

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**.

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- ◆ **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.

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- ◆ **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.

IRB/IEC

- ◆ **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.

IRB/IEC

- ◆ **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.

INVESTIGATOR

- ◆ **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.

INVESTIGATOR

- ◆ **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.

INVESTIGATOR

- ◆ **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.

INVESTIGATOR

- ◆ **4.3 Medical Care of Trial Subjects**
- ◆ 4.3.1 investigator or sub-investigator should be responsible for all trial-related medical decisions.
- ◆ 4.3.2 investigator/institution should ensure that adequate medical care is provided.
- ◆ 4.3.3 investigator need to inform the subject's primary physician about the subject's participation in the trial

INVESTIGATOR

- ◆ **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.

INVESTIGATOR

- ◆ **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.

INVESTIGATOR

- ◆ **4.6 Investigational Product(s)**
- ◆ 4.6.3 The investigator/institution and/or a pharmacist should maintain records of the product's on site.
- ◆ 4.6.4 The investigational product(s) should be stored as specified by the sponsor and in accordance with applicable regulatory requirement(s).
- ◆ 4.6.5 The investigator should ensure that the investigational product(s) are used only in accordance with the approved protocol.

INVESTIGATOR

- ◆ **4.7 Randomization Procedures and Unblinding**
- ◆ The investigator **should follow the trial's randomization procedures**, if any, and should ensure that the code is broken only in accordance with the protocol and should promptly document and explain to the sponsor any premature unblinding of the investigational product(s) (e.g., accidental unblinding, unblinding due to a serious adverse event).

INVESTIGATOR

- ◆ **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.

INVESTIGATOR

- ◆ **4.8 Informed Consent of Trial Subjects**
- ◆ 4.8.6 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**

INVESTIGATOR

- ◆ **4.8 Informed Consent of Trial Subjects**
- ◆ 4.8.9 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.

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 (1 to 20):

- 1) That the trial involves research.
- 2) The purpose of the trial.
- 3) The trial treatment(s) and the probability for random assignment to each treatment.
- 4) The trial procedures to be followed, including all invasive procedures.
- 5) The subject's responsibilities.

INVESTIGATOR

- 6) Those aspects of the trial that are experimental.
- 7) The reasonably foreseeable risks or inconveniences to the subject and, when applicable, to an embryo, fetus, or nursing infant.
- 8) The reasonably expected benefits. When there is no intended clinical benefit to the subject, the subject should be made aware of this.
- 9) The alternative procedure(s) or course(s) of treatment that may be available to the subject, and their important potential benefits and risks.
- 10) The compensation and/or treatment available to the subject in the event of trial-related injury.

INVESTIGATOR

- 11) The anticipated prorated payment, if any, to the subject for participating in the trial.
- 12) The anticipated expenses, if any, to the subject for participating in the trial.
- 13) That the subject's participation in the trial is voluntary and that the subject may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the subject is otherwise entitled.

INVESTIGATOR

- 14) That the monitor(s), the auditor(s), the IRB/IEC, and the regulatory authority(ies) will be granted direct access to the subject's original medical records for verification of clinical trial procedures and/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 informed consent form, the subject or the subject's legally acceptable representative is authorizing such access.

INVESTIGATOR

- 15) That records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the trial are published, the subject's identity will remain confidential.
- 16) That the subject or the subject's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the subject's willingness to continue participation in the trial.

INVESTIGATOR

- 17) The person(s) to contact for further information regarding the trial and the rights of trial subjects, and whom to contact in the event of trial-related injury.
- 18) The foreseeable circumstances and/or reasons under which the subject's participation in the trial may be terminated.
- 19) The expected duration of the subject's participation in the trial.
- 20) The approximate number of subjects involved in the trial.

INVESTIGATOR

- ◆ **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);

INVESTIGATOR

- ◆ 4.9.4 The investigator/institution should maintain the trial documents as specified in Essential Documents for the Conduct of a Clinical Trial. The investigator/institution should take measures to prevent accidental or premature destruction of these documents.
- ◆ 4.9.5 Essential documents should be retained **until at least 2 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 2 years have elapsed since the formal discontinuation of clinical development of the investigational product.

