



دائرة الصحة  
DEPARTMENT OF HEALTH

# DOH GUIDELINES FOR CONDUCTING CLINICAL TRIALS WITH INVESTIGATIONAL PRODUCTS AND MEDICAL DEVICES

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## I. GENERAL PROVISIONS FOR CLINICAL TRIALS

### 1. PURPOSE & SCOPE

#### 1.1 Purpose:

This guideline provides guidance on the regulatory and good clinical practice (GCP) requirements when conducting clinical trials in Abu Dhabi using ‘unapproved’ investigational therapeutic goods or products.

It describes the schemes under which clinical trials involving ‘unapproved’ investigational therapeutic goods may be conducted in Abu Dhabi.

It assists trial sponsors (pharma, or others), Human Research Ethics Committees (RECs), investigators and approving authorities (institutions) to understand their roles and responsibilities.

It does not describe all of the requirements for conducting clinical trials in Abu Dhabi. It refers to other relevant previous circulars, memos, policies, standards published throughout that should be read in conjunction with this guidance.

#### 1.2 Scope:

The guideline can be used by all DOH-licensed healthcare entities, public and private, seeking to conduct clinical trials using investigational products.

### 2. Definitions

For the purposes of this Guideline, the following definitions apply:

- 2.1 **Adverse event** means any untoward medical occurrence in a subject to whom a medicinal product is administered and which does not necessarily have a causal relationship with this treatment.
- 2.2 **Adverse Device Effect (ADE)** means an adverse event related to the use of an investigational medical device.
- 2.3 **Assent** means a child’s affirmative agreement to participate in a clinical trial. Mere failure to object may not, absent affirmative agreement, be construed as assent.
- 2.4 **Authorized investigational product** means a medicinal product authorized in accordance with UAE Regulation, irrespective of changes to the labelling of the product, which is used as an investigational product.
- 2.5 **Auxiliary medicinal product** means a medicinal product used for the needs of a clinical trial as described in the protocol, but not as an investigational product.
- 2.6 **Clinical study/ trial** means any investigation in relation to humans intended:
  - 2.6.1 to discover or verify the clinical, pharmacological and/or other pharmacodynamics effects of one or more investigational products;
  - 2.6.2 to identify any adverse reactions to one or more investigational products; or



- 2.6.3 to study the absorption, distribution, metabolism and excretion of one or more investigational products; with the objective of ascertaining the safety and/or efficacy of those investigational products. The terms clinical study and clinical trial are synonymous.
- 2.7 **Clinical study report** means a written description of a trial/study of any therapeutic, prophylactic, or diagnostic agent conducted in human subjects, in which the clinical and statistical description, presentations, and analyses are fully integrated into a single report.
- 2.8 **Clinical trial temporary on hold** means an interruption not provided in the protocol of the conduct of a clinical trial with the intention of resuming it later
- 2.9 **Contract Research Organization (CRO)** a person or an organization (commercial, academic, or other) contracted by the Sponsor to perform one or more of a Sponsor's trial-related duties and functions.
- 2.10 **Early termination of a clinical trial** means the premature end of a clinical trial due to any reason before the conditions specified in the protocol are complied with.
- 2.11 **End of a clinical trial** means the last visit of the last subject or at a later point in time as defined in the protocol.
- 2.12 **Good Clinical Practice (GCP)** means a standard for design, conduct, performance, monitoring, auditing, recording, analysis, and reporting clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.
- 2.13 **Good Laboratory Practice (GLP)** is a set of principles intended to assure the quality and integrity of non-clinical laboratory studies that are intended to support research or marketing permits for products regulated by government agencies.
- 2.14 **Good Manufacturing Practice (GMP)** is a system for ensuring that products are consistently produced and controlled according to quality standards. It is designed to minimize the risks involved in any pharmaceutical production that cannot be eliminated through testing the final product.
- 2.15 **Impartial Witness** is a person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the subject or the subject's legally acceptable representative cannot read, and who reads the informed consent form and any other written information supplied to the subject.
- 2.16 **Incapacitated subject** means a subject who is, for reasons other than the age of legal competence to give informed consent, incapable of giving informed consent according to the law of the UAE.
- 2.17 **Independent Ethics Committee (EC)** means an independent body constituted of medical, scientific, and nonscientific members, whose responsibility is to ensure the protection of the rights, safety, and well-being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trials, of protocols and amendments, and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects. This body (ies) is established in Abu Dhabi



- commensurate with the recommendations of this Guideline to give opinions taking into account the views of laypersons, in particular patients or patients' organizations.
- 2.18 **Informed consent** means a subject's free and voluntary expression of his or her willingness to participate in a particular clinical trial, after having been informed of all aspects of the clinical trial that are relevant to the subject's decision to participate or, in case of minors and of incapacitated subjects, an authorization or agreement from their legally designated representative to include them in the clinical trial.
- 2.19 **Inspection** means the act by a regulatory authority (DOH) of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority to be related to the clinical trial and that may be located at the clinical trial site, at the Sponsor's (2.37) and/or contract research organization's (CRO's) facilities, or at other establishments deemed appropriate by regulatory authority (DOH).
- 2.20 **Investigator (principal investigator)** means a person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.
- 2.21 **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. The terms investigational medicinal product (IMP) and investigational product (IP) are synonymous.
- 2.22 **Investigator's brochure** means a compilation of the clinical and non-clinical data on the investigational product or products, which are relevant to the study of the product or products in humans.
- 2.23 **Legally acceptable representative means an individual or juridical or other body authorized according** to the law of the UAE, to consent, on behalf of a prospective subject, to the subject's participation in the clinical trial.
- 2.24 **Manufacturing** means total and partial manufacture, as well as the various processes of dividing up, packaging and labelling (including blinding).
- 2.25 **Medical device** means any instrument, apparatus, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific medical purpose(s) of:
- 2.25.1 Diagnosis, prevention, monitoring, treatment or alleviation of disease,
  - 2.25.2 Diagnosis, monitoring, treatment, alleviation of or compensation for an injury,
  - 2.25.3 Investigation, replacement, modification, or support of the anatomy or of a physiological process,
  - 2.25.4 Supporting or sustaining life,
  - 2.25.5 Control of conception,
  - 2.25.6 Disinfection of medical devices,
  - 2.25.7 Providing information by means of in vitro examination of specimens derived from the human body,



