to ascertain the reason, while fully respecting the subject's rights. (ICH-GCP 4.3.4)
  - **4.3.8.** Where allowed or required, the PI may assign some or all duties for investigational articles accountability at the trial sites to an appropriate pharmacist or another appropriate individual who is under the supervision of the PI. (ICH-GCP 4.6.2)
  - **4.3.9.** The PI and the investigational pharmacist will, in accordance with hospital policy, maintain records of a drug or biological product delivery to the 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 will include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique

code numbers assigned to the investigational products and trial subjects. The PI will 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. (ICG-GCP 4.6.3)

- **4.3.10.** The PI, or other designated individual, will maintain records of an investigational device, delivery to the 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 will include dates, quantities, serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational device and trial subjects. The PI will maintain records that document adequately that the investigational device has been used as specified by the protocol and reconcile all investigational products received from the sponsor. (ICG-GCP 4.6.3)
- **4.3.11.** The PI will permit monitoring and auditing by the sponsor, and inspection by the appropriate regulatory authority. (ICH-GCP 4.1.4)
- **4.3.12.** The PI will ensure the accuracy, completeness, legibility, and timeliness of the data reports to the sponsor. (ICH-GCP 4.9.1)
- **4.3.13.** The PI will report all serious adverse events (SAEs) or abnormal laboratory findings identified in the protocol as critical to safety evaluations to the sponsor according to the reporting requirements and within the time period specified by the sponsor in the protocol. The PI will follow regulatory requirements related to the reporting of unexpected serious adverse drug reactions to the regulatory authority and the IRB. (ICH-GCP 4.11.1)
- **4.3.14.** The PI will report to the sponsor, IRB, and, as applicable, the Organization (ICH GCP 4.10.2):
  - **4.3.14.1.** Any new information that may adversely affect the safety of the subject or the conduct of a clinical trial.
  - **4.3.14.2.** Any changes significantly affecting the conduct of the clinical trial, or increasing risk to subjects.
- **4.3.15.** The PI will maintain the clinical trial documents as specified in Essential Documents for the Conduct of a Clinical Trial and as required by the applicable regulatory requirements. (ICH-GCP 4.9.4). Essential documents will be retained until at least two years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least two years have elapsed since the formal discontinuation of clinical development of the investigational product. (ICH-GCP 4.9.5)
- **4.3.16.** If the PI terminates or suspends a clinical trial without prior agreement of the sponsor, the PI will inform the Organization, sponsor and the IRB. (ICH-GCP 4.12.1)
- **4.3.17.** If the IRB terminates or suspends its approval of the clinical trial, the PI will promptly notify the sponsor. (ICH-GCP 4.12.3)
- **4.3.18.** Upon completion of the trial, the PI will inform the IRB with a summary of the trial’s outcome, and the regulatory authority with any reports required. (ICH-GCP 4.13)
- **4.3.19.** The PI will maintain a list of appropriately qualified persons to whom the PI has delegated significant trial-related duties. (ICH-GCP 4.1.5)
- **4.3.20.** For reports of deaths, the PI will supply the sponsor and the IRB with any additional requested information (e.g., autopsy reports and terminal medical reports). (ICH-GCP 4.11.3)

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