



دائرة الصحة  
DEPARTMENT OF HEALTH

# DOH STANDARD ON HUMAN SUBJECT RESEARCH

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<b>Related Laws, Policies, Standards, Circulars &amp; Guidelines</b>	This Standard should be read in conjunction with related UAE laws, DOH Standards, Policies and Manuals especially but not limited to: <ul style="list-style-type: none"> <li>• DOH Regulator Manual</li> <li>• DOH Consent Guideline</li> <li>• Federal Law on Medical Liability</li> <li>• Guidelines for conducting Clinical Trial with investigational products and medical devices (MOHAP)</li> </ul> For more information, kindly visit: <a href="http://www.mohap.gov.ae">http://www.mohap.gov.ae</a> and <a href="http://www.doh.gov.ae">www.doh.gov.ae</a>
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## 1. Purpose

- 1.1 To define the regulatory requirements for the conduct of clinical research involving human subjects in the Emirate of Abu Dhabi.
- 1.2 This Standard replaces the DOH Standard Operating Procedures for Research Ethics Committees Version 1.0.

## 2. Scope

- 2.1 This Standard applies to:
  - 2.1.1. Any type of facility or organization seeking to undertake research involving human subjects in the Emirate of Abu Dhabi, healthcare providers and healthcare professionals, educational institutions and pharmaceutical firms.



- 2.1.2. Clinical Trials of Investigational Medicinal Products (CTIMPs).
- 2.1.3. Any research involving vulnerable persons (see Definitions & Abbreviations).
- 2.1.4. All other research involving human participants.
- 2.1.5. Research that does not involve human participants but has ethical considerations.
- 2.1.6. Clinical Trial with Medical Devices.
- 2.2 This Standard does not apply to:
  - 2.2.1 CTIMPs for gene therapy;
  - 2.2.2 Phase I CTIMPs;
  - 2.2.3 Any research exclusively involving animal subjects;
  - 2.2.4 Bio banking of umbilical cord blood, tissue stem cells, or the use of any stored tissues for diagnostic, therapeutic, or other human applications.
  - 2.2.5 Procedures for CTIMPs for gene therapy, Phase I CTIMPs, and clinical investigations involving medical devices or ionizing radiation may be added to this Standard in the future.
- 2.3 All paragraphs relating to authorization for clinical trials, Investigational Medicinal Products (IMPs) and Suspected Unexpected Serious Adverse Events (SUSARs) apply to CTIMPs only.

### 3. Definitions & Abbreviations

- 3.1 **Abu Dhabi Health Research and Technology Committee (ADHRTC):** Is an oversight committee that has been established by DOH to oversee and support critical human subject research carried out by various healthcare providers from public or private healthcare providers, and to advise on and promote health research in the Emirate of Abu Dhabi.
- 3.2 **Adverse reaction/event:** In a Clinical Trial of an Investigational Medical Product (IMP) any untoward and unintended response in a subject to an IMP which is related to any dose administered to that subject.
  - 3.2.1 **Unexpected Adverse Reaction:** An adverse reaction is considered to be “unexpected” if its nature and severity are not consistent with the information about the medicinal product set out in the trial documentation.
  - 3.2.2 **Serious Adverse Reaction/Event:** is an untoward and unintended response to an IMP at any dose that:
    - Results in death;
    - Is life threatening;
    - Requires hospitalisation or prolongation of existing hospitalisation;
    - Results in persistent or significant disability or incapacity;
    - Consists of a congenital anomaly or birth defect;
    - Or is otherwise considered medically significant by the investigator.
  - 3.2.3 **Suspected Serious Adverse Reaction (SSAR):** An adverse reaction is “serious” if it:
    - Results in death
    - Is life-threatening
    - Requires hospitalisation or prolongation of existing hospitalisation
    - Results in persistent or significant disability or incapacity
    - Consists of a congenital anomaly or birth defect.



- 3.2.4 **Suspected unexpected serious adverse reaction (SUSAR):** A “suspected unexpected serious adverse reaction” (SUSAR) is a SSAR which is also “unexpected”, meaning that its nature and severity are not consistent with the information about the medicinal product in question as set out:
- In the case of a product with a marketing authorisation, in the summary of product characteristics for that product
  - In the case of any other investigational medicinal product, in the investigator’s brochure relating to the trial in question
- 3.3 **Amendment:** A change made to the application to the facility’s REC for its approval of the research project, the research protocol or any other supporting documentation after the study has started. (See Appendix 9).
- 3.3.1 **Modified amendment:** Following the issue of an unfavourable opinion on a substantial amendment, the re-submission of the amendment in modified form.
- 3.3.2 **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 authorised 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 favourable opinion.
- 3.3.3 **Minor amendment:** An amendment which is not a substantial amendment, not requiring review by a REC.
- 3.4 **Approval conditions:** Are the conditions to be observed by the applicant in the conduct of the research.
- 3.5 **Authorised health professional:** could be licenced doctor, dentist, nurse or pharmacist.  
Note: The Principal Investigator and any investigator at a site in a CTIMP must be one of the above.
- 3.6 **Benefits:** Refers to the direct advantages subjects may obtain by participating in the research. (See Appendix 11).
- 3.7 **Care organization:** Is the organization(s) responsible for providing care to patients and/or users and carers participating in the research/study. Care organizations remain liable for the quality of care, and for their duty towards anyone who might be harmed by a study.
- 3.8 **Chair:** The head of the REC carrying ultimate responsibility for all actions and decisions taken by the Committee. Note: all references in this Standard to “the Chair” should be interpreted as referring also to the vice-Chair when acting in place of the Chair.
- 3.9 **Clinical Research Organization (CRO):** provide clinical trial services for PI’s, Institutions or pharmaceutical companies on an outsource basis.



**3.10 Clinical Trial:** Any investigation in human subjects, other than a non-interventional trial, intended to discover or verify the clinical, pharmacological or other pharmacodynamics effects of one or more medicinal products, identify any adverse reactions to one or more such products and/ or study absorption, distribution, metabolism and excretion of one or more such products with the object of ascertaining the safety or efficacy of those products.

**3.10.1 Types of Trials:**

3.10.1.1 **CTIMP: Clinical trial of an investigational medicinal product.** (Any other type of research is known as a non-CTIMP).

3.10.1.2 **Non-CTIMP:** Any **research** study that is not a CTIMP.

**3.10.2 Phases of Trials:**

3.10.2.1 **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

3.10.2.2 **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.

3.10.2.3 **Phase II trials:** further assess safety and effectiveness of a drug. The drug is often tested among patients with a specific type of condition. 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.

3.10.2.4 **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.

3.10.2.5 **Phase IV trial: Phase IV trials** test new drugs approved by the United States Food and Drug Administration (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.

**3.10.3 Conducting a clinical trial (see Appendix 1):**

3.10.3.1 **Administering,** or giving directions for the administration of, an investigational medicinal product to a subject for the purposes of that trial; or

3.10.3.2 **Giving a prescription** for an investigational medicinal product for the purposes of that trial; or

3.10.3.3 **Carrying out** any other medical or nursing procedure in relation to that trial; or

3.10.3.4 **Carrying out** any test or analysis:

i. to discover or verify the clinical, pharmacological or other pharmacodynamics effects of the investigational medicinal products administered in the course of the trial

ii. to identify any adverse reactions to those products, or

iii. to study absorption, distribution, metabolism or excretion of those products.



It does not include activity undertaken prior to the commencement of a trial, which consists of making such preparations for the trial as are necessary or expedient.

3.10.4 **Sponsor of a clinical trial:** The person who takes on the ultimate responsibility for the initiation, management and financing (or arranging the financing) of a clinical trial. Where two or more persons take responsibility for the functions of the sponsor, one of the sponsors should take responsibility for each of the following group of functions:

- 3.10.4.1 **communications** relating to substantial amendments, modified amendments and the conclusion of the trial;
- 3.10.4.2 **communications** relating to urgent safety measures; and
- 3.10.4.3 **Pharmacovigilance** reporting.

The Principal Investigator is considered the sponsor if he/she independently plans, conducts, and is totally responsible for a clinical trial.

- 3.11 **Committee:** The Research Ethics Committee (REC).
- 3.12 **DOH:** Department of Health - Abu Dhabi.
- 3.13 **Deception:** There are two types of deception: passive, wherein the investigator does not fully disclose the purpose or expectations of the research (also referred to as deception by omission), and active, wherein the investigator deliberately misleads the subject (also referred to as deception by commission).
- 3.14 **European Union Drug Regulating Authorities Clinical Trials Database (EudraCT):** is the European database for all interventional clinical trials on medicinal products authorized in the European Union (EEA) and outside the EU/EEA.
- 3.15 **Facility:** Facility/organization seeking to undertake research involving human subjects in the Emirate of Abu Dhabi, including healthcare providers and healthcare professionals, educational institutions and pharmaceutical firms.
- 3.16 **Healthcare Provider:** Any person who operates a healthcare facility.
- 3.17 **Human embryonic stem cell (HESC):** one of the cells that are self-replicating, are derived from human embryos or human fetal tissue, and are known to develop into cells and tissues of the three primary germ layers.
- 3.18 **Human subject: A living individual about whom an investigator obtains:**
  - 3.18.1 Data from intervention or interaction with and/or
  - 3.18.2 Identifiable private information (e.g. examining student records to ascertain grade point averages).
- 3.19 **Human Tissue:** Any part of the human body, which has been separated from a human being (whether living or dead).



- 3.20 Informed Consent:** Refers to a written document that informs subjects about what they can expect from participating in a research study.
- 3.21 Institutional Review Board (IRB):** Is equivalent to the Research Ethics Committee (REC). It is an administrative body established within the facility that is intending to conduct clinical research, to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under their facility, in addition to the legal protection for the investigators and the facility itself.
- 3.22 ICH GCP:** International Conference on Harmonisation Guideline for Good Clinical Practice (ICH GCP), is a set of standards used internationally for the conduct of clinical trials, delineating the responsibilities and expectations of all participants in the conduct of clinical trials, including investigators, monitors, sponsors and ethics committees. ICH GCP sets internationally accepted standards for monitoring, reporting and archiving of clinical trials. (See [Efficacy Guidelines: Good Clinical Practice \(E6\)\(R2\)](#)<sup>1</sup>).
- 3.23 Investigator:** The authorized health professional responsible for the conduct of a clinical trial at a trial site, and if the trial is conducted by a team of authorized health professionals at a trial site, the investigator is the leader responsible for that team.
- 3.23.1 Principal investigator (PI):** Principal Investigator is the primary individual responsible for the preparation, conduct, and administration of a research project at a study/trial site in compliance with applicable laws and regulations and facility policy governing the conduct of research.
- 3.23.1.1 A PI is preferably to be from one of the following health specialties; physician, dentist, nurse or pharmacist.
- 3.23.1.2 Where research projects involve collaboration among many individuals, one person must be designated as the principal investigator (PI).
- 3.23.1.3 The PI will be the investigator responsible for the research site in a multi-site study. There should also be one PI for each research site.
- 3.23.1.4 In the case of a single-site study, the PI and the key investigator will normally be the same person.
- 3.23.1.5 The PI is the “point person” for communicating with the REC and all applications for review by the REC should be submitted by the PI.
- 3.23.2 Co-investigator or Sub-investigator:** Is any individual member of the research project designated and supervised by the PI to perform the tasks, procedures, to make important decisions related to the study and to assume responsibilities above those of other personnel and is recognized by the facility.