- 2.25.8 And does not achieve its primary intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its intended function by such means (i.e. pharmacological, immunological or metabolic).
- 2.26 **Medical device incident** is any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labeling or the instructions for use which, directly or indirectly, might lead to or might have led to the death of a patient, or user or of other persons or to a serious deterioration in their state of health.
- 2.27 **Minor** means a subject who is, according to the law of the UAE, under the age of legal competence to give informed consent to treatments or procedure involved in clinical trials.
- 2.28 **Non-interventional study** is a clinical study in which:
- 2.28.1 The medicinal product is prescribed in the usual manner in accordance with the terms of the marketing authorization;
  - 2.28.2 Inclusion of a subject into a clinical trial should take into consideration the patient's medication history in order to influence results;
  - 2.28.3 Once accepted into a clinical trial the assignment of that patient to a particular therapeutic strategy is not decided in advance by a trial protocol but takes into consideration current and past medication history;
  - 2.28.4 No additional diagnostic or monitoring procedures are applied to the patients and epidemiological methods are used for the analysis of collected data.
- The terms Non-interventional study (NIS) and observation study (OBS) are synonymous.
- 2.29 **Normal clinical practice** means the treatment regime followed to treat, prevent, or diagnose a disease or a disorder.
- 2.30 **Post-Authorization Efficacy Study (PAES)** is any study conducted where concerns relating to some aspects of the efficacy of the investigational product are identified and can only be resolved after the investigational product has been marketed.
- 2.31 **Post-Authorization Safety Study (PASS)** is any study relating to an authorized investigational product conducted with the aim of identifying, characterizing or quantifying a safety hazard, confirming the safety profile of the investigational product, or of measuring the effectiveness of risk management measures.
- 2.32 **Protocol** means a document that describes the objectives, design, methodology, statistical considerations and organization of a clinical trial. The term 'protocol' encompasses successive versions of the protocol and protocol modifications.
- 2.33 **Serious adverse event** means any untoward medical occurrence that at any dose requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability or incapacity, results in other important medical event, results in a congenital anomaly or birth defect, is life-threatening, or results in death.
- 2.34 **Serious deterioration in the state of health** can include:
- 2.34.1 Life-threatening illness;
  - 2.34.2 Permanent impairment of a body function or permanent damage to a body structure;



- 2.34.3 A condition necessitating medical or surgical intervention to prevent a) or b); examples: - clinically relevant increase in the duration of a surgical procedure - a condition that requires hospitalization or significant prolongation of existing hospitalization;
- 2.34.4 Any indirect harm as a consequence of an incorrect diagnostic or In-Vitro Diagnostic (IVD) test results when used within manufacturer's instructions for use;
- 2.34.5 Fetal distress, fetal death or any congenital abnormality or birth defects.
- 2.35 **Start of a clinical trial** means the first act of recruitment of a potential subject for a specific clinical trial, unless defined differently in the protocol.
- 2.36 **Standard Operating Procedures (SOPs)** are a set of step-by-step instructions compiled by an organization to help workers carry out routine operations. SOPs aim to achieve efficiency, quality output and uniformity of performance, while reducing miscommunication and failure to comply with industry regulations.
- 2.37 **Sponsor** means an individual, company, institution or organization, which takes responsibility for the initiation, for the management and for setting up the financing of the clinical trial. The sponsor should be a person established on the territory of the Emirates of Abu Dhabi with accordance of the federal law or his licensed legally authorized representative.
- 2.38 **Subject / participant** means an individual who participates in a clinical trial, either as recipient of an investigational product or as a control. A subject may be either a healthy human or a patient.
- 2.39 **Substantial amendment** Are defined in terms of regulatory authorization and not terms of the REC application or research protocols and are amendments that are likely significantly to impact the safety or physical or mental integrity of the human subjects, or the quality or safety of any investigational medicinal product used in the trial or the scientific value of the trial. Where the sponsor proposes to make a substantial amendment to an authorized research protocol which consists of, or includes, an amendment to the terms of the REC application or the supporting documentation, the amendment may be made only if the REC has given a favorable opinion.
- 2.40 **Suspension of a clinical trial** means interruption of the conduct of an ongoing clinical trial by DOH or the investigator for reasons related to patient safety.
- 2.41 **Vulnerable Subjects:** include, but are not limited to:
- 2.41.1 The mentally ill
  - 2.41.2 Prisoners and young offenders
  - 2.41.3 Children under 18.
  - 2.41.4 Those in an overtly dependent situation (for example those in care)
  - 2.41.5 Patients with incurable diseases
  - 2.41.6 Persons in nursing homes
  - 2.41.7 Patients in emergency situations
  - 2.41.8 Those incapable of giving consent
  - 2.41.9 Also include individuals whose decision may be influenced by the expectation of a retaliatory response from senior members of a hierarchy in case of refusal



to participate (medical, pharmacy, dental, and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention).