INVESTIGATOR

- ◆ 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.

INVESTIGATOR

- ◆ 4.11.3 For reported deaths, the investigator should supply the sponsor and the IRB/IEC with any additional requested information (e.g., autopsy reports and terminal medical reports).
- ◆ **4.12 Premature Termination or Suspension of a Trial**
- ◆ If the trial is prematurely terminated or suspended for any reason, the investigator/institution should promptly inform the trial subjects, should assure appropriate therapy and follow-up

SPONSOR

5.1 Quality Assurance and Quality Control

- ◆ 5.1.1 The sponsor is responsible for implementing and maintaining quality assurance and quality control systems
- ◆ 5.1.2 The sponsor is responsible for securing agreement from all involved parties to ensure direct access (see 1.21) to all trial related sites, source data/documents , and reports for the purpose of monitoring and auditing by the sponsor, and inspection by domestic and foreign regulatory authorities.

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.

SPONSOR

- ◆ **5.3 Medical Expertise**
- ◆ The sponsor should designate appropriately qualified medical personnel who will be readily available to advise on trial related medical questions or problems. If necessary, outside consultant(s) may be appointed for this purpose.

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

SPONSOR

- ◆ **5.5 Trial Management, Data Handling, and Record Keeping**
- ◆ 5.5.1 The sponsor should utilize appropriately qualified individuals to supervise the overall conduct of the trial, to handle the data, to verify the data, to conduct the statistical analyses, and to prepare the trial reports.

SPONSOR

- ◆ 5.5.3 When using electronic trial data handling the sponsor should:
 - ◆ (a) Ensure and document that the electronic data processing system(s) conforms to the sponsor's established requirements for completeness, accuracy, reliability, and consistent intended performance (i.e. validation).
 - ◆ (b) Maintains SOPs for using these systems.
 - ◆ (c) Ensure that the systems are designed to permit data changes in such a way that the data changes are documented and that there is no deletion of entered data (i.e. maintain an audit trail, data trail, edit trail).

SPONSOR

- ◆ (d) Maintain a security system that prevents unauthorized access to the data.
- ◆ (e) Maintain a list of the individuals who are authorized to make data changes (see 4.1.5 and 4.9.3).
- ◆ (f) Maintain adequate backup of the data.
- ◆ (g) Safeguard the blinding, if any (e.g. maintain the blinding during data entry and processing).

SPONSOR

- ◆ **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.

SPONSOR

- ◆ **5.13 Manufacturing, Packaging, Labelling, and Coding Investigational Product(s)**
- ◆ 5.13.2 The sponsor should determine, for the investigational product(s), acceptable storage temperatures, storage conditions (e.g. protection from light), storage times, reconstitution fluids and procedures, and devices for product infusion, if any. The sponsor should inform all involved parties (e.g. monitors, investigators, pharmacists, storage managers) of these determinations.

SPONSOR

- ◆ 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.

SPONSOR

◆ 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

SPONSOR

◆ 5.16 Safety Information

- 5.16.1 The sponsor is responsible for the ongoing safety evaluation of the investigational product(s).
- 5.16.2 The sponsor should promptly notify all concerned investigator(s)/institution(s) and the regulatory authority(ies) of findings that could affect adversely the safety of subjects, impact the conduct of the trial, or alter the IRB/IEC's approval/favourable opinion to continue the trial.

SPONSOR

◆ 5.17 Adverse Drug Reaction Reporting

- 5.17.1 The sponsor should expedite the reporting to all concerned investigator(s)/institutions(s), to the IRB(s)/IEC(s), where required, and to the regulatory authority(ies) of all adverse drug reactions (ADRs) that are both serious and unexpected.
- 5.17.3 The sponsor should submit to the regulatory authority(ies) all safety updates and periodic reports, as required by applicable regulatory requirement(s).

MONITOR

◆ 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).

MONITOR

- ◆ **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).