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[https://www.ich.org/fileadmin/Public\\_Web\\_Site/ICH\\_Products/Guidelines/Efficacy/E6/E6\\_R2\\_Step\\_4\\_2016\\_110\\_9.pdf](https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2_Step_4_2016_110_9.pdf)



- 3.24 Investigator's brochure:** A document containing a summary of the clinical and non-clinical data relating to an investigational medicinal product which are relevant to the study of the product in human subjects.
- 3.25 Investigational medicinal product (IMP):** Is a pharmaceutical form of an active substance or placebo being tested, or to be tested, or used, or to be used, as a reference in a clinical trial, and includes a medicinal product, which has a marketing authorization but is, for the purposes of the trial:
- used or assembled (formulated or packaged) in a way different from the form of the product authorized under the authorization
  - used for an indication not included in the summary of product characteristics under the authorization for that product
  - used to gain further information about the form of that product as authorized under the authorization.
- 3.26 Non-interventional trial:** A study of one or more medicinal products, which have a marketing authorization, where all of the following conditions are met:
- The products are prescribed in the usual manner in accordance with the terms of that authorization
  - The assignment of any patient involved in the study to a particular therapeutic strategy is not decided in advance by a clinical trial protocol
  - The decision to prescribe a particular medicinal product is clearly separated from the decision to include the patient in the study
  - No diagnostic or monitoring procedures are applied to the patients included in the study, other than those which are ordinarily applied in the course of the particular therapeutic strategy in question
  - Epidemiological methods are to be used for the analysis of the data arising from the study.
- 3.27 Participant:** Anyone who consents to take part in a study.
- 3.28 Protocol/Research Protocol:** Is a document that describes the background, rationale, objectives, design, methodology, statistical considerations, and organization of a research project.
- 3.29 Protocol Deviation:** Is any change or alteration from the procedures stated in the study's original protocol, consent document, recruitment process, or study materials (e.g. questionnaires) that were submitted to the healthcare providers' Research Ethical Committee (REC) and approved by it. Protocol deviations can be either major (important protocol deviations) or minor. Repeated failure by an investigator not to report protocol deviations may be viewed as non-compliance with the federal and local regulations and with the guidelines that govern ethical conduct of research. (see Appendix 10).
- 3.30 Regulatory Authority:** A body responsible for the approval, regulation and monitoring of CTIMPs and non-CTIMPs.



- 3.31 Research:** A “systematic investigation designed to develop or contribute to generalizable knowledge beyond a particular setting. This includes findings that are presented as a poster or paper at a conference, at Student Symposium, on a website, or that may be published, and student work presented outside of the classroom.
- 3.32 Human Subject Research:** Any activity falling within one or more of the following categories:
- 3.32.1 Studies of a physiological, biochemical or pathological process, or of the response to a specific intervention – whether physical, chemical or psychological – in healthy subjects or in patients.
  - 3.32.2 Controlled trials of diagnostic, preventive or therapeutic measures in larger groups of persons, designed to demonstrate a specific generalizable response to these measures against a background of individual biological variation.
  - 3.32.3 Studies designed to determine the consequences for individuals and communities of specific preventive or therapeutic measures.
  - 3.32.4 Studies concerning human health-related behaviour in a variety of circumstances and environments.
- Activities that are not considered “research” for the purpose of this Standard include:
- Research on normal educational practices such as instructional strategies, curricula or classroom management techniques. Experiments with class format and/or use of student evaluation to improve teaching.
  - Journalism: Journalists and investigative reporters who are writing stories for news publications unless ethical approval is required.
- 3.33 Research Authorization:** Regulatory permission granted by DOH to a DOH-licensed Healthcare Provider authorizing Human Subject Research to be conducted at a Facility operated by it.
- 3.34 Research site:** The organization or unit responsible for conducting any of the research procedures in a study at a particular locality.
- 3.35 Revision of application:** Any changes made to the terms of an application following the meeting or, following issue of an opinion, before the research has started. Revision is not permitted prior to the REC meeting once the application has been validated.
- 3.36 Risk:** Is the probability of physical, psychological, legal, social or economic harm occurring as a result of participating in a research study. (see Appendix 11).
- 3.37 Unanticipated Event:** (see Appendix 8)
- 3.38 Vulnerable persons: Vulnerable persons include, but are not limited to:**
- The mentally ill.
  - Prisoners and young offenders.
  - Children under 18.
  - People of determination.
  - Those in an overtly dependent situation (for example those in care).
  - Patients with incurable diseases



- Persons in nursing homes
- Patients in emergency situations
- Those incapable of giving consent
- 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).

#### 4. Duties of Healthcare Provider/Facility Conducting Human Subject Research

##### 4.1 Obtaining a Facility Research Authorization:

A healthcare provider or facility seeking to conduct human subject research must apply for and have a Facility Research Authorization granted by DOH for that Facility to conduct Human Subject Research.

- 4.1.1. A facility must not permit Human Subject Research to be carried out at a the premises operated by it unless:
  - 4.1.3.1. It holds a valid Facility Research Authorization granted by DOH, applicable to that Facility, and
  - 4.1.3.2. The Human Subject Research carried out at the Facility is within the description of research that is permitted to be carried out in accordance with the Facility Research Authorisation.
- 4.1.2. To obtain a Facility Research Authorisation, a healthcare provider/facility must comply with DOH's requirements as part of the Application for Authorization to Conduct Human Subject Research which include:
  - 4.1.2.1. Application form;
  - 4.1.2.2. Establishment of a Research Ethics Committee;
  - 4.1.2.3. Completion of a Research Ethics Training course.
- 4.1.3. Any Healthcare Provider applying for or holding a Facility Research authorization must comply with any other duties set out in the DOH Application for Authorization to Conduct Human Subject Research.

##### 4.2 Establishing and Operating a Facility Research Ethics Committees (Facility REC)

Research Ethics Committee are authorized by DOH to ensure the protection of human subjects in research projects conducted or sponsored (see Appendix 1 on DOH Guidelines for the Structure and Function of REC) by the facility.

- 4.2.1 A healthcare provider/facility seeking DOH authorization to Conduct Human Subject Research must ensure that a Research Ethics Committee is established and maintained for each facility that holds a Facility Research Authorization.
- 4.2.2 The Research Ethics Committee must, at a minimum:
  - 4.2.2.1. Include members from departments which are more active in clinical research;
  - 4.2.2.2. Be multi-representative and multi-disciplinary;
  - 4.2.2.3. Have clear SOP's and protocols;
  - 4.2.2.4. Have protocols for different levels of research approvals;



- 4.2.3 When establishing of Research Ethics Committees, facilities and investigators must comply with The Integrated Addendum to the International Conference on Harmonization Good Clinical Practice (E6) (R2), the International Standard for Ethical Research Conduct, Chapter VII of the Health Regulator Manual, and all other applicable Laws and Regulations.
- 4.2.4 The facility must ensure that the REC is constituted and operates in accordance with DOH published rules and regulation.
- 4.2.5 Before confirming a favorable opinion on any research (including both CTIMPs and non-CTIMPs), the REC shall assure itself that the sponsor and investigators have appropriate insurance or indemnity cover for the potential legal liability arising from the research due to either injury or death attributable to the research especially in the case of CTIMP.
- 4.2.6 As authorized by DOH, the Research Ethics Committee should:
- 4.2.6.1 Review the research application and ensure its compliance with national laws and standards, international research standards and DOH regulations;
  - 4.2.6.2 Give an ethical opinion on proposed research projects;
  - 4.2.6.3 Refer to DOH for its approval all proposals for proposed research in critical areas;
  - 4.2.6.4 Monitor of the research process and review regular reports from the PI;
  - 4.2.6.5 Be notified of any serious breach of Good Clinical Practice or the research protocol;
  - 4.2.6.6 Review protocol deviations for approval/rejection;
  - 4.2.6.7 Communicate any change in its ethical position to DOH;
  - 4.2.6.8 Notify DOH where one of the following is suspected:
    - 4.2.6.8.1. Conduct of a trial without regulatory authorization or favorable REC opinion.
    - 4.2.6.8.2. Provision of false or misleading information to the REC in relation to an application for ethical opinion or notification of substantial amendment.
    - 4.2.6.8.3. Implementation of a substantial amendment without authorization and/or a favorable opinion as appropriate.
    - 4.2.6.8.4. Failure to notify SUSARs occurring in a trial in an expedited manner or to provide an Annual Safety Report.
    - 4.2.6.8.5. Failure to notify urgent safety measures.
    - 4.2.6.8.6. Failure to notify the early termination or conclusion of the trial.
    - 4.2.6.8.7. A serious breach of ICH GCP or the research protocol. A breach of the conditions and principles of ICH GCP or the research protocol should be regarded as “serious” if it is likely to affect to a significant degree the safety or physical or mental integrity of the participants or the scientific value of the trial.
    - 4.2.6.8.8. Any other fraud or serious misconduct.
    - 4.2.6.8.9. Consideration should also be given to notifying the authorities where a pattern emerges of repeated minor breaches of ICH GCP or the research protocol.
- 4.3 Data and Record Keeping: A Healthcare Provider must ensure that all information related to Human Subject Research for which it is responsible is recorded, handled and stored in a



way that allows its accurate reporting, interpretation, and verification in accordance with all applicable Regulations on document retention, information management and data protection and confidentiality.

#### 4.4 Duties of Facilities' Research Ethics Committees with Respect to Studies with Special Considerations:

- 4.3.1. Applications involving critical subjects, mentioned below, must be approved in principle by REC, then forwarded to ADHRTC for its review and approval prior to the execution of the study.
  - 4.3.1.1. Multi-center studies;
  - 4.3.1.2. Clinical Trials/studies;
  - 4.3.1.3. Any pharmaceutical sponsored research;
  - 4.3.1.4. Any research that carries significant or potential risk to human subjects (patients);
  - 4.3.1.5. Any research with genetic material;
  - 4.3.1.6. Processing of medical data outside UAE for research purpose;
  - 4.3.1.7. Genomics-related research;
- 4.3.2. Facilities must ensure that Human Subject Research complies with all UAE laws, DOH policies and standards, and the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, Guideline for Good Clinical Practice E6(R2) (ICH GCP).<sup>2\*</sup>
- 4.3.3. Facilities must comply with DOH requests to inspect and audit records and cooperate with DOH-authorized auditors, as required for inspections and audits by DOH.