- 2.42 **Suspected unexpected adverse reaction (SUSAR)** is any unexpected adverse reaction that at any dose.
- 2.43 **Phases of Trials:**
- 2.43.1. **Phase 0 trials:** are the basic phase of clinical trials aiming to learn how a drug is processed in the body and how it affects the body. In these trials, a very small dose of a drug is given to about 10 to 15 people
  - 2.43.2. **Phase I trials:** are small trials recruiting only a few patients with the aim of testing a drug's safety and at what level. If a drug is found to be safe enough, it can be tested in a phase II clinical trial.
  - 2.43.3. **Phase II trials:** further assess safety and effectiveness of a drug. The drug is often tested among patients with a specific type of cancer. Phase II trials are done in larger groups of patients compared to Phase I trials. Often, new combinations of drugs are tested. However, the new drug is rarely compared to the current (standard-of-care) drug that is used. If a drug is found to work, it can be tested in a phase III clinical trial.
  - 2.43.4. **Phase III trials: compare a new drug to the standard-of-care drug.** These trials assess the side effects of each drug and which drug works better. Phase III trials enroll 100 or more patients. Often, these trials are randomized.
  - 2.43.5. **Phase IV trial:** Phase IV trials test new drugs approved by the FDA. The drug is tested in several hundreds or thousands of patients. This allows for better research on short-lived and long-lasting side effects and safety.
- 2.44 **Abu Dhabi Health, Research and Technology Council (ADHRTC):** It is an oversight Central Committee that has been established by the department of health.

## II. CLINICAL TRIALS BACKGROUND

### 3. Clinical trials background

- 3.1 Clinical testing on humans should be carried out subject to the fundamental principles of the protection of human rights and dignity in accordance with the Declaration of Helsinki.
- 3.2 All clinical trials of medicinal products on humans, including trials of bioavailability and bioequivalence, should be planned, carried out and reported in compliance with the rules of Good Clinical Practice, the requirements of this Guidelines, Joint Commission International (JCI) requirements and ISO 14155 for clinical investigation of medical devices for human Subjects–Good Clinical Practice.
- 3.3 All considerations which are made in Federal Law No. (4) of 2016 (in respect of medical liability) should be taken into account during review and approval of any activities under this Guidelines.





#### 4. Subjects' Rights

- 4.1 The rights, safety and health of the subjects in a clinical trial should be placed above the interests of science and the public.
- 4.2 Any available preclinical and/or clinical data about the medicinal product tested should be adequate to justify the clinical trial being carried out.

#### 5. Scientific Justification & Description

- 5.1 A clinical trial should be scientifically justified and described in a clear and detailed way in the testing protocol.
- 5.2 Sponsor and investigator should take into account all available Department of Health (Abu Dhabi), Federal and international guidelines and best-practices such as those published by the US Food and Drug Administration, the European Medicines Agency, World Health Organization and the scientific committees attached to them when developing the documentation and when carrying out the clinical trial for a medicinal product.

#### 6. Information Recording

- 6.1 Clinical testing of medicinal products on humans should be guided by DOH procedures outlined in this document for assuring the quality of every aspect of clinical testing.
- 6.2 All information pertinent to the clinical trial and related tests should be recorded, monitored, processed and stored in a way that will ensure its accurate reporting, interpretation and validation, the personal data of subjects being protected.

### III. SUITABILITY OF INDIVIDUALS AND SITES INVOLVED IN CONDUCTING THE CLINICAL TRIAL

#### 7. Individuals involved in conducting the clinical Trial-Qualification & Experience:

- 7.1 All persons conducting a clinical trial should have relevant professional qualification, training and experience, in order to undertake their delegated activities in compliance with Good Clinical Practice.
- 7.2 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.
- 7.3 The Investigator should have sufficient time to conduct and complete the trial properly within the agreed time period.
- 7.4 The Investigator, for the foreseen duration of the trial, should have adequate staff and facilities available to conduct the trial properly and safely.
- 7.5 The clinical testing of a medicinal product should take place under the supervision of a physician or a doctor of dental medicine with a recognized medical specialization in the respective area, who shall be aware of the available preclinical and/or clinical data about the product and the study risks and procedures.



- 7.6 A physician or a doctor of dental medicine with suitable qualifications and license from Department of Health - Abu Dhabi (DOH) should be responsible for the medical or dental care provided to test subjects during the clinical trial, and for making medical or dental decisions.
- 7.7 An updated, recent GCP certification, provided by an approved GCP training organization for investigator is expected to have been completed.

## 8. Suitability of sites involved in conducting the clinical trial

- 8.1 Clinical study/ trial may be carried out in Out/In-patient care establishments/centers that are licensed by and under the terms and conditions of the Department of Health - Abu Dhabi (DOH).
- 8.2 The study site should have adequate resources, staffing, and facilities to conduct the proposed clinical study/ trial
- 8.3 The Institution in which a medicinal product is to be tested should give consent for the participation of the investigator and for the conducting of the trial.

## 9. Approvals

- 9.1 Regulatory and ethical approvals for the following situations should be obtained prior to the conduct of clinical study/ trial on humans:
  - 9.1.1 Medicinal products not authorized in the United Arab Emirates;
  - 9.1.2 Medicinal products that have been authorized in the UAE when tested for an unauthorized indication, for a pharmaceutical form other than the authorized one, in a group of patients who have not been studied so far or for obtaining additional information.
- 9.2 Medicinal products authorized in the UAE, as per items 9.1, 9.1.2, should be those that have obtained marketing authorization in compliance with the MOHAP Regulations.

## 10. Investigational Products

- 10.1 Clinical study/ trial on humans should be carried out with medicinal products that have been manufactured, maintained and stored in accordance with the rules of Good Manufacturing Practice (GMP) for medicinal products under development and research.
- 10.2 An investigational product that has been subjected to pharmacological and toxicological studies in accordance with the requirements of Good Laboratory Practice (GLP) may be proposed for clinical study/ trial.
- 10.3 Adequate chemical and pharmaceutical information should be provided to ensure the proper identity, purity, quality & strength of the investigational product, the amount of information needed may vary with the Phase of the clinical trials, proposed duration of trials, dosage forms and the amount of information otherwise available.



