THE PRINCIPLES OF ICH E6 GCP

- 2.1 Clinical trials should be conducted in accordance with the Declaration of Helsinki
- 2.2 A trial should be initiated and continued only if the anticipated benefits justify the risks.
- 2.3 The rights, safety, and well-being of the trial subjects are the most important considerations and should prevail over interests of science and society.
- 2.4 The available nonclinical and clinical information on an investigational product should be adequate to support the proposed clinical trial.
- 2.5 Clinical trials should be a detailed protocol E3.
THE PRINCIPLES OF ICH E6 GCP

- **2.6** A trial should have received prior institutional review board (IRB)/independent ethics committee (IEC) approval/favourable opinion.

- **2.7** The medical care given to, and medical decisions made on behalf of, subjects should always be the responsibility of a qualified physician or, when appropriate, of a qualified dentist.

- **2.8** Each individual involved in conducting a trial should be qualified by education, training, and experience to perform his or her respective task(s).

- **2.9** Freely given informed consent should be obtained from every subject prior to clinical trial participation.
THE PRINCIPLES OF ICH E6 GCP

- **2.10** All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification.

- **2.11** The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules.

- **2.12** Investigational products should be manufactured, handled, and stored in accordance with applicable good manufacturing practice (GMP).

- **2.13** Systems with procedures that assure the quality of every aspect of the trial should be implemented.
3.1.1 Institutional review board/independent ethics committee (IRB/IEC) should safeguard the rights, safety, and well-being of all trial subjects.

3.1.2 The IRB/IEC should obtain: trial protocol(s) / amendment(s), written informed consent form(s), subject recruitment procedures, written information to be provided to subjects, Investigator's Brochure (IB), available safety information, information about payments and compensation available to subjects, the investigator's current curriculum vitae and/or other documentation evidencing qualifications.
3.1.4 The IRB/IEC should conduct continuing review of each ongoing trial at intervals appropriate to the degree of risk to human subjects, but at least once per year.
4.1 Investigator's Qualifications and Agreements

4.1.1 The investigator(s) should be qualified by education, training, and experience to assume responsibility for the proper conduct of the trial, should meet all the qualifications specified by the applicable regulatory requirement(s), and should provide evidence of such qualifications through up-to-date curriculum vitae and/or other relevant documentation requested by the sponsor, the IRB/IEC, and/or the regulatory authority(ies).
INVESTIGATOR

4.1 Investigator's Qualifications and Agreements

4.1.2 The investigator should be thoroughly familiar with the appropriate use of the investigational product(s), as described in the protocol, in the current Investigator's Brochure, in the product information and in other information sources provided by the sponsor.

4.1.3 The investigator should be aware of, and should comply with, GCP and the applicable regulatory requirements.
• 4.1 Investigator's Qualifications and Agreements
  • 4.1.4 The investigator/institution should permit monitoring and auditing by the sponsor, and inspection by the appropriate regulatory authority(ies).
  • 4.1.5 The investigator should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.
4.2 Adequate Resources

4.2.1 a potential for recruiting the required number of suitable subjects within the agreed recruitment period.

4.2.2 sufficient time to properly conduct and complete the trial within the agreed trial period.

4.2.3 an adequate number of qualified staff and adequate facilities for the foreseen duration of the trial to conduct the trial properly and safely.
4.3 Medical Care of Trial Subjects

4.3.4 Although a subject is not obliged to give his/her reason(s) for withdrawing prematurely from a trial, the investigator should make a reasonable effort to ascertain the reason(s), while fully respecting the subject's rights.
4.5 Compliance with Protocol

4.5.1 The investigator/institution should conduct the trial in compliance with the protocol. The investigator/institution and the sponsor should sign the protocol, or an alternative contract, to confirm agreement.
4.8 Informed Consent of Trial Subjects

4.8.1 In obtaining and documenting informed consent, the investigator should comply with the applicable regulatory requirement(s), and should adhere to GCP and to the ethical principles that have their origin in the Declaration of Helsinki.

4.8.3 Neither the investigator, nor the trial staff, should coerce or unduly influence a subject to participate or to continue to participate in a trial.
4.8 Informed Consent of Trial Subjects

The language used in the oral and written information about the trial, including the written informed consent form, should be as non-technical as practical and should be understandable to the subject or the subject's legally acceptable representative and the impartial witness, where applicable.
INVESTIGATOR

- **4.8 Informed Consent of Trial Subjects**
  - **4.8.7** Before informed consent may be obtained, the investigator, or a person designated by the investigator, should provide the subject or the subject's legally acceptable representative ample time and opportunity to inquire about details of the trial and to decide whether or not to participate in the trial.
  - **4.8.8** Prior to a subject’s participation in the trial, the written informed consent form should be signed and personally dated by the subject and the investigator.
4.8 Informed Consent of Trial Subjects

4.8.10 Both the informed consent discussion and the written informed consent form and any other written information to be provided to subjects should include explanations of the following:

- (a) That the trial involves research.
- (b) The purpose of the trial.
- (c) The trial treatment(s) and the probability for random assignment to each treatment.
- (d) The trial procedures to be followed, including all invasive procedures.
- (e) The subject's responsibilities.
4.9 Records and Reports

4.9.1 The investigator should ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports.

4.9.2 Data reported on the CRF, that are derived from source documents, should be consistent with the source documents or the discrepancies should be explained.