### 5. Specific Responsibilities of Healthcare Providers/Investigators with Respect to Human Subject Research

#### 5.1. Securing Approval of the Facility's REC:

- 5.1.1. The principal investigator must obtain REC approval prior to beginning to work with human subjects.
- 5.1.2. The standard approval conditions apply to CTIMPs and all other research.
- 5.1.3. The principal investigator should inform co-investigators and subjects of the REC's approval and contact information.
- 5.1.4. As the research progresses, the principal investigator must obtain REC approval for any changes in methodology or protocol before the changes are implemented.
- 5.1.5. The principal investigator must contact the REC if any incidents that harm or may harm a human subject arise during the research.
- 5.1.6. The principal investigator must inform the REC when the research project has been completed.
- 5.1.7. Insurance, Indemnity & Compensation:

<sup>2</sup> International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, Guideline for Good Clinical Practice E6(R2) (ICH GCP). (Available at URL: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ICH\\_Products/Guidelines/Efficacy/E6/E6\\_R2\\_Step\\_4\\_2016\\_1109.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2_Step_4_2016_1109.pdf))



- 5.1.7.1. Research institutions, investigators and sponsors are responsible for ensuring that insurance cover is adequate to protect the investigators and the institutions from legal liability in case of injury or death.
- 5.1.7.2. Applicants and the facilities in which they are conducting the research must show that:
  - 5.1.7.2.1. The financial arrangements, including insurance or indemnity, cover the research study concerned.
  - 5.1.7.2.2. The sponsor, research protocol authors, investigators/collaborators and, where applicable, Site Management Organizations will all be protected by insurance or indemnity arrangements.
  - 5.1.7.2.3. The arrangements will provide adequate cover to meet the potential liability assessed by the sponsor.
- 5.2. **Responsibility for Securing Review**
  - 5.2.1. Research on human subjects conducted as a requirement for an undergraduate course is the responsibility of the staff member(s) supervising the project.
  - 5.2.2. Research on human subjects conducted by a postgraduate student (as part of a postgraduate course or a PhD, under official requirement by the institute) as principal investigator is the responsibility of that student investigator.
  - 5.2.3. Research on human subjects conducted by a staff or staff principal investigator(s) is the responsibility of the staff member(s) performing the research.
- 5.3. **Appealing REC decisions**
  - 5.3.1. In the event that an application is denied and the investigator disagrees with the committee's disapproval decision, the investigator may initiate an appeal by submitting a letter presenting the researcher's arguments for approval, and any other pertinent information in support of the appeal.
- 5.4. **Complaints or Unanticipated Problems**
  - 5.4.1. If the investigator encounters unanticipated problems involving risks to subjects or complaints about the research, the investigator should immediately report these problems to the Chair of the REC. These problems may result in a possible amendment, suspension or termination of the research project.
- 5.5. **Changes in Protocols**
  - 5.5.1. Investigators who want to make significant changes in a previously approved protocol must obtain prior permission from the REC (see Appendix 10).
- 5.6. **Commencement of CTIMP**
  - 5.6.1. The sponsor will obtain authorization from DOH before the commencement of the clinical trial.
  - 5.6.2. Evidence of the authorization should be forwarded to the facility's REC when available (if not already provided to the Committee).
  - 5.6.3. Where DOH requests significant changes to the research protocol before confirming authorization, or attaches any other condition requiring substantial amendments to be made to the terms of the REC application or the supporting



documentation, a Notification of Substantial Amendment form should be submitted to the facility's REC.

- 5.6.4. Creating Clinical Trials Registry and include the commenced CTIMP in addition to patients' information registry

#### 5.7. Changes to Research Sites of CTIMP

- 5.7.1. Where it is proposed to make important changes in the management of a site (in particular, the appointment of a new PI), a Notification of Substantial Amendment form should be submitted to DOH for information, together with the CV of the new PI if applicable.

#### 5.8. Urgent Safety Measures Taken in Cases of CTIMP

- 5.8.1. The Principal Investigator or sponsor at a trial site may take appropriate urgent safety measures in order to protect the trial participants against any immediate hazard to their health or safety.
- 5.8.2. DOH and the facility REC must be notified that such measures have been taken, the reasons why and the plan for further action.

#### 5.9. Reporting of CTIMP-Related Events (see Appendix 7)

- 5.9.1. DOH mandates reporting of adverse events or any other pharmaceutical, medicinal and/or device related problems in accordance with the DOH Policies on 'Reporting Adverse Reactions<sup>3</sup>' and 'Reporting Medication Errors<sup>4</sup>'.
- 5.9.2. The following occurrences should be reported to the REC and DOH:
- 5.9.2.1. An increase in the rate of occurrence or a qualitative change of an expected serious adverse reaction, which is judged to be clinically important.
- 5.9.2.2. Post-study SUSARs that occur after the patient has completed a trial and are reported by the investigator to the sponsor.
- 5.9.2.3. A new event, related to the conduct of the trial or the development of the IMP, that is likely to affect the safety of subjects, such as:
- 5.9.2.3.1. A serious adverse event which could be associated with the trial; procedures and which could modify the conduct of the trial (for example a SAE occurring during the run-in period);
- 5.9.2.3.2. A significant hazard to the subject population such as lack of efficacy of an IMP used for the treatment of a life threatening disease;
- 5.9.2.3.3. A major safety finding from a newly completed animal study (such as carcinogenicity);
- 5.9.2.3.4. Any anticipated end or temporary halt of a trial for safety reasons where the trial is conducted with the same IMP by the same sponsor in another country;

<sup>3</sup> DOH Policy on Reporting Adverse Reactions is available at URL:

<https://www.haad.ae/haad/Portals/0/Reporting%20Adverse%20Reactions-updated24-june%20.pdf>

<sup>4</sup> DOH policy on Reporting Medication Errors is available at URL:

<https://www.haad.ae/haad/Portals/0/Reporting%20Medictaion%20Errors-updated24-june.pdf>



- 5.9.2.3.5. The conclusions or recommendations of a Data Monitoring Committee, where relevant for the safety of subjects.
- 5.9.3. Any information that materially alters the current risk/benefit assessment of the IMP or merits changes in the way the IMP is administered or the overall conduct of the trial should also be reported to the REC and DOH (DOH Adverse Drug Reaction Reporting Form).
- 5.10. Reporting of Non-CTIMP Related Serious Adverse Events** (see Appendix 7)
- 5.10.1. Reports of SAEs should be notified using the DOH Adverse Drug Reaction Reporting Form.
- 5.11. Conclusion or Early Termination of the Trial**
- 5.11.1. Unless otherwise specified in the research protocol, the conclusion of the trial is normally defined as the last visit of the last participant or the completion of any follow-up monitoring and data collection described in the research protocol.
- 5.11.2. The sponsor should notify the facility REC and DOH in writing that the trial has ended.
- 5.11.3. Any change to the definition of the conclusion of the trial should also be notified to the facility REC and DOH as a Substantial Amendment.
- 5.12. Final Report**
- 5.12.1. The sponsor or Principal Investigator should provide the facility REC with a summary of the clinical trial report in order to be reported to DOH.
- 5.13. Other Important Topics for Researchers** in Appendix 9 & 10.

## 6. Special Consideration –Joint Responsibilities of REC and the Investigators

### 6.1. Genomics Studies

The Facility REC must:

- 6.1.1. Provide ethical review of research using human tissue collected, stored and used at the Facility.
- 6.1.2. Undertake ethical review in a proportionate way, taking account of any material risk of harm or distress to donors, their families and other research participants.
- 6.1.3. Facilitate valuable research using human tissue of benefit to society, within the legal framework of the UAE.

### 6.2. Processing and Handling of Genomic Samples

- 6.2.1. Processing and handling of genomic samples and data should be conducted in a manner that protects the confidentiality of subjects' individual data.
- 6.2.2. Highest security measures using coding schemata and restriction of access should be implemented at each step of analysis and storage.
- 6.2.3. Storage of genetic data outside the institutional premises (e.g. universities and non-health institutions within UAE) needs approval from ADHRTC.
- 6.2.4. Suitable consideration should also be given to data protection and confidentiality legislation and policies from DOH and UAE federal laws.



### 6.3. Access to Genomics Samples and Data

Use of genomic samples and data may involve repeated access over time in accordance with the informed consent. Therefore,

- 6.3.1. Strategies and procedures involving systems that ensure strict control of access rights with access logs should be established for all genomic samples and data for each project, similar to that for other clinical data.
- 6.3.2. When outsourcing sample storage, genomic analysis or data storage outside the institutional premises, contractual agreements must specify that the responsible party will supervise the outsourced facility in an appropriate manner to ensure that the samples and/or data are properly safeguarded.
- 6.3.3. ADHRTC must be notified of these outsourcing arrangements
- 6.3.4. The outsourcing of Genomics analysis or data outside UAE is strictly prohibited.

### 6.4. Transparency and Communication of Findings

- 6.4.1. Research PIs and sponsors who generate genomic data in a study must adopt a position regarding return of findings to subjects and their primary healthcare providers.
- 6.4.2. The position must articulate whether the intended research findings, incidental findings, neither or both will be communicated. Ideally, the position would describe the timing of such communication (during or after the clinical study) and to whom (subject or in case of children and incapacitated individuals) as appropriate.

### 6.5. Returning results to Research Participants

- 6.5.1. The decision on whether to return research results to participants must be made by the study investigator in consultation with REC. This decision, including the format and process for returning results, must be clearly communicated.
- 6.5.2. If results are agreed to be communicated, it must be communicated by a genetic counsellor accompanied by the PI.
- 6.5.3. The applied assay and its level of validation must also be considered before communicating any results.
- 6.5.4. The PI is not to communicate a genomics related results to the affected individual without prior consideration to the short and long term effects and proper consultation with subject matter experts.
- 6.5.5. The person(s) responsible for communicating the findings will also need consideration and usually this would be the investigator, with a link to the informed consent.
- 6.5.6. The subject's desire and consent to receive such information or not must be respected.
- 6.5.7. Arrangements should be in place for appropriate counselling (if required) and offered following disclosure of information to participants

### 6.6. Data Security

- 6.6.1. Information Governance policy should be in place at the Healthcare facility and strictly adhered to.
- 6.6.2. **Storage of Genomic Data:**  
In order to assure confidentiality, the investigator must take the following measures:
  - 6.6.2.1. Identifying information or coding keys must be destroyed as soon as possible.  
(However, Consent Forms must be kept for a minimum of three years after the



research project ends, or more if required by specific authorizing or sponsoring agencies.)

- 6.6.2.2. Raw data must be archived in a secure location within the Emirate.
- 6.6.2.3. Paper records must be kept in a secure locked file or office.
- 6.6.2.4. Portable electronic records (e.g., laptop computer, PDA, flash or zip drive, CD or DVD, external hard drive) must be kept in a locked office or password protected and communicated through secure mail.
- 6.6.2.5. Non-portable electronic records (e.g. data accessed via the Web) must be maintained on a Local network with restricted access (e.g., a shared drive).
- 6.6.2.6. Storage of genetic analysis raw data outside health facility is not allowed unless permitted by ADHRTC.
- 6.6.2.7. Usage of cloud storage solutions is prohibited.