**11. Criteria for Commencing and Conducting Clinical Trials to commence and conduct a clinical trial:**

- 11.1 The expected therapeutic benefits for trial subjects, for present and future subjects and the benefits for health care justify the foreseeable risks;
- 11.2 The available non-clinical and clinical information on an investigation product should be adequate to support the proposed clinical trial;
- 11.3 The physical and mental integrity of the trial subject, his/her right to privacy and personal data protection, are guaranteed;
- 11.4 An insurance or compensation covering investigator or Sponsor liability has been ensured.

**12. The Sponsor and the investigator have to make a local insurance covering their liability available to the trial subjects in the event of any trial-related injury or death during the course of the trial.**

**13. Potential Liability Issues:**

- 13.1 The Sponsor may be held liable in case of health deterioration or death during or on the occasion of clinical testing where the trial is not carried out in accordance with the requirements and procedures based on the protocol approved by the Ethics Committee.
- 13.2 The investigator may be held liable in case of health deterioration or death during or on the occasion of clinical testing where the requirements and procedures based on the protocol approved by the Ethics Committee were changed without having informed the DOH of the changes.

**14. Institution & Contract Research Organization**

- 14.1 The Sponsor and the investigator/institution may be the same person.
- 14.2 The Contract Research Organization involved in the clinical trial should have valid DOH healthcare facility license.

**15. The Sponsor should ensure that the tested medicinal product(s) and all articles required for its administration are free of charge for any case of interventional design.**

**IV. PROTECTION OF SUBJECTS AND INFORMED CONSENT**

**16. Research Subjects**

- 16.1 Clinical testing of medical products should only be permitted on an individual who is/has:
  - 16.1.1 Been informed, in a preliminary conference with a physician, i.e., a member of the research team, of the purposes, risks and inconveniences of testing, and of the terms under which it is to be carried out;



- 16.1.2 Been informed of his right to withdraw from testing at any time, without any penalty for him and is being informed about no loss of treatment as a regular patient even after the withdrawal.
- 16.1.3 Personally given consent in writing to take part, having been made aware of the nature, significance, effects and possible risks of the clinical testing.
- 16.1.4 Been given adequate time to complete the clinical trial.
- 16.1.5 Been provided with a copy of the testing protocol (or the record).
- 16.2 Where the individual is illiterate (that is cannot read or write), informed consent for the participation in a clinical trial should be given orally in the presence of legally acceptable representative who should certify in writing that the individual has personally given informed consent for taking part in the clinical trial.
- 16.3 The informed consent for participation in a clinical trial may be withdrawn at any time.
- 16.4 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.
- 16.4.1 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 impartial witness should sign and personally date the consent form.
- 16.4.2 By signing the consent form, the impartial 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.
- 16.5 With respect to incapacitated adults, information should be provided to them on the trial, its possible risks and benefits in a way that corresponds to their ability for understanding.
- 16.6 The declared wish of an incapacitated adult to refuse taking part or to withdraw at any time from the clinical trial should be respected by the physician.

## 17. Information and Consent

- 17.1 To carry out clinical trial on a minor, written informed consent should be obtained from both parents or from the legal guardian(s) of the minor. The minor should be involved in the process if he/she is able to "assent" by first having the study explained to him/her and/or by reading a simple form about the study, followed by giving verbal consent on whether he/she wants to participate or not. Where one of the parents is unknown, deceased or deprived of parental rights or, in case of divorce no such rights have been given to him/her, the written informed consent should be given by the minor and by the parent exercising parental rights.
- 17.2 The consent of the parents and legal guardians represent the presumed will of the minor and may be withdrawn at any time without any penalty for him.



- 17.3 The investigator should take into consideration the declared wish of minors to refuse taking part or to withdraw at any time from the clinical trial.
- 17.4 The assent of the minor, and the consent of the parents or of the legally acceptable representative may be withdrawn at any time without any penalty for the minor.
- 17.5 The minor should be given information about the trial and about the possible risks and benefits in a way that will ensure understanding by a physician who has experience with minors.

**18. Obtaining informed consent in the event the subject is unable to do so himself or herself:** The information given to the subject or, to his or her legally acceptable representative for the purposes of obtaining informed consent in the event the subject is unable to do so himself or herself, should:

- 18.1 Enable the subject or his or her legally acceptable representative to understand:
  - 18.1.1 The nature, objectives, benefits, implications, risks and inconveniences of the clinical trial;
  - 18.1.2 The subject's rights and measures regarding his or her protection, in particular his or her right to refuse to participate and the right to withdraw from the clinical trial at any time without any resulting penalty and without having to provide any justification;
  - 18.1.3 The conditions under which the clinical trial is to be conducted, including the expected duration of the subject's participation in the clinical trial; and the possible treatment alternatives, including the follow-up measures if the participation of the subject in the clinical trial is discontinued;
- 18.2 Be kept comprehensive, concise, clear, relevant, and understandable to a layperson and should be in or her vernacular language.
- 18.3 Be provided in a prior interview with a member of the investigating team who is a physician and appropriately qualified.

**19. Compassionate Use of the Investigational Product:**

- 19.1 If immediate use of the investigational product is, in the investigator's opinion, required to preserve the life of the subject (Compassionate use):
  - 19.1.1 The decision should be taken by at least two physicians not involved in the research team and should be documented.
  - 19.1.2 And if the time is not sufficient to obtain the independent determination specified in under item 19.1.1 in advance of using the investigational product, the determinations of the clinical investigator should be made and, within 5 working days after the use of the product, be reviewed and evaluated in writing by a physician who is not participating in the clinical investigation. This should be documented.
- 19.2 The documentation in support of items 19.1, 19.1.1 or 19.1.2 should be submitted to the IRB/REC within 5 working days after the use of the investigational product.