MONITOR

◆ 5.18.4 Monitor's Responsibilities

- (a) Acting as the main line of communication between the sponsor and the investigator.
- (b) Verifying that the investigator has adequate qualifications and resources
- (c) Verifying, for the investigational product(s):
 - (i) That storage times and conditions are acceptable, and that supplies are sufficient throughout the trial.
 - (ii) That the investigational product(s) are supplied only to subjects who are eligible to receive it and at the protocol specified dose(s).

MONITOR

- ◆ (c) Verifying, for the investigational product(s):
 - (iii) That subjects are provided with necessary instruction on properly using, handling, storing, and returning the investigational product(s).
 - (iv) That the receipt, use, and return of the investigational product(s) at the trial sites are controlled and documented adequately.
 - (v) That the disposition of unused investigational product(s) at the trial sites complies with applicable regulatory requirement(s) and is in accordance with the sponsor.

MONITOR

- ◆ (d) Verifying that the investigator follows the approved protocol and all approved amendment(s), if any.
- ◆ (e) Verifying that **written informed consent** was obtained before each subject's participation in the trial.
- ◆ (f) Ensuring that the investigator receives the current Investigator's Brochure, all documents, and all trial supplies needed to conduct the trial properly and to comply with the applicable regulatory requirement(s).
- ◆ (g) Ensuring that the investigator and the investigator's trial staff are adequately informed about the trial.

MONITOR

- (h) Verifying that the investigator and the investigator's trial staff are performing the specified trial functions, **in accordance with the protocol** and any other written agreement between the sponsor and the investigator/institution, and have not delegated these functions to unauthorized individuals.
- (i) Verifying that the investigator is enrolling only eligible subjects.
- (j) Reporting the subject recruitment rate.
- (k) Verifying that source documents and other trial records are accurate, complete, kept up-to-date and maintained.

MONITOR

- ◆ (l) Verifying that the investigator provides all the required reports, notifications, applications, and submissions, and that these documents are accurate, complete, timely, legible, dated, and identify the trial.
- ◆ (n) **Informing the investigator of any CRF entry error, omission, or illegibility.** The monitor should ensure that appropriate corrections are done by Investigator.

MONITOR

◆ 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.

AUDIT

- ◆ **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.

AUDIT

◆ 5.19.3 Auditing Procedures

- (b) The sponsor's audit plan and procedures for a trial audit should be guided by the importance of the trial to submissions to regulatory authorities, the number of subjects in the trial, the type and complexity of the trial, the level of risks to the trial subjects, and any identified problem(s).
- (c) The observations and findings of the auditor(s) should be documented.
- (d) To preserve the independence and value of the audit function, the regulatory authority(ies) should not routinely request the audit reports.

REPORT

- ◆ **5.22 Clinical Trial/Study Reports**
- ◆ Whether the trial is completed or prematurely terminated, the sponsor should ensure that the clinical trial reports are prepared and provided to the regulatory agency(ies) as required by the applicable regulatory requirement(s).

PROTOCOL

◆ 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.

PROTOCOL

◆ 6.4 Trial Design

- 6.4.1 A specific statement of the primary endpoints and the secondary endpoints,
- 6.4.2 A description of the type/design of trial to be conducted (e.g. double-blind, placebo-controlled, parallel design) and a schematic diagram of trial design, procedures and stages.
- 6.4.3 A description of the measures taken to minimize/avoid bias, including:
 - (a) Randomization.
 - (b) Blinding.

PROTOCOL

- 6.4.4 A description of the trial treatment(s)
- 6.4.5 The expected duration of subject participation, and a description of the sequence and duration of all trial periods, including follow-up, if any.
- 6.4.6 A description of the "stopping rules" or "discontinuation criteria" for individual subjects, parts of trial and entire trial.

PROTOCOL

- ◆ **6.5 Selection and Withdrawal of Subjects** : inclusion criteria. exclusion criteria, withdrawal criteria
- ◆ **6.6 Treatment of Subjects**
 - 6.6.1 The treatment(s) to be administered,
 - 6.6.2 Medication(s)/treatment(s) permitted and not permitted
- ◆ **6.7 Assessment of Efficacy**
 - 6.7.1 Specification of the efficacy parameters.
 - 6.7.2 Methods and timing for assessing, recording, and analysing of efficacy parameters.