#### 6.6.3. Access to Genomic Data:

- 6.6.3.1. The investigator must specify which additional individuals will have access to identifiable data.
- 6.6.3.2. Each of these individuals must sign a confidentiality form to be kept by the investigator.
- 6.6.3.3. In this context, temporary employee, part time employee or an external employee who does not belong to the same institution as that of the PI will not be allowed to have access to the secure identifiable data of the subjects.

#### 6.6.4. Reporting of Genomic Data:

- 6.6.4.1. Identifiable information about individual subjects should not be disclosed during any phase of the clinical trial without the subject's explicit consent
- 6.6.4.2. Aggregated (grouped) data will be reported with potentially-identifiable information (e.g., demographic descriptors) removed.

### 6.7. Children and Adolescents as Research Subjects:

Special considerations apply when children or adolescents are the research subjects.

- 6.7.1. Minors (less than 18 years of age) cannot give legal permission to participate in research. In these instances, the researcher must prepare an Informed Consent form for parents (or legal guardians) to sign on their child's behalf.
- 6.7.2. Additionally, children must be assessed by the PI before obtaining consent and they must also agree (assent) to participate in the research study, either in writing or verbally.
- 6.7.3. Written assent will typically be appropriate for children aged 8 and above.

### 6.8. Deception and Incomplete Disclosure

- 6.8.1. Withholding information from or providing incomplete or erroneous information to research subjects is only allowed if the study's scientific or educational merit specifically requires the deception, and subjects are placed at no more than minimal risk due to the deception.
- 6.8.2. Approval will not be given if deception involves matters such as physical or psychological risks that would affect the subject's willingness to participate in the study.
- 6.8.3. Deception may not be used to recruit subjects to a study. When feasible the consent form should indicate that deception may be used or that full disclosure of the research protocol is not possible until completion of the study.



- 6.8.4. Subjects must be informed of the deception and of the actual purpose of the research and procedures as soon as feasible either at the end of their participation or upon completion of the study and documented in subjects' health records.
- 6.8.5. Procedures must also be in place to relieve any distress subjects may encounter due to the deception.
- 6.8.6. Applications involving deception must include a justification for the deception, a full description of the debriefing process and procedures for relieving possible distress to the subject caused by the deception.
- 6.8.7. REC may not approve research that entails more than minimal risk where participants are deceived or not given complete information that they would consider material to the decision to participate in the study.
- 6.8.8. REC must determine that the research qualifies for a waiver or alteration of the required elements of informed consent, in accordance with criteria provided in local regulations.

## 7. Enforcement and Sanctions

- 7.1. Healthcare Provider, Insurers, Pharmaceutical companies and Institutes of Higher Education (Academia) must comply with the terms and requirements of this Standard.
- 7.2. DOH may impose sanctions and/or disciplinary actions in relation to any breach of requirements under this standard in accordance with the DOH Policy on Inspections, Complaints, Appeals and Sanctions and the chapter on Complaints, Investigations, Regulatory Action and Sanctions Policy, Healthcare Regulator Manual.





## 8. APPENDICES

### APPENDIX 1: Guideline on SOP's for Conducting Clinical Trials for Investigational Medicinal Products (CTIMPs)

The aim of the following appendix is to provide guidance to researchers on how the regulatory and other requirements for the conduct of Clinical Trials for Investigational Products can be implemented.

#### 1. Communications with the Research Ethics Committee

- a. Further communications during the trial with the Research Ethics Committee that gave the favorable ethical opinion (hereafter referred to in this appendix as “the Committee”) are generally the responsibility of the lead sponsor. However, the sponsor may delegate responsibility to the Principal Investigator or another representative.
- b. Where there is more than one sponsor for the trial, it is recommended that the lead sponsor or its representative takes responsibility for all communications with the Committee.
- c. However, one of the co-sponsors may take responsibility for each of the following group of functions:
  - (i) Substantial amendments, modified amendments, and the conclusion of the trial.
  - (ii) Urgent safety measures.
  - (iii) Pharmacovigilance reporting.

#### 2. Commencement of the Trial

- a. It is assumed that the trial will commence (i.e. the initiation of any research protocol procedures) upon the favorable ethical opinion.
- b. The sponsor will obtain authorization from the Regulatory Authority (DOH) before the commencement of the clinical trial.
- c. Evidence of the authorization should be forwarded when available (if not already provided to the Committee).
- d. Where the regulatory authority requests significant changes to the research protocol before confirming authorization, or attaches any other condition requiring substantial amendments to be made to the terms of the REC application or the supporting documentation, a Notification of Substantial Amendment form should be submitted to the Regulatory Authority and the Committee.
- e. Should the trial not commence within 12 months, the sponsor should give the Committee a written explanation for the delay. It is open to the Committee to allow a further period of up to 12 months within which the trial must commence.
- f. Should the trial not commence within 24 months, the Committee may review its opinion and may recommend to the regulatory authority that the authorization should be suspended or terminated.

#### 3. Duration of Ethical Opinion

- a. The favorable opinion generally applies for the duration of the trial.
- b. If the duration of the trial is to extend beyond the term specified in the application form, the Committee should be notified.

#### 4. Progress Reports

- a. A facility Research Ethics Committee is required to keep a favorable opinion under review in the light of progress reports and any developments in the trial.



- b. A progress report should be submitted to the Committee 12 months after the date on which the favorable opinion was given. Annual progress reports should be submitted thereafter until the end of the trial is declared.
  - c. The Committee should be kept informed of any significant findings or recommendations by an independent Data Monitoring Committee or equivalent body established for the trial.
  - d. The Principal Investigator may be requested to attend a meeting of the Committee or Sub-Committee to discuss the progress of the trial.
5. **Amendments** (see Appendix 9)
- a. If the sponsor proposes to make a substantial amendment to the Clinical Trial Authorization, a signed “Notification of Substantial Amendment” form should be submitted to the Committee and the regulatory authority.
  - b. A substantial amendment is any amendment to the terms of the request for clinical trial authorization, or to the terms of the application for ethical review, or to the research protocol or other supporting documentation approved by the Committee, that is likely to affect to a significant degree the:
    - i. Safety or physical or mental integrity of the trial participants;
    - ii. Scientific value of the trial;
    - iii. Conduct or management of the trial;
    - iv. Quality or safety of any investigational medicinal product used in the trial.
  - c. A substantial amendment on which an ethical opinion has been requested should not be implemented until a favorable ethical opinion has been given by the Committee, unless the changes to the trial are urgent safety measures.
  - d. Amendments that are not substantial amendments (“minor amendments”) may be made at any time and do not need to be notified to the Committee.
6. **Changes to the Protocol** (see Appendix 10)
- a. **Changes to sites**
    - i. Where it is proposed to make important changes in the management of a site (in particular, the appointment of a new PI), a “Notification of Substantial Amendment” form should be submitted to the Committee (and to the regulatory authority for information), together with the CV of the new PI if applicable.
    - ii. The Committee should be notified when a site is closed or withdrawn prematurely.
  - b. **Urgent safety measures**
    - i. The sponsor or the Principal Investigator at a trial site may take appropriate urgent safety measures in order to protect the trial participants against any immediate hazard to their health or safety.
    - ii. The Committee and the Regulatory Authority must be notified within three days that such measures have been taken, the reasons why and the plan for further action.
  - c. **Pharmacovigilance**
    - i. Reporting of adverse events or any other pharmaceutical, medicinal and/or device related problems must be in accordance with the DOH Policies on ‘Reporting Adverse Reactions’ and ‘Reporting Medication Errors’.



## 7. Periodic Safety Report

- a. For each IMP being tested in the trial, the sponsor should provide the REC with an annual report on the safety of subjects.
- b. The report, should be no longer than 10 pages excluding line listings and should:
  - i. Give a concise description and analysis of all new and relevant findings that could have a significant impact on the trial population;
  - ii. Analyse the safety profile of the IMP and its implications for subjects' exposure, taking into account all safety data including drop-outs for safety reasons;
  - iii. Take into account supporting results of non-clinical studies or other experience with the IMP that are likely to affect the subjects' safety;
  - iv. Provide an updated risk-benefit evaluation for the trial;
  - v. Describe any measures taken or proposed to minimise risks;
  - vi. Consider the need to amend or update the research protocol, participant information sheet, consent form and investigator brochure.
- c. Periodic reports should be accompanied by a line listing of all Suspected Serious Adverse Reactions (SSARs) occurring in relevant trials during the year, including both expected and unexpected reactions.
- d. Periodic reports should be sent to the REC as soon as practicable after the end of the reporting period.

## 8. Expedited Safety Reporting

- a. Suspected Unexpected Serious Adverse Reactions: Suspected Unexpected Serious Adverse Reactions (SUSARs) occurring during the trial must be notified to the Committee and the Regulatory Authority in an expedited fashion. (See DOH Adverse Drug Reaction Reporting Form5).
- b. A SUSAR which is fatal or life-threatening should be reported as soon as possible and in any event after the sponsor becomes aware of the event.
- c. Any additional relevant information should be reported within a specific timeline after sending the first report.
- d. A SUSAR which is not fatal or life-threatening should be reported as soon as possible and in any event after the sponsor first becomes aware of the event.
- e. In the case of double-blinded trials, all reports of adverse reactions should be unblended.
- f. Pharmacovigilance reports may be provided to the Committee by either the sponsor, or the sponsor's representative, or the Principal Investigator.
- g. The Principal Investigator and representatives of the sponsor may be requested to attend a meeting of the Committee or Sub-Committee to discuss any concerns about the health or safety of trial participants arising from pharmacovigilance reports.

## 9. Other Events

- a. DOH mandates reporting of adverse events or any other pharmaceutical, medicinal and/or device related problems in accordance with the DOH Policies on 'Reporting Adverse Reactions<sup>6</sup>' and 'Reporting Medication Errors<sup>7</sup>'.

<sup>5</sup> DOH Adverse Drug Reaction Reporting Form is available at URL:

[https://www.haad.ae/HAAD/LinkClick.aspx?fileticket=xS8\\_YnH4avE%3d&tabid=1399](https://www.haad.ae/HAAD/LinkClick.aspx?fileticket=xS8_YnH4avE%3d&tabid=1399)

<sup>6</sup> DOH Policy on Reporting Adverse Reactions is available at URL:

<https://www.haad.ae/haad/Portals/0/Reporting%20Adverse%20Reactions-updated24-june%20.pdf>



- b. The following occurrences should be reported to the REC and regulatory authority within 15 days:
  - i. An increase in the rate of occurrence or a qualitative change of an expected serious adverse reaction, which is judged to be clinically important;
  - ii. Post-study SUSARs that occur after the patient has completed a trial and are reported by the investigator to the sponsor;
  - iii. A new event, related to the conduct of the trial or the development of the IMP, that is likely to affect the safety of subjects, such as:
    - (1) A serious adverse event which could be associated with the trial procedures and which could modify the conduct of the trial (for example a SAE occurring during the run-in period);
    - (2) A significant hazard to the subject population such as lack of efficacy of an IMP used for the treatment of a life-threatening disease;
    - (3) A major safety finding from a newly completed animal study (such as carcinogenicity);
    - (4) Any anticipated end or temporary halt of a trial for safety reasons where the trial is conducted with the same IMP by the same sponsor in another country;
    - (5) The conclusions or recommendations of a Data Monitoring Committee, where relevant for the safety of subjects;
    - (6) Any information that materially alters the current risk/benefit assessment of the IMP or merits changes in the way the IMP is administered or the overall conduct of the trial shall also be reported to the REC and regulatory authority. (DOH Adverse Drug Reaction Reporting Form).