**20. Request for Information**



- 20.1 In case the subject during the trial requested additional information, an independent person from the Sponsor has to provide it.
- 20.2 To provide written information to subjects of clinical trials of a medicinal product which contain contact details of the independent person (member of the Ethics Committee, but not part of the study team) for additional information.

## V. CLINICAL TRIALS WITH VULNERABLE GROUPS (VULNERABLE SUBJECTS) OF PATIENTS

### 21. Minors—Clinical trials on minors may be undertaken provided that:

- 21.1 The protocol has been approved by the IRB/REC after discussion of the clinical, moral and psycho-social of the impact on childhood, in which at least two pediatricians have taken part;
- 21.2 A direct benefit is expected from the clinical trial for the group of patients that will be included in it;
- 21.3 The clinical trial is directly related to the clinical condition of the minors;
- 21.4 The medicinal product tested is intended to be used for diagnosis, treatment or prevention of diseases that are specific to minors;
- 21.5 The purpose of the trial is to verify data obtained from clinical trials on individuals that are able to give informed consent or data obtained through other research methods, and the results obtained from clinical trials on adults and their interpretation may not also be considered valid for minors and young persons;
- 21.6 The trial is planned in a way to minimize pain, inconvenience, fear and other foreseeable risks associated with the disease, and the level of risk and physical pain have been predefined and are constantly controlled during testing;
- 21.7 No financial or other incentives are provided.

### 22. Adults Unable to Give Consent

- 22.1 Clinical trials on individuals, who are not able to give informed consent, should be carried out in accordance with the requirements under item 11.
- 22.2 Other than the requirements under item 22.1, the participation of adults who are not able to give informed consent in clinical trials should be allowed, provided that:
  - 22.2.1 The IRB/REC, involving specialists with competence in respect to the disease concerned or to the group of patients, has approved the protocol after discussing the clinical, moral and psycho-social aspects of relevance to the particular disease and to the group of patients;
  - 22.2.2 It may be expected that taking the medicinal product tested would bring benefits exceeding the risks or that risks have been fully eliminated;
  - 22.2.3 The purpose of the trial is to check data obtained through clinical trials on humans who are able to give informed consent or of data obtained through other research methods;



- 22.2.4 The trial is directly connected to a life-threatening or disabling disease or any other diseases of which the adult person concerned who is not able to give informed consent suffers;
- 22.2.5 The clinical trials have been planned so that pain, inconvenience, fear and other foreseeable risks associated with the disease have been reduced to a minimum and the level of risk and the degree of physical pain have been set in advance and are constantly monitored during the trial;
- 22.2.6 No financial and other incentives are provided.

### 23. Pregnant & Breastfeeding Mothers

No clinical trials of a medicinal product may be conducted on pregnant and breast-feeding women, unless the medicinal product concerned is required for their treatment and may not be tested on any other group of patients.

## VI. ETHICS AND RESEARCH COMMITTEES

### 24. Clinical trial scope, purpose, type and design determine the appropriate body or bodies, which should be involved in the assessment of the application.

- 24.1 This includes the involvement of Ethics and Regulatory Committees within the timelines for the authorization of that clinical trial as set out in this Guideline.
- 24.2 When determining the appropriate body or bodies, DOH should ensure that the necessary expertise is available to assess the application.
- 24.3 In accordance with international guidelines, the assessment should be done jointly by a quorum (as stipulated in the Committees Standard Operating Procedures (SOPs)).
- 24.4 Members should collectively have the necessary qualifications, experience and represent a quorum of membership list.
- 24.5 The Committees should be independent of the Sponsor, the clinical trial site, and the investigators involved, as well as free from any other undue influence.

## VII. REC/IRB

### 25. Composition

- 25.1 A REC/IRB (Internal) should ideally include a minimum of five members, having the qualifications and experience required to examine and evaluate the scientific, medical and ethical aspects of the proposed clinical trial.
- 25.2 REC/IRB should be set up within one single clinical establishment and its composition should be specified by an order of the Institution Head.
- 25.3 The committee should comprise:
  - 25.3.1 At least one member whose primary area of interest is in a nonscientific area and
  - 25.3.2 At least one member who is independent of the institution/trial site



- 25.3.3 Representing both genders and being financially and administratively independent of the treatment establishment in which the clinical trial takes place.
- 25.4 The REC/IRB may use the services of external experts for the needs of their work.
- 25.5 While conducting clinical trials on minors, the REC/IRB should ensure involvement of pediatrician as regular member or external experts.
- 25.6 The term of office as well as the rules of renewing the members of the REC/IRB should be clearly determined in writing.

## 26. Scope of activities and responsibilities

The REC/IRB should give an opinion for all clinical trials with interventional and non-interventional design when this is requested by the ADHRTC and when it is involving only one investigational site.

## 27. Functions and operations

- 27.1 The REC/IRB should produce written standard operational procedures in compliance with the rules of Good Clinical Practice within one month of being set up, thereby fixing the terms and conditions of their work. These standard operational procedures should be approved by the respective Abu Dhabi Health, Research and Technology Council (ADHRTC) as part of an accreditation process.
- 27.2 The sessions of the REC/IRB should be conducted in closed sessions. Where necessary, the chairperson of the REC/IRB may invite the Sponsor or investigator to take part therein.
- 27.3 Only those members of the REC/IRB who do not participate directly in a specific trial and are administratively and financially independent of the Sponsor and investigator may vote and take part in deliberations.
- 27.4 Members of the REC/IRB should sign a statement of conflict of interests.