PROTOCOL

◆ 6.8 Assessment of Safety

- 6.8.1 Specification of safety parameters.
- 6.8.2 The methods and timing for assessing, recording, and analysing safety parameters.
- 6.8.3 Procedures for eliciting reports of and for recording and reporting adverse event and intercurrent illnesses.
- 6.8.4 The type and duration of the follow-up of subjects after adverse events.

PROTOCOL

◆ 6.9 Statistics

- 6.9.1 A description of the statistical methods
- 6.9.2 The number of subjects planned to be enrolled. Reason for choice of sample size, including reflections on (or calculations of) the power of the trial and clinical justification.
- 6.9.3 The level of significance to be used.
- 6.9.4 Criteria for the termination of the trial.
- 6.9.7 The selection of subjects to be included in the analyses

PROTOCOL

- ◆ **6.10 Direct Access to Source Data/Documents**
- ◆ **6.11 Quality Control and Quality Assurance**
- ◆ **6.12 Ethics**
- ◆ **6.13 Data Handling and Record Keeping**
- ◆ **6.14 Financing and Insurance**
- ◆ **6.15 Publication Policy**

INVESTIGATOR'S BROCHURE

- ◆ 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

INVESTIGATOR'S BROCHURE

- ◆ The IB should contain the following sections, each with literature references where appropriate:
- ◆ 7.3.4 Physical, Chemical, and Pharmaceutical Properties and Formulation
- ◆ 7.3.5 Nonclinical Studies
 - (a) Nonclinical Pharmacology
 - (b) Pharmacokinetics and Product Metabolism in Animals
 - (c) Toxicology

INVESTIGATOR'S BROCHURE

- ◆ 7.3.6 Effects in Humans
 - (a) Pharmacokinetics and Product Metabolism in Humans
 - – Pharmacokinetics
 - – Bioavailability of the investigational product
 - – Population subgroups (e.g., gender, age, and impaired organ function).
 - – Interactions (e.g., product-product interactions and effects of food).
 - – Other pharmacokinetic data (e.g., results of population studies performed within clinical trial(s)).
 - (b) Safety and Efficacy
 - (c) Marketing Experience

ESSENTIAL DOCUMENTS FOR THE CONDUCT OF A CLINICAL TRIAL

Before the Clinical Phase of the Trial Commences

- ◆ **8.2.1 investigator's brochure**
- ◆ **8.2.2 signed protocol and amendments, and sample crf**
- ◆ **8.2.3 informed consent form** (including translations)
- ◆ **8.2.4 financial aspects of the trial**
- ◆ **8.2.5 insurance statement**
- ◆ **8.2.6 signed agreement between involved parties**
- ◆ **8.2.7 dated, documented approval/favourable opinion of institutional review board (irb) /independent ethics committee (iec) of the following:**
- ◆ **8.2.8 institutional review board/independent ethics committee composition**
- ◆ **8.2.9 regulatory authority(ies) authorisation/approval/ notification of protocol**
- ◆ **8.2.10 curriculum vitae and/or other relevant documents evidencing qualifications of investigator(and sub-investigator(s))**
- ◆ **8.2.11 normal value(s)/range(s) for medical/ laboratory/technical procedure(s) and/or test(s) included in the protocol**
- ◆ **8.2.12 medical/laboratory/technical procedures /tests**

ESSENTIAL DOCUMENTS FOR THE CONDUCT OF A CLINICAL TRIAL

- ◆ **8.2.13 sample of label(s) attached to investigational product container(s)**
- ◆ **8.2.14 instructions for handling of investigational product(s) and trial-related materials**
- ◆ **8.2.15 shipping records for investigational product(s) and trial-related materials**
- ◆ **8.2.16 certificate(s) of analysis of investigational product(s) shipped**
- ◆ **8.2.17 decoding procedures for blinded trials**
- ◆ **8.2.18 master randomisation list**
- ◆ **8.2.19 pre-trial monitoring report**
- ◆ **8.2.20 trial initiation monitoring report**