4.9.3 Any change or correction to a CRF should be dated, initialed, and explained and should not obscure the original entry (i.e. audit trail should be maintained);
4.9.7 Upon request of the monitor, auditor, IRB/IEC, or regulatory authority, the investigator/institution should make available for direct access all requested trial-related records.
INVESTIGATOR

- 4.11 Safety Reporting
  - 4.11.1 All serious adverse events (SAEs) should be reported immediately to the sponsor …/… The immediate reports should be followed promptly by detailed, written reports. The investigator should also comply with the applicable regulatory requirement(s) related to the reporting of unexpected serious adverse drug reactions to the regulatory authority(ies) and the IRB/IEC.
  - 4.11.2 Adverse events and/or laboratory abnormalities identified in the protocol as critical to safety evaluations should be reported to the sponsor.
SPONSOR

5.2 Contract Research Organization (CRO)

5.2.1 A sponsor may transfer any or all of the sponsor's trial-related duties and functions to a CRO, but the ultimate responsibility for the quality and integrity of the trial data always resides with the sponsor.

5.2.4 All references to a sponsor in this guideline also apply to a CRO to the extent that a CRO has assumed the trial related duties and functions of a sponsor.
5.4 Trial Design

5.4.1 The sponsor should utilize qualified individuals (e.g. biostatisticians, clinical pharmacologists, and physicians) as appropriate, throughout all stages of the trial process.
5.6 Investigator Selection

5.6.1 The sponsor is responsible for selecting the investigator(s)/institution(s). Each investigator should be qualified by training and experience.

5.9 Financing

The financial aspects of the trial should be documented in an agreement between the sponsor and the investigator/institution.
5.13.4 In blinded trials, the coding system for the investigational product(s) should include a mechanism that permits rapid identification of the product(s) in case of a medical emergency, but does not permit undetectable breaks of the blinding.
5.15 Record Access

- 5.15.1 The sponsor should ensure that it is specified in the protocol or other written agreement that the investigator(s)/institution(s) provide direct access to source data/documents for trial-related monitoring, audits, IRB/IEC review, and regulatory inspection.

- 5.15.2 The sponsor should verify that each subject has consented, in writing, to direct access to his/her original medical records for
5.18 Monitoring

5.18.1 Purpose
The purposes of trial monitoring are to verify that:

- (a) The rights and well-being of human subjects are protected.
- (b) The reported trial data are accurate, complete, and verifiable from source documents.
- (c) The conduct of the trial is in compliance with the currently approved protocol/amendment(s), with GCP, and with the applicable regulatory requirement(s).
5.18.2 Selection and Qualifications of Monitors

(a) Monitors should be appointed by the sponsor.

(b) Monitors should be appropriately trained, and should have the scientific and/or clinical knowledge needed to monitor the trial adequately. **A monitor’s qualifications should be documented.**

(c) Monitors should be thoroughly familiar with the investigational product(s), the protocol, written informed consent form and any other written information to be provided to subjects, the sponsor’s SOPs, GCP, and the applicable regulatory requirement(s).
5.18.6 Monitoring Report

(a) The monitor should submit a written report to the sponsor after each trial-site visit or trial-related communication.

(c) Reports should include a summary of what the monitor reviewed and the monitor's statements concerning the significant findings/facts, deviations and deficiencies, conclusions, actions taken or to be taken and/or actions recommended to secure compliance.
5.19 Audit

The purpose of a sponsor's audit, which is independent of and separate from routine monitoring or quality control functions, should be to evaluate trial conduct and compliance with the protocol, SOPs, GCP, and the applicable regulatory requirements.

5.19.2 Selection and Qualification of Auditors

(a) The sponsor should appoint individuals, who are independent of the clinical trials/systems, to conduct audits.
6. CLINICAL TRIAL PROTOCOL AND PROTOCOL AMENDMENT(S)

6.1 General Information: Protocol title, protocol identifying number, and date, Name and address ...

6.2 Background Information: on investigational product(s). A statement that the trial will be conducted in compliance with the protocol, GCP and the applicable regulatory requirement(s). Description of the population to be studied.

6.3 Trial Objectives and Purpose: a detailed description of the objectives and the purpose of the trial.
The Investigator's Brochure (IB) is a compilation of the clinical and nonclinical data on the investigational product(s) that are relevant to the study of the product(s) in human subjects.

- The information should be presented in a concise, simple, objective, balanced, and non-promotional form.
- The IB should be reviewed at least annually. More frequent revision may be appropriate depending on the stage of development and the generation of relevant data.