## VIII. AUTHORIZATION TO CONDUCT CLINICAL TRIALS

### 28. Submission Process

- 28.1 Procedures at the Ethics Committee (ADHRTC or REC/IRB) and the DOH may take place simultaneously, at the Sponsor's choice.
- 28.2 The granted opinion of the ADHRTC should be valid for all entities within DOH to the committee and only those included in the application. Any REC decision should be considered as a Single Opinion of the IRB/REC.
- 28.3 A clinical trial should be conducted in compliance with the protocol that has obtained a positive opinion from the Ethics Committee (ADHRTC or REC/IRB), and subject to the terms specified in the documentation filed.
- 28.4 The IRB/REC may collect a fee for the submission of applications requesting an opinion. The fee should be in the amount determined in the tariff.





## IX. ETHICS COMMITTEE APPLICATION FOR A CLINICAL TRIAL

### 29. The Ethics Committee's Opinion

- 29.1 The Ethics Committee (ADHRTC or REC/IRB) should provide an opinion, taking the following into account the:
- 29.1.1 The significance of the clinical trial;
  - 29.1.2 The positive evaluation of the ratio between the expected benefits and the risks in accordance with items 11, 1, and the extent to which the conclusions are justified;
  - 29.1.3 The clinical trial protocol;
  - 29.1.4 The extent to which the investigator and the research team are suitable to conduct the clinical trial;
  - 29.1.5 The Investigator's Brochure;
  - 29.1.6 The consistency and completeness of written information to be provided and the procedure for obtaining informed consent, as well as the extent to which the trial on humans incapable of giving informed consent is justified in the cases under items 21 and 22;
  - 29.1.7 The foreseen compensation or restitution in case of damages or death that may result from the clinical trial;
  - 29.1.8 The Insurance covering the investigator's and sponsor's liability;
  - 29.1.9 Where necessary, the terms and conditions of remunerating or compensating investigators and subjects in the clinical trial and the elements of the contract between the Sponsor and the institution;
  - 29.1.10 The terms and conditions of recruiting subjects.
- 29.2 The Ethics Committee (ADHRTC or REC/IRB) should:
- 29.2.1 Give a positive opinion;
  - 29.2.2 Provide justification for refusal, OR
  - 29.2.3 Request some modification as a condition for obtaining a positive opinion.

### 30. Documentation and Its Evaluation

- 30.1 When evaluating the documentation, the Ethics Committee (ADHRTC or REC/IRB) may require, on a one-off basis, the applicant to provide additional documentation, which may delay the commencement of the trial.
- 30.2 The procedure for examination of the study should terminate where, within 60 calendar days of receiving a request for additional information, the Sponsor fails to submit the documentation requested by the committee.

### 31. Appeal of the Committee's Decision

- 31.1 Where the opinion of the Abu Dhabi Health, Research and Technology Council (ADHRTC) is negative, the investigator may, within a period of 90 calendar days of the date of notification, appeal its decision.
- 31.2 Where the opinion of the REC/IRB is negative, the Investigator may, within a period of 60 calendar days of the date of notification, appeal its decision before the ADHRTC.



31.3 The opinion of the ADHRTC should be final and binding.

## X. TIMELINES FOR REVIEW

### 32. The following timelines are as per international benchmarks:

- 31.4 Interventional Clinical Trial reviewed by ADHRTC: Within a period of 90 calendar days of filing an application, the REC concerned should rule, issuing an opinion, which should be send to the applicant.
- 31.5 Non-interventional Clinical Trial reviewed by ADHRTC: Within a period of 45 calendar days of filing an application, the REC concerned should rule, issuing an opinion, which should be send to the applicant.
- 31.6 Interventional Clinical Trial reviewed by REC/IRB: Within a period of 60 calendar days of filing an application, the REC/IRB concerned should rule, issuing an opinion, which should be send to the applicant and ADHRTC.
- 31.7 Non-interventional Clinical Trial reviewed by REC/IRB: Within a period of 30 calendar days of filing an application, the REC/IRB concerned should rule, issuing an opinion, which should be send to the applicant and ADHRTC

## XI. AMENDMENTS IN CLINICAL TRIALS

### 32. Changes to the Protocol- Substantial Amendments:

The Sponsor through the principal investigator (PI) may introduce changes to the clinical trial protocol at any time, other than significant ones that affects:

- 32.1 the safety or the physical and mental integrity of the subjects;
- 32.2 the scientific value of the study;
- 32.3 the conduct or the organization of the study;
- 32.4 the quality or the safety of one of the medicinal products tested.

### 33. Planned Substantial Amendments

- 33.1 The Sponsor through the principal investigator (PI) may apply planned substantial amendments in the trial protocol and in the documentation under item 37, where:
  - 33.1.1 The respective Ethics Committee has given a written positive opinion;
  - 33.1.2 The DOH has issued a written approval for this in respect to interventional clinical trials.
- 33.2 The provision of item 41.1 does not apply to changes in the approved protocol, which are required in order to protect the subjects from imminent danger when new information is discovered pertaining to the conduct of the trial, or to the development of the tested medicinal product.



- 33.3 In case of change of approved protocol, the investigator should immediately notify the REC/IRB, while Sponsor notify the ADHRTC of the available new information, of the measures taken and of the changes introduced in the protocol.

#### 34. Applying for Substantial Amendments

- 34.1 When planning substantial amendments in the clinical trial and in the documentation under 37, the principal investigator (PI) should file a written application, based on a model, with the REC/IRB.
- 34.2 The application should be accompanied by documentation required to justify the changes and certifying that after applying the change, the evaluation of the ratio between the benefits and the risks under item 11 should be kept.
- 34.3 Substantial amendment is considered whenever there is a change in the information pointed in the item 6 of Appendix 2, of the “DOH STANDARD ON HUMAN SUBJECTS RESEARCH” document (Example list of information changes considered as substantial).
- 34.4 The requirements to the application and the documentation about the amendments is specified in item 7 of Appendix 2 of the “DOH STANDARD ON HUMAN SUBJECTS RESEARCH” document (The requirements to the application and the documentation about the amendments).