ESSENTIAL DOCUMENTS FOR THE CONDUCT OF A CLINICAL TRIAL

During the clinical conduct of the trial

- ◆ **8.3.1 investigator's brochure updates**
- ◆ **8.3.2 any revision to: - protocol/amendment(s) and crf ; informed consent form**
- ◆ **8.3.3 dated, documented approval/favourable opinion of (IRB) /(IEC)**
- ◆ **8.3.4 regulatory authority(ies) authorisations/approvals/notifications**
- ◆ **8.3.5 curriculum vitae for new investigator(s) and/or sub-investigator(s)**
- ◆ **8.3.6 updates to normal value(s)/range(s) for medical/ laboratory/ technical procedure(s)/test(s) included in the protocol**
- ◆ **8.3.7 updates of medical/laboratory/ technical procedures/tests**
- ◆ **8.3.8 documentation of investigational product(s) and materials shipment**
- ◆ **8.3.9 certificate(s) of analysis for new batches of investigational products**
- ◆ **8.3.10 monitoring visit reports**
- ◆ **8.3.11 relevant communications other than site visits**

ESSENTIAL DOCUMENTS FOR THE CONDUCT OF A CLINICAL TRIAL

- ◆ **8.3.12 signed informed consent forms**
- ◆ **8.3.13 source documents**
- ◆ **8.3.14 signed, dated and completed case report forms (crf)**
- ◆ **8.3.15 documentation of crf corrections**
- ◆ **8.3.16 notification by originating investigator to sponsor of SAE and reports**
- ◆ **8.3.17 notification to regulatory authority(ies) and irb(s)/iec(s) of unexpected serious adverse drug reactions and of other safety information**
- ◆ **8.3.18 notification by sponsor to investigators of safety information**
- ◆ **8.3.19 interim or annual reports to irb/iec and authority(ies)**
- ◆ **8.3.20 subject screening log**
- ◆ **8.3.21 subject identification code list**
- ◆ **8.3.22 subject enrolment log**
- ◆ **8.3.23 investigational products accountability at the site**
- ◆ **8.3.24 signature sheet**
- ◆ **8.3.25 record of retained body fluids/ tissue samples (if any)**

ESSENTIAL DOCUMENTS FOR THE CONDUCT OF A CLINICAL TRIAL

After completion or termination of the trial

- ◆ **8.4.1 investigational product(s) accountability at site**
- ◆ **8.4.2 documentation of investigational product destruction**
- ◆ **8.4.3 completed subject identification code list**
- ◆ **8.4.4 audit certificate**
- ◆ **8.4.5 final trial close-out monitoring report**
- ◆ **8.4.6 treatment allocation and decoding documentation**
- ◆ **8.4.7 final report by investigator to irb/iec where required**
- ◆ **8.4.8 clinical study report**

ESSENTIAL DOCUMENTS FOR THE CONDUCT OF A CLINICAL TRIAL

- ◆ **8.3.12 signed informed consent forms**
- ◆ **8.3.13 source documents**
- ◆ **8.3.14 signed, dated and completed case report forms (crf)**
- ◆ **8.3.15 documentation of crf corrections**
- ◆ **8.3.16 notification by originating investigator to sponsor of SAE and reports**
- ◆ **8.3.17 notification to regulatory authority(ies) and irb(s)/iec(s) of unexpected serious adverse drug reactions and of other safety information**
- ◆ **8.3.18 notification by sponsor to investigators of safety information**
- ◆ **8.3.19 interim or annual reports to irb/iec and authority(ies)**
- ◆ **8.3.20 subject screening log**
- ◆ **8.3.21 subject identification code list**
- ◆ **8.3.22 subject enrolment log**
- ◆ **8.3.23 investigational products accountability at the site**
- ◆ **8.3.24 signature sheet**
- ◆ **8.3.25 record of retained body fluids/ tissue samples (if any)**