#### 10. Serious Adverse Events (Non-CTIMP Research Only)

- a. A Serious Adverse Event occurring to a research participant should be reported to the Committee where in the opinion of the Principal Investigator the event was related to administration of any of the research procedures, and was an unexpected occurrence.
- b. Reports of SAEs should be provided to the Committee within 24 hours of the Principal Investigator becoming aware of the event. If applicable, the regulatory authority should also be notified. (Use DOH Adverse Drug Reaction Reporting Form).

#### 11. Conclusion or Early Termination of the Trial

- a. If the trial is terminated early, the sponsor should notify the Committee. An explanation of the reasons for early termination should be given.

#### 12. Final Report

- a. The sponsor or Principal Investigator should provide the Committee and, therefore, DOH with a summary of the clinical trial report upon the conclusion of the trial.
- b. The Committee should also be notified of the arrangements for publication or dissemination of the research including any feedback to participants.
- c. For non-CTIMP research the final report should include information on whether the study achieved its objectives, the main findings, and arrangements for publication or dissemination of the research including any feedback to participants.

#### 13. Further Reporting after the Conclusion of the Trial

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<sup>7</sup> DOH policy on Reporting Medication Errors is available at URL:  
<https://www.haad.ae/haad/Portals/0/Reporting%20Medictaion%20Errors-updated24-june.pdf>



- a. If after the conclusion or early termination of a trial the risk/benefit analysis is considered to have changed, the sponsor or Principal Investigator should notify the main REC in case this affects the planned follow-up of trial participants.
- b. The plan for further action to inform or protect participants should be described.

#### 14. Review of Ethical Opinion

- a. The Committee may review its opinion at any time in the light of any relevant information it receives.
- b. It has no power to legally withdraw the opinion it has given but may draw the attention of the Regulatory Authority to any serious concerns and may recommend that consideration is given to suspending or terminating the Regulatory Authorization.
- c. The sponsor or Principal Investigator may at any time request that the Committee reviews its opinion, or seek advice from the Committee on any ethical issue relating to the trial.

#### 15. Serious Breaches of Good Clinical Practice or the Research Protocol

- a. The Committee should be promptly notified of any serious breach of the conditions or principles of International Conference on Harmonization Good Clinical Practice (ICH GCP) or of the research protocol.
- b. A breach should be regarded as serious if it is likely to affect to a significant degree the safety or physical or mental integrity of the subjects of the trial, or the scientific value of the trial. The sponsor should notify the Committee and the Regulatory Authority of the matter coming to their attention. There is no need to notify minor breaches of ICH GCP or the research protocol.
- c. A minor deviation from the research protocol to deal with unforeseen circumstances is not considered to be a serious breach of the research protocol provided that it is approved by the Principal Investigator, either in advance or after the event. However, if the deviation would meet the criteria for a substantial amendment it should be notified to the Committee.

#### 16. Breach of Approval Conditions

- a. These approval conditions are not legally binding but they set out important guidance which Principal Investigators and sponsors are expected to follow.
- b. Failure to comply with the conditions may lead to a change of the Committee's opinion and a recommendation to the regulatory authority that the authorization should be suspended or terminated.

#### 17. Substantial Amendments to CTIMPs are detailed in Appendix 9.



## APPENDIX 2: The following points are in specific reference to “Guidelines for Conducting Clinical Trials with Investigational Products and Medical Devices”

1. Clinical trials with interventional design, may begin when the following conditions are fulfilled:
  - a. the Ethics Committee (ADHRTC and REC/IRB) has given a positive opinion,
  - b. the Regulatory Committee at the Department of Health (DOH) has issued a written approval and
  - c. Drug Control Department at the Ministry of Health and Prevention (DCD) in addition to drug and medical product department in DOH has issued an import license.
2. Clinical trials with non-interventional design may begin when the following conditions are fulfilled:
  - a. the Ethics Committee (ADHRTC or REC/IRB) has given a positive opinion, and
  - b. the Regulatory Committee at the Department of Health (DOH) has been notified in writing prior to the first subject being enrolled.
3. In order to obtain an opinion, the investigator should submit to the Ethics Committee (ADHRTC or REC/IRB):
  - a. administrative documentation;
  - b. information about subjects;
  - c. documentation concerning the trial protocol;
  - d. documentation about the medicinal product tested;
  - e. documentation about the technical requirements and the staff;
  - f. data about funding and the administrative organization of trials.
4. The content, format and requirements to the documentation submitted to Ethics Committee (ADHRTC or REC/IRB)
  - a. Administrative documentation
    - i. Ethics Committee Application (ECA): an electronic pre-defined form on an official portal contains mandatory and optional fields and allowing embedding additional files.
    - ii. Cover Letter: The applicant should submit as an attachment to an ECA a signed cover letter. The cover letter should contain, the protocol number and title and a full list of all essential documents accompanied the proposed clinical trial.
    - iii. List of Regulatory Authorities and Ethics Committees apart from DOH, to which the application has been submitted and information about their decisions.
    - iv. List of all study centers and investigators planned to participate in the Emirate of Abu Dhabi.
    - v. Power of Attorney or Agreement authorizing the applicant of the submission on behalf of the Sponsor, in cases where the applicant is not the Sponsor of the trial.
    - vi. Statement, according to item 46 in the “Guidelines for Conducting Clinical Trials with Investigational Products and Medical Devices” document.
    - vii. Evidence of registration of the clinical trial on one of the international clinical trial data system.
    - viii. Certified copy of the Contract Research Organization (CRO).
  - b. Information about subjects
    - i. Information for the patient/ subject and Informed Consent Form (in English; in Arabic and any other language that will be used).



- ii. Description of the procedures for obtaining informed consent from a legal representative, where applicable.
  - iii. Ethical grounds for enrolling participants incapable to give informed consent, as outlined in items 1, 5, 21 and 22 of the “Guidelines for Conducting Clinical Trials with Investigational Products and Medical Devices” document, where applicable.
  - iv. Any other information that will be used for subject enrolment and/ or presented to patients before or during the course of a study (in English and in Arabic). Project-specific documents for the trial subjects could be any of the following:
    - 1) Patient diary.
    - 2) Patient card.
    - 3) Adverse Events diary.
    - 4) Instructions for medication application or for handling medical device;
    - 5) Scales and Questionnaires (including Quality of Life questionnaires);
    - 6) Calendar(s).
    - 7) Patient advertisement.
    - 8) Additional trial information given in writing & / or multimedia technology to the subject.
    - 9) Copies or pictures of any materials intended to be given to the patient.
- c. Documentation concerning the trial protocol;
- i. Study Protocol and all current amendments, developed in accordance with ICH-GCP requirements and items 3 and 5 of the “Guidelines for Conducting Clinical Trials with Investigational Products and Medical Devices” document and contains as minimum:
    - 1) Clear justification of the known and potential risks and benefits, if any, to human subjects.
    - 2) Selection of Subjects – inclusion and exclusion criteria.
    - 3) Description of and justification for the selected subject population, especially in case of vulnerable subject group.
    - 4) Withdrawal of Subjects.
    - 5) Description of informed consent process in case of enrolment of subject temporary or permanent enable to be consented.
    - 6) The trial procedures to be followed, including all invasive procedures and all criteria for assessment and decisions.
    - 7) Planned monitoring and other control.
    - 8) Statistical, safety and ethical considerations.
  - ii. Study Protocol summary in English.
  - iii. Peer review of the scientific value of the trial, where available.
  - iv. Protocol pages signed by the Sponsor and by the Investigator from each study site participating in the trial.
  - v. Case Report form.
- d. Documentation about the medicinal product tested
- i. Investigator’s brochure (issued not later than one year before application submission).
  - ii. Summary of Product Characteristics, when applicable.
  - iii. Outline/ summary of all currently active clinical trials with the investigated product.
- e. Documentation about the technical requirements and the staff



- i. Description of the equipment and/ or the technical requirements necessary to perform the Protocol procedures.
      - ii. Certificates for external quality assessments (for the local laboratories) or Certificate for successful accreditation procedure (for the Central laboratories). Those documents are submitted for each laboratory that will be participating in the study procedures.
      - iii. CV and/ or other documents confirming the qualification, experience and training of study staff members (Investigator and Sub-Investigators) and their compliance with the requirements according to items I, 7 of the “Guidelines for Conducting Clinical Trials with Investigational Products and Medical Devices” document.
      - iv. GCP training certificates of all study staff members.
      - v. Financial Disclosure of Principal Investigator.
      - vi. Confidentiality agreement of Principal Investigator.
      - vii. Documents, confirming the circumstances as described in items I, 8, of the “Guidelines for Conducting Clinical Trials with Investigational Products and Medical Devices” document – Accreditation of the Institution.
  - f. Data about funding and the administrative organization of trials
    - i. Insurance covering the liability of the Sponsor and the Principal investigator(s) in case of property or non-property damages caused to the subjects related to their participation in the trial.
    - ii. Provision for compensation or a sample agreement between Sponsor and study subjects, when such compensation is considered.
    - iii. Sample Agreement between Sponsor, Institution and investigator, defining terms and conditions of conducting the clinical trial.
    - iv. Written approval as outlined in items I, 8.2 of the “Guidelines for Conducting Clinical Trials with Investigational Products and Medical Devices” document- Statement by the Director of the Institution regarding permission for conducting the study (if applicable).
    - v. Information about a clinical trial finance resource in case the Sponsor is a non-profit organization.
    - vi. Pre-site assessment report signed by the Sponsor or its representative.
    - vii. Evidence for payment of the required fee.
5. Change in the Conduct of a Clinical Trial (Also refer to Appendix 9)
  - a. A change in the way a clinical trial is conducted could be requested by the Ethics Committee (ADHRTC or REC/IRB) whenever necessary, in order to ensure the safety of subjects, the scientific value of the trial and/or compliance with Good Clinical Practice.
  - b. A substantial amendment in the way a study is conducted shall be any change in the protocol and/or in the information and the documentation under items 37 and 41 of the “Guidelines for Conducting Clinical Trials with Investigational Products and Medical Devices” document that affects:
    - i. the safety or the physical and mental integrity of the subjects;
    - ii. the scientific value of the study;
    - iii. the conduct or the organization of the study;
    - iv. the quality or the safety of one of the medicinal products tested.
6. List of information changes considered as substantial