35. **Notification:** Within a period of up to 30 calendar days of receiving an application for amendment, the REC/IRB, if applicable should notify the applicant of its resolution, issuing:

- 35.1 A positive opinion on the requested changes and issuing an approval, or  
35.2 A motivated refusal of changes in the clinical trial.

#### 36. Modification of a Proposed Amendment

- 36.1 In the cases under items 44, 2, the Sponsor may submit a modification of the proposed amendment, in line with the reasons, within 14 calendar days after receiving a rejection.
- 36.2 Within a period of 14 calendar days of the date of receiving the changed documentation under item 44.1, the body initially issuing a refusal should issue a change to the authorization for a clinical trial involving medicinal products, or a refusal. Both of these decisions are final.

## XII. SUSPENSION OF THE CLINICAL TRIAL

#### 37. Urgent Measures

- 37.1 The Sponsor or the investigator may undertake urgent measures in order to protect the subjects of the clinical trial against any suddenly appearing risks to their safety and health.
- 37.2 In the cases under item 45.1, the REC/IRB should be immediately notified by the principal investigator (PI) of the action undertaken and of their causes.



### 38. Provisional suspension

- 38.1 When the trial is conducted under terms other than those specified upon issuance of the authorization, or information is available that the scientific validity of the study is discredited, or there is a risk to the safety of the subjects, or any serious concerns about the protection of rights and wellbeing of the trial subject, the ADHRTC/ REC/IRB may provisionally suspend the trial or terminate it.
- 38.2 The termination may be imposed on a particular center or on all centers.
- 38.3 In case of termination of the clinical trial in all centers on the territory of the Emirates of Abu Dhabi, the ADHRTC, prior to taking action under item 47.1, should notify in writing the Sponsor and the investigator.
- 38.4 Within seven calendar days of receiving the notification, the investigator may give an opinion on the measures taken by ethics committee.
- 38.5 The provision of item 46.3 should not apply where there is immediate risk to the health and safety of trial subjects.

## XIII. SAFETY FOLLOW-UP AND REPORTING AS PART OF CLINICAL TRIAL

### 39. Reporting

- 39.1 The investigator should immediately notify the Sponsor in writing, of any serious adverse event that has occurred in the course of the clinical trial with a subject in the center of which he is in charge as per the protocol.
- 39.2 After the notification under item 47.1, a detailed report in writing should be submitted to the Sponsor.
- 39.3 When a notification under item 47.1 or a report under item 51.2, the trial subject should be identified by a unique code specified in the trial protocol.
- 39.4 The investigator should report to the Sponsor and the ethics committee all adverse events (Adverse Event of Special Interest - AESI) or laboratory deviations specified in the protocol as critical to safety, within the period and in the format compliant to the requirements of the protocol.

**40. Adverse Event:** When the outcome of an adverse event during the conducting of a clinical trial is fatal, the investigator should be obligated to provide the Sponsor and the Ethics Committee with all additional information requested.

### 41. Suspected Serious Adverse Event

- 41.1 The principal investigator (PI) should notify the Ethics Committees, respectively, of any suspected unexpected serious adverse reaction that has occurred in the course of a clinical and has resulted in death or has proven to be life threatening, within seven calendar days at the latest of receiving the information about it.
- 41.2 The Sponsor and principal investigator (PI) respectively should provide the bodies under item 49.1 with additional information about the case within 7 calendar days of the date on which a notification was sent.



- 41.3 The principal investigator (PI) respectively is responsible to notify the Ethics Committees of all suspected unexpected serious adverse reactions other than those specified in item 49.1 that have occurred in the course of the clinical trial, 15 calendar days at the latest from receiving the information about their occurrence.
- 41.4 When some information is not available at the time of report, e.g. causality assessment by medical monitor of Sponsor/ Contract Research Organization (CRO), compensation provided for study related injury or death, the same has to be provided as a follow-up report.

#### **42. Suspected Unexpected Adverse Reaction**

- 42.1 The format and the content of the notifications of SUSARs (both initial as well as follow-up reports) should be submitted to the Ethic Committees along with a covering letter (printed on the company's/ Contract Research Organization's (CRO's) letterhead). A template of covering letter is specified in Appendix 03.
- 42.2 The Sponsor should inform the investigators carrying out the clinical trial with an investigational product of any suspected unexpected adverse reaction associated with the tested medicinal product, irrespective of its origin.

#### **43. Suspected Serious Adverse Reactions**

- 43.1 Once a year the principal investigator (PI) should submit to the REC/IRB a list of all suspected serious adverse reactions that have occurred within the past period and a report on the safety of trial subjects.
- 43.2 Once a year the principal investigator (PI) should submit to the REC/IRB an update of Investigator's brochure or other relevant information concerning the safety profile of the investigational product.

44. **The Ethic Committee** should record all information provided about the suspected unexpected serious adverse reactions caused by investigational products tested.

### **XIV. NOTIFICATION OF COMPLETION OF THE CLINICAL TRIAL**

#### **45. When to Notify**

- 45.1 The principal investigator (PI) should notify REC/IRB in writing of the termination or completion of the trial.
- 45.2 The notification should be filed within 90 calendar days of the completion of the study.
- 45.3 Unless otherwise specified in the protocol approved by the REC/IRB, the last visit of a subject should be considered as the completion of the trial.
- 45.4 Where a trial terminates early, the principal investigator (PI) should notify the REC/IRB within up to 15 calendar days of making a decision, stating the reasons for it.

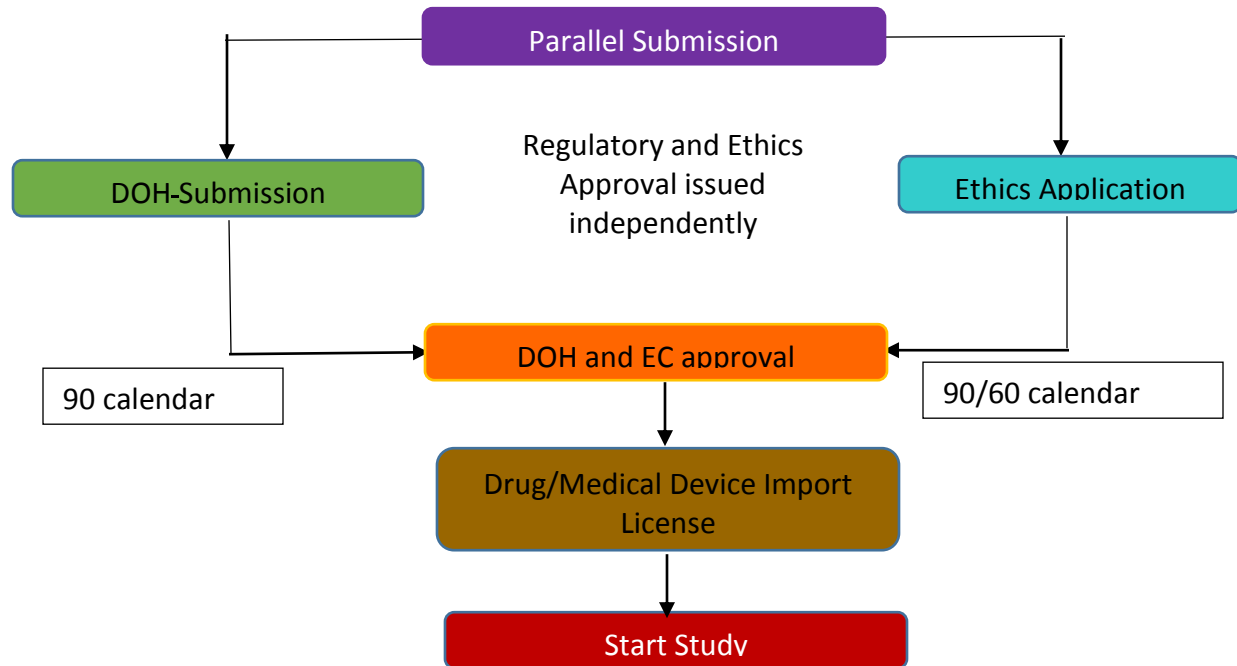


#### 46. Final Report

46.1 The principal investigator (PI) to the REC/IRB with a final report on the clinical trial within one year from the end of the trial.

## Appendix 1: Flow Chart of the Authorization Process

### 1. Process for Interventional Clinical Trial approved by DOH and ADHRTC / REC/IRB



### 2. Process for Non-Interventional Clinical Trial, approved by ADHRTC or REC/IRB





## Appendix 2: Data Elements for Reporting Serious Adverse Event (SAE) Occurring in a Clinical Trial

1. Subject details
  - a. Subject initials & identifier
  - b. Country
  - c. Gender
  - d. Age and/or date of birth
2. Suspected Drug(s)
  - a. Generic name of the suspect drug
  - b. Indication(s) for which suspect drug was prescribed or tested
  - c. Dosage form and strength
  - d. Daily dose and regimen (specify units - e.g., mg, ml, mg/kg)
  - e. Route of administration
  - f. Starting date and time of day
  - g. Stopping date and time, or duration of treatment
3. Other Treatment(s) Provide the same information for concomitant drugs (including non-prescription/ OTC drugs) and non-drug therapies, as for the suspected drug(s).
4. Details of Serious Adverse Event (s)
  - a. Start date (and time) of onset of event
  - b. Stop date (and time) or duration of event
  - c. De-challenge and re-challenge information
  - d. Results of specific tests and/or treatment that may have been conducted
5. Outcome

Information on recovery and any sequelae; for a fatal outcome, cause of death and a comment on its relationship to the suspected reaction; any post-mortem findings other information: anything relevant to facilitate assessment of the case, such as medical history including allergy, drug or alcohol abuse; family history; findings from special investigations etc.

Details of compensations provided for injury or death. In case no compensation has been paid, reason for the same should be submitted. It is pertinent to mention that in case of study related injury or death, complete medical care as well as compensation for the injury or death should be provided.
6. Details about the Investigator
  - a. Name, Address & Telephone number
  - b. Date of receipt by the investigator
  - c. Date of reporting the event to Licensing Authority
  - d. Date of reporting the event to Ethics Committee overseeing the site:
  - e. Signature of the Investigator





### Appendix 3: Covering Letter Elements for Reporting SUSAR Reporting in a Clinical Trial to the Ethics Committee

1. CT number.
2. Phase of clinical trial.
3. Protocol or Study No. / Code / ID and the study title.
4. Adverse event term / diagnosis (Whenever possible provide a “preferred term”).
5. A brief narrative of the event, not exceeding 10 lines. A detailed narrative may be enclosed, if available.
6. Causality assessment by investigator and the medical monitor of Sponsor/CRO. The assessment report should clearly mention whether the SAE occurred is related or not related (Situations like unlikely, possibly, suspected, doubtful etc. should not be used).
7. Whether the outcome is fatal.
8. Details of compensations provided for injury or death. In case no compensation has been paid, reason for the same should be submitted. It is pertinent to mention that in case of study related injury or death, complete medical care as well as compensation for the injury or death should be provided.