- a. Changes related to the study protocol
  - i. Change in the study endpoint/ objective.
  - ii. Change in the study design and/or methodology or background scientific information, based on which the study is conducted.
  - iii. Changes in the following study subject documents:
    - 1) Subject/ patient information sheet and Informed Consent Form;
    - 2) Information related to a legal representative;
    - 3) Questionnaires, invitation letters, notification letters to the treatment or other physicians.
  - iv. Change in the schedule/ methodology of biological sampling related to the study.
  - v. Adding or removing of examination and/or testing.
  - vi. Change in the subject aging limits.
  - vii. Change in the inclusion and/or exclusion criteria.
  - viii. Change in the safety following procedure.
  - ix. Change in the prolongation of using the investigational product.
  - x. Change in the route or the dose of investigational product administration.
  - xi. Change in the drug comparator.
  - xii. Any change related to safety and physical and/or intellectual integrity of subjects or study risk/ benefit rationality.
  - xiii. Change in the study end schedule.
- b. Changes related to the administrative organization of the study:
  - i. Change in the study Sponsor and/or his legal representative.
  - ii. Change in the approved investigational site.
  - iii. New investigator.
  - iv. Including a new clinical site.
  - v. Change of investigator in the approved investigational site.
  - vi. Change in the insurance or the way of subject compensation.
  - vii. Other significant changes in the protocol and/ or other supplementary documents part of initial application.
- c. Changes related to quality of the investigational product:
  - i. Change in the investigational product name from Sponsor code into international non-proprietary name (INN).
  - ii. Change in the materials in the primary package.
  - iii. Change in the investigational product manufacture.
  - iv. Change in the specification of investigational product, when includes extension of permitted limits and/or tests drop out.
  - v. Change in the specification of additional supplements, when this could interfere the final product.
  - vi. Significant change in the manufacturing process.
  - vii. Limitation in the IP storage condition.
  - viii. Decreasing of expiration period of the investigational product after opening or diluting.
  - ix. Change in the procedures for active substance testing, including additional method.
  - x. Change in the procedures for non-pharmacopeia ingredients, including adding a new method.



- d. All amendments in non-clinical data for investigational product, which could lead to change of the ratio risk/ benefit.
  - e. All amendments in clinical data for investigational product, which could lead to change of the ratio risk/ benefit.
7. Requirements to the application and the documentation about the amendments:
- a. Ethics Committee (ADHRTC or REC/IRB)
    - i. In case of planned substantial amendments in a clinical trial, the principal investigator (PI) or his authorized representative should submit an Ethics Committee Application (ECA) to the respective EC: an electronic pre-defined form on an official portal contains mandatory and optional fields and allowing embedding additional files.
    - ii. The application should be accompanied by the following documents:
      - 1) Cover Letter.
      - 2) Summary of the proposed amendment.
      - 3) List of modified documents with their effective dates and version numbers.
      - 4) Pages from the amended documents according to Appendix 02 -#4 (Initial submission) with previous and new wording.
      - 5) Comments of any novel aspect of the amendment (if any).
      - 6) Document for paid fee.
8. Notification under item 53 of the “Guidelines for Conducting Clinical Trials with Investigational Products and Medical Devices” document should contain:
- a. Full name and study protocol number.
  - b. Name and contact details of the principal investigator (PI) and its authorized representative.
  - c. Name and contact details of the Sponsor and its authorized representative.
  - d. Name and contact details of the Contract Research Organization, if any.
  - e. Details about initial and all subsequent approvals with reference number and authorizing body.
  - f. Details about exact initiation of the study.
  - g. Number and name of all approved sites on the territory of the Emirates of Abu Dhabi participated in the study.
  - h. Number of subject participating in the study (screened, enrolled, and completed).
  - i. Number of occurred serious adverse events per site.
  - j. Details of compensations provided for injury or death. In case no compensation has been paid, reason for the same.
  - k. In case of early termination of the study a reason(s) and justification of this decision; relation between early termination and ratio risk/benefit of the investigational product.



## APPENDIX 3: Guideline on REC/IRB Functions and Structure

The Research Ethics Committee, also known as the Institutional Review Board, is an administrative body established within the facility that is intending to conduct clinical research, to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under their facility, in addition to the legal protection for the investigators and the facility itself.

The following Appendix provides guidance on the functions and structure of IRBs.

### 1. REC/IRB Functions

- a. Develop, disseminate, and implement nationally and internationally compliant and institutionally-appropriate procedures for ensuring protection of human subjects in all research projects conducted or sponsored involving the collection and analysis of data from human subjects.
- b. Conduct reviews of research project proposals involving the collection and analysis of data involving human subjects when required to ensure that such research will be carried out in a manner which protects the rights and well-being of the subjects.
- c. Forward critical researches for ADHRTC decision.
- d. Gives ethical opinion on proposed research projects. It is not necessary for evidence of Regulatory Approval to be provided to the REC before it confirms the final ethical opinion.
  - i. Where a favourable ethical opinion is given before regulatory approval and the regulator requires significant changes to be made to the terms of the REC application or the supporting documentation, a Notice of Substantial Amendment form shall be submitted to the REC for review.
  - ii. The Committee is not required to undertake its own expert scientific or safety assessment of CTIMP or seek advice on safety issues from scientific referees. The quality and safety of CTIMP is the responsibility of the facility and investigator.
  - iii. The Committee should make an ethical assessment of the information provided in the application about the potential risks and benefits to participants and any measures in place to minimise the risks. The ethical review must also ensure that the potential risks and benefits of the trial are fully and clearly explained in the participant information sheet.
- e. Findings of the continuous review and compliance are discussed within the REC, and are communicated to the DOH, which may take further appropriate action if required.
- f. The facility REC provides post approval support to researchers by assessing and helping to manage post approval events through on-site reviews of studies and directed investigations.

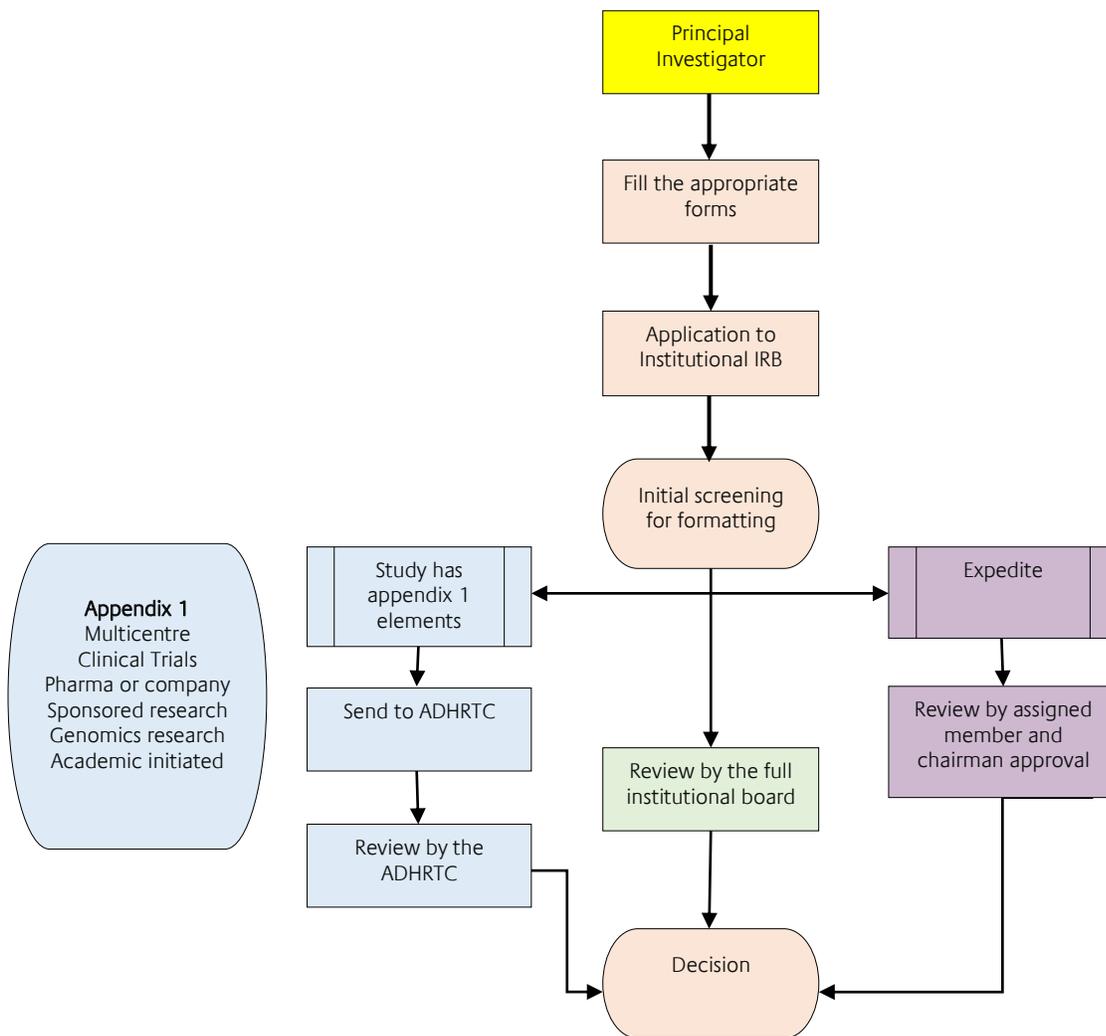
### 2. IRB/REC Structure:

- a. The facility REC committee members are selected to assure continual diversity and experience on the REC, and are to include both males and females of various backgrounds and professions.
- b. Committee members are selected from departments that have the most active clinical research programs. Committee members must have a research interest and a record of indexed publications to qualify to be a REC member (with exception to the outside/lay member).
- c. However, the Committee also keeps in mind the need for expertise in all areas and should make sure they have appropriate representation. Membership of REC should be multidisciplinary and include to the extent possible: experts from within the facility, members with relevant clinical and/or methodological expertise, lay members and members who are independent of the facility

itself. With the exception of the lay member, all others should have completed a course in research ethics accredited by DOH.

### 3. Initiating the IRB Review Process

- a. REC will work with applicants on meeting the requirements.
- b. Sponsor (if present) should not interact with REC directly for any issues during submission and review process.
- c. Prior review is necessary to ensure compliance with DOH and internationally defined criteria for ethical treatment of human subjects.



Thus, Research Done Without Prior Rec Approval Must Not Be Used in Any Public Presentation or Publication.



#### 4. Application for Approval of the Research Project

- a. Staff members, or postgraduate students (residents, fellows) who are planning research projects involving human subjects are responsible for beginning the review process by submitting the Application for Approval of Human Subjects Research form to the Chair of the REC through the secretary of REC committee at least 4 weeks before the next scheduled meeting to be included therein. Meetings should be scheduled once a month and the meeting schedules should be published and communicated within it's the facility.
- b. Researchers should submit a fully-developed research plan and accompanying documentation (e.g. a questionnaire or scripts when the subjects are likely to be interviewed; as well as the Informed Consent Form).
- c. In cases where Residents, Fellows, Master or Ph.D. students are the investigators, the applications should be approved by their program director or the institute DIO (or equivalent).
- d. Pharma Sponsored clinical trials or projects that will use the hospital resources (laboratory, pharmacy, diagnostic equipment), should be submitted and approved by both the ADHRTC and the facility's research director or equivalent, before commencing with the trial/project.

#### 5. After Submission: The Review Process & Outcomes

- a. All submitted proposals should be assigned by the REC to one of three review categories: Exempt, Expedited, or Full.
- b. The 'level of the review' can only be determined by the REC. Even if the investigator believe that the research proposal is exempt, the investigator must submit it so that the REC has the opportunity to make this determination.
- c. Furthermore, to fully protect subjects, the REC should approve a research project before investigators begin to recruit subjects, since recruitment strategies are part of the review.

#### 6. Levels of Review

##### a. Exempt

- i. Research may be **Exempt** from REC review because it either makes use of existing records, involves standard educational/psychological tests, improvement of current practices of education and quality of healthcare set ups, or for other reasons. However, it is up to REC (not the researcher) to determine whether a project is Exempt.
- ii. In the case of Exempt research, REC Chair should review the proposal and advise the principal investigator of the outcome.
- iii. In general, procedures that are free of foreseeable risk to the subject are likely to be Exempt.
- iv. The following are examples likely to be considered Exempt from review:
  - 1) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behaviour, where information is recorded anonymously (i.e., so that the human subject cannot be identified, directly or indirectly through identifiers linked to the subject). All survey/interview/observational research in which elected or appointed public officials or candidates for public office serve as subjects should be Exempt, whether or not data collection is anonymous. Such research should be Exempt unless any disclosure of the human subjects' responses outside the research could place the subjects at risk of criminal or civil liability or be damaging to the subject's financial standing, employability, or reputation.
  - 2) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens. These sources should be either publicly



available or the information should be recorded anonymously (i.e., in such a manner that subjects cannot be identified, directly or through identifiers linked to the subject).

- 3) Research evaluating: public benefit or service programs procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures; or possible changes in methods or levels of payment for benefits or services under those programs. Such research that also involves interaction with human subjects (e.g., interviewing, surveying) should not automatically Exempt.
- 4) Research on instructional strategies conducted in educational settings, involving normal educational practices (such as research on regular and special education strategies, or research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods).

**b. Expedited**

Research that poses only minimal risk to participants can be handled as Expedited. “Minimal risk” means that the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

- i. In case of Expedited research, the REC Chair and one other member of REC should review the proposal and advise the principal investigator of the outcome.
- ii. Activities approved for Expedited review include:
  - 1) Collection of biological specimens through non-invasive means; for example, electrocardiography, electroencephalography, thermography, Doppler blood flow, echocardiography, functional magnetic resonance imaging;
  - 2) Clinically routine non-invasive procedures such as muscular strength testing, moderate exercise, body composition assessment, flexibility testing involving health subjects;
  - 3) Research on individual or group characteristics or behaviour (including but not limited to research involving perception, cognition, surveys, interviews, and focus groups) as follows:
    - involving adults, where (i) the research does not involve stress to subjects; and (ii) identification of the subjects and/or their responses would not reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation;
    - involving children, where (i) the research involves neither stress to subjects nor obtaining of sensitive information about themselves, or their family; (ii) parents/guardians will complete the usual consent form (i.e. there is no request for a waiver); (iii) identification of the subjects and/or their responses would not reasonably place them or their family members at risk of criminal or civil liability or be damaging to the financial standing, employability, or reputation of themselves or their family members;
  - 4) Collection of data from voice, video, digital or image recordings, as long as identification of the subjects and/or their responses does not place them at risk for criminal or civil liability, or damage their financial standing, employability or reputation;
  - 5) Research involving existing identifiable data, documents, records, or biological specimens (including pathological or diagnostic specimens), where these materials have been collected prior to the research for a purpose other than the proposed research, confidentiality should be strictly maintained, and information should not be recorded anonymously (e.g., use will be made of audio or videotapes, names will be recorded, even if



they are not directly associated with the data); (In case where, data or human subject's bio-specimens, whether collected prospectively or retrospective, banked, are shared outside the supervision of the REC, a data and material sharing agreement should be required \* between the parties involved with sufficient information with confidential material transfer agreement, both in Arabic and English languages). Furthermore, Certificate of Confidentiality should be signed.

- 6) Continuing review of non-exempt research previously approved by the REC, where no new subjects will be enrolled or where the research involves no greater than minimal risk. \*Data and material sharing agreement.

### c. Full Board Review

- i. All research that is not exempt or expedited should be given a Full Review. This means that the proposal is reviewed during a convened meeting of the REC, during which discussion of the proposal occurs. A majority of the REC members, and specifically, the Emirates of Abu Dhabi community member, should be present.
- ii. These are some of the situations likely to require Full Review:
  - 1) The proposed research involves active or passive deception;
  - 2) The investigator asks for a waiver of written Informed Consent;
  - 3) The proposed research involves vulnerable populations (there may be instances of research with children that do not require full review; refer to Expedited category above);
  - 4) The proposed research involves topics of a sensitive nature (sexual behaviours, illegal behaviours, drug or alcohol use, sensitive demographic data, etc.). The key principle used to determine whether a project involves sensitive information is that it has the potential for provoking a negative emotional reaction from a subject;
  - 5) The procedures of the research involve more than minimal risk to the subject (where more than minimal risk means that the probability and magnitude of harm or discomfort anticipated in the proposed research is greater than that ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests);
  - 6) The proposed research involves observation where the individual could reasonably expect privacy (i.e. in the individual's home);
  - 7) The proposed research requires links between the individual and his/her behaviour (e.g. a longitudinal study);
  - 8) The proposed research includes collection of data from voice, video, or image recordings where identification of the subjects and/or their responses could place them at risk for criminal or civil liability, or damage their financial standing, employability or reputation;
  - 9) The proposed research involves pharmaceuticals, nutraceuticals or other chemical agents;
  - 10) The research involves physically invasive procedures (e.g. blood drawing, other tissue collection or implantable medical devices);
  - 11) The research involves transport or shipment of human subject's biological specimens outside the UAE, either collected prospectively or through banked specimens.

### 7. Criteria in Evaluating REC Proposals

The REC should consider the following factors in reviewing research proposals:

- a. Have the risks to subjects been minimized?
- b. Are the risks reasonable in relation to anticipated benefits?
- c. Is the selection of subjects equitable (e.g., free from racial, gender or other types of bias)?



- d. Can the Informed Consent be easily understood? Does it adequately reflect what the subject can expect?
- e. Has the investigator indicated how the data will be protected (to assure the privacy of the research subjects)?
- f. Are any of the participants vulnerable to coercion or undue influence?

## 8. Review Outcomes

There are four possible outcomes to a review:

- a. **Approved:** No further action is required from the investigator prior to initiating the study.
- b. **Accepted pending Clarifications:** Project is not accepted or granted approval until the clarifications to the comments is submitted by the investigator in written form, to the comments raised by the Committee. The primary reviewers of the project or REC Chair should review the response as soon as the clarification(s) is submitted, and approval granted.
- c. **Revise (Reassessment) and Resubmit:** Changes are required before the study can begin. Additional or revised information should be submitted to the REC prior to approval. The written response by the investigator requires review by the full board at its next meeting.
- d. **Denied/Reject:** Because of the level of risk involved, the proposed research project cannot be initiated. Rejected projects may be given re-submission advice.
- e. The results of the REC review should be promptly communicated to the investigator in writing by the Chair of the REC specifying the REC decision, the reasons/opinions for this decision and the procedure the investigator can take to repeal this decision. A copy of this letter will be sent to the Chairman of the department of the principal investigator, who will communicate all approved REC research projects. In case the chairman of the department or other staff members of the department have concerns about the approved research project, those concerns should be reported to ADHRTC.

## 9. Monitoring of Research Process

- a. The REC shall keep under review the favourable ethical opinion given to any research study in the light of regular progress reports and significant developments in the research.
- b. Other than by means of the reports that the sponsor and investigators are required to submit; the REC has no responsibility for proactive monitoring of research studies. The accountability for this lies with the sponsor and the employing organization.

## 10. Commencement of the Research

- a. Research shall normally commence within 12 months of the date on which a favorable ethical opinion is given by a REC.
- b. Should the study not commence within 12 months, the Principal Investigator should give the REC a written explanation for the delay in the first annual progress report. It is open to the Chair to allow a further period of 12 months within which the trial should commence.
- c. Should the study not commence within 24 months, the matter should be discussed at a meeting of the REC. At the discretion of the REC, the favourable ethical opinion may be terminated and the Principal Investigator required to submit a new application. Alternatively, a further period may be allowed.

## 11. Duration of the Ethical Opinion

- a. The favourable ethical opinion of the REC applies for the duration of the research, except where action is taken to suspend or terminate the opinion.



- b. Where the duration of the study is to be extended beyond the period specified in the application form, the REC should be notified by letter, giving reasons for the extra time needed to complete the research.
- c. Annual progress reports should continue to be submitted if the study duration is extended in this way.
- d. Extension of the study period is not in itself a substantial amendment, except where it is related to other amendments that would be substantial, such as an increase in target recruitment, addition of new procedures or extension of follow-up.
- e. It should not be necessary to obtain formal approval for extension of the study period, though the REC may review its favourable opinion of the study at any time.

## 12. Reviewing Reports

The following paragraphs suggests the responsibilities for review of reports submitted to the REC. The primary responsibility for monitoring the safety of research participants lies with the trial sponsor and/or investigators.

The REC shall receive the following reports from the Principal Investigator:

- a. Progress reports and the final report should be reviewed at least by the Chair or, at the Chair's discretion, by one or more members of the Committee or a Scientific Officer before sending it to the regulator.
- b. Periodic safety reports should be reviewed at least by the Chair and, unless the Chair has appropriate expertise, by an expert member or referee.
- c. The purpose of the review of periodic safety reports should be to:
  - i) Check the accuracy of the risk/benefit analysis as described in the patient information sheet.
  - ii) Consider the possible need for new information to be given to patients and their consent sought to continue in the study.
  - iii) Consider any other issue that may be relevant to the ethics of the trial.
- d. Where concerns arise about any of the above, the REC may contact the Principal Investigator or sponsor to express its concerns, and may request further information. The Principal Investigator may be requested to attend a meeting of the Sub-Committee or Committee to discuss the concerns of the REC.
- e. Where findings and recommendations from Data Monitoring Committees are received by the REC, they should be reviewed in the same way as periodic safety reports.

## 13. Urgent Safety Measures and Expedited Reports

- a. Notifications of urgent safety measures should be reviewed at a meeting of the REC or Sub-Committee but not by the Chair acting alone.
- b. The REC should consider whether the measures taken are appropriate in relation to the apparent risk to participants, and what further action the sponsor and investigator(s) propose to take.
- c. Where any concern arises about the safety or welfare of participants or the conduct of the research, the REC should address these with the sponsor or Principal Investigator in writing.
- d. Expedited reports of SUSARs or other occurrences should be acknowledged and filed by the Coordinator. They do not need to be seen by the Chair. There is no need for the Committee to be notified routinely of the receipt of expedited reports, or for any review to be carried out, as the overall safety of the trial cannot be assessed on the basis of such limited data.

## 14. Serious Breaches of Good Clinical Practice or the Research Protocol



- a. The REC should be notified of serious breaches of the research protocol or of the conditions or principles of Good Clinical Practice (ICH GCP) as set out in the regulations. Any such report should be considered at a meeting of the Committee or Sub-Committee.
- b. There is no statutory provision for the Committee to approve proposed deviations from the research protocol for individual subjects. It is the responsibility of the sponsor and/or investigator to consider whether research protocol amendments should be made in such cases. Where the amendment is substantial, it should be notified.

#### 15. Review of a Favorable Ethical Opinion

- a. The REC may review its favorable ethical opinion of a study at any time. In particular, this might be prompted by safety reports, progress reports or any other information received about the conduct of the study.
- b. The Principal Investigator or sponsor may ask the REC to review its opinion, or seek advice from the REC on any ethical issue relating to the study.

#### 16. Review of Opinion on a CTIMP

- a. The REC has no power to legally withdraw the ethical opinion given previously. However, the REC may review its opinion in the light of new ethical concerns following any new information received about the trial. It may also notify the regulatory authority and the ADHRTC that it no longer has a favourable opinion of the trial. Any such notification should be based on a decision taken at a quorate meeting of the full Committee.
- b. Where the REC decides that it no longer has a favorable opinion of a trial, the Chair should write to the Regulatory Authority or the ADHRTC. The REC may recommend that consideration is given to suspending or terminating the trial authorisation. Any such recommendation should relate to serious concern about one or more of the following:
  - i) Scientific validity of the trial.
  - ii) Health or safety of participants.
  - iii) Competence or conduct of the investigator(s).
  - iv) A delay of at least 2 years in the commencement of the trial leading to doubts about the continuing validity of the ethical opinion given on the original application.
  - v) Adequacy of the site or facilities.

#### 17. Suspension or Termination of Opinion on a Non-CTIMP

- a. A favorable ethical opinion on a non-CTIMP may be suspended or terminated by the Committee due to serious concern about one of the following:
  - i) Scientific validity of the study.
  - ii) Health or safety of participants.
  - iii) Competence or conduct of the investigator(s).
  - iv) Serious or repeated breach of approval conditions.
  - v) A delay of at least 2 years in the commencement of the study leading to doubts about the continuing validity of the ethical opinion given on the original application.
  - vi) Adequacy of the site or facilities.
  - vii) Suspension or termination of regulatory approval for the study.
- b. A decision by the REC to suspend or terminate a favorable ethical opinion should be taken only at a quorate meeting of the full Committee. Before taking this course the REC should weigh carefully the implications for any research participants already recruited. The Principal Investigator should be notified of the decision by the Chair.



#### 18. Research-related Fraud and Misconduct

- a. Where a REC receives information suggesting that any kind of fraud or misconduct may have occurred in relation to an application for ethical review or the conduct of research, the Chair or Committee Coordinator should pass the information confidentially to the facility management, sponsor and the regulatory authority.
- b. It is for the REC to consider whether any action needs to be taken in relation to the ethical opinion for the research, in particular where there could be an immediate risk to the safety of participants. The opinion on a non-CTIMP may be suspended pending the outcome of further investigation by other bodies. Such a decision should only be taken after careful consideration of the implications for research participants already recruited.
- c. A member of a REC who becomes aware of possible fraud or misconduct in research should report this to the Chair and Coordinator of the REC, who will be responsible for reporting the matter to DOH.

#### 19. Non-compliance in CTIMPs

RECs should draw serious concerns about compliance issues in CTIMPs to the attention of the appointing authority under the procedures for notifying possible fraud or misconduct.



## APPENDIX 4: LIST OF REC FORMS

- a) REC form 001 (Application Checklist)
- b) REC form 002 (Application)
- c) REC form 003 (Studies with Medical Devices Use)
- d) REC form 004 (Use of Drugs and/or Biological Products in Research)
- e) REC form 005 (Use of Stem Cell, Zygotes, Gametes and Fetuses in Research)
- f) REC form 006 (Study Progress Report)
- g) REC form 007 (Request to Amend a Currently-Approved Project)
- h) REC form 008 (ADHRTC Risk Assessment)
- i) DOH form (Adverse Event Reporting form) Available on the below link:  
[https://www.haad.ae/HAAD/LinkClick.aspx?fileticket=xS8\\_YnH4avE%3d&tabid=1399](https://www.haad.ae/HAAD/LinkClick.aspx?fileticket=xS8_YnH4avE%3d&tabid=1399)
- j) REC CV template
- k) Conflict of Interest Form
- l) Certificate of Confidentiality

Note: These are mandatory for all projects submitted to REC as full board review. Informed Consent Forms must be provided in both Arabic and English languages, and both should have same text (descriptions).



1. Application Forms to the IRB/Facility REC

<div style="border: 1px solid black; padding: 5px; background-color: #f0f0f0;"> <p style="color: red; font-weight: bold;">Institute logo</p> </div>	<p><b>REC/Institutional Review Board</b> لجنة أخقيات لبحوث لا علمي</p>	 دائرة الصحة DEPARTMENT OF HEALTH	For REC/IRB use only: For Review [    ] FOR ADHRTC [    ] Proposal No. _____
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**Application Checklist Form # REC 001**

YES	NO	N/A	CHECKLIST	COMMENTS
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	“Proposal Application for Research Involving Human Participants” (Form # REC 001) is completed, signed and dated by the Principal Investigator and the Co-Investigators?	
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	“Research Proposal Form” (REC 002) is completed, signed and dated by the Principal Investigator?	
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Signed and dated “Curriculum Vitae” for each senior personnel in the research project are attached in the appendix to the Research Proposal Form?	
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Valid “Good Clinical Practice” (GCP) for each clinical personnel in the research project, Valid “Good Laboratory Practice” (GLP) for each clinical personnel in the research project are attached to the Research Proposal Form?	
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	“Informed Consent Checklist” (REC) is attached?	
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	If the study is Clinical Trial: appropriate “Informed Consent Forms” (REC) is filled, signed and attached?	
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	If the study is Medical/Scientific Research: appropriate “Informed Consent Forms” (REC) is filled, signed and attached?	
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	If the proposal is genetics or genomics studies: appropriate “Informed Consent Forms” (REC) is filled, signed and attached?	
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	If the study includes the use of stem cells: “Use of Stem Cell in Research” Form (REC) is attached in the appendix to the Research Proposal Form?	
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	If the study includes the use of devices: “Devices Use” Form (REC) is attached in the appendix to the Research Proposal Form?	
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	If the study includes the use of drugs and/or biological products: “Use of Drugs and/or Biological Products in Research” Form (REC) is attached in the appendix to the Research Proposal Form?	
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	If the study is sponsored from a pharmacological or medical industry company, please attach relevant documents	
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	If the includes the use of artificial intelligence, data analysis, computed analysis of EHR data, please attach relevant documents	

Principal Investigator Name \_\_\_\_\_

Signature \_\_\_\_\_

Date \_\_\_\_\_



<div style="border: 1px solid black; padding: 5px; display: inline-block;">Institute logo</div>	<p><b>REC/Institutional Review Board</b> لجنة أخقيات لبحوث لالغدي</p>	 دائرة الصحة DEPARTMENT OF HEALTH	For REC/IRB use only: For Review [    ] FOR ADHRTC [    ] Proposal No. _____
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Research Proposal Form **Form # REC 002**

**SECTION I: GENERAL INFORMATION**

Study Centres in the institute (if you applicable, list all branches of the hospital)			
	<input type="checkbox"/>		
1- Title of Study:			
English:			
Arabic:			
2- Contact information:			
1. Principle investigator (PI)			
Name			
ID		Department/ Hospital	
Phone No.		Mobile No.	
E-mail			
Status	<input type="checkbox"/> Undergraduate student		<input type="checkbox"/> Hospital Staff
	<input type="checkbox"/> Graduate Student \ Post-Doctoral		<input type="checkbox"/> University Faculty
	<input type="checkbox"/> Resident/Fellow		<input type="checkbox"/> Other (specify)
2. Co-Investigators and Members of Research Team:			
Name	Email Address	Department/Hospital	Role in Project



Study expected start date (Day/Month/Year) H. G.	--/--/-- H	--/--/--G
Study estimated end date (Day/Month/Year) H. G.	--/--/-- H	--/--/--G
Study completion date (Day/Month/Year) H. G.	--/--/-- H	--/--/--G
Submission date (Day/Month/Year) H. G.	--/--/-- H	--/--/--G
Others: (please specify)		

## SECTION II: COLLABORATING INSTITUTIONS/FACILITIES AND OTHER REC REVIEWS

Will the research be conducted only at the premises of your institute with no involvement of a collaborating institution?			
<input type="checkbox"/> Yes (if yes, skip to section III)		<input type="checkbox"/> No	
If you are collaborating with other sites, provide the name of each institution/facility and describe the type of involvement of each institution (e.g. recruitment, enrolment, consenting, study procedures, follow-up, and data analysis). Indicate if REC approval/site permission is attached			
<b>National Collaboration</b>			
Institution Name	Describe Involvement	REC Approval/Site Permission Attached?	
<b>International Collaboration</b>			
Will any aspect of the study take place outside UAE? If yes, complete the table below.		<input type="checkbox"/> Yes	<input type="checkbox"/> No
List Location(s)	Name of Collaborating Institution/Facility/Hospital	Describe Involvement	REC/Ethics Approval and/or Site Permission Attached?



### SECTION III: FUNDING INFORMATION

1. Is this research being funded?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. If yes, please specify:		
<b>Funding agency</b>		
<input type="checkbox"/> Governmental funding within UAE		
<input type="checkbox"/> Private sector funding within UAE		
<input type="checkbox"/> International government funding		
<input type="checkbox"/> International private sector funding		
<input type="checkbox"/> Under graduate / post graduate student funding		
Total budget of the project:		

### SECTION IV: DRUGS/BIOLOGICAL PRODUCTS/DEVICES, BIOLOGICAL SAMPLES, GENETIC TESTING, RADIATION and RADIOISOTOPES, AND EXPERIMENTAL ANIMALS

Type of Research			
Audit	<input type="checkbox"/>	Registry	<input type="checkbox"/>
Retrospective Chart Review	<input type="checkbox"/>	Device Study	<input type="checkbox"/>
Case Report Review	<input type="checkbox"/>	Clinical Trial, if yes	<input type="checkbox"/>
Health Related Survey	<input type="checkbox"/>	Phase I <input type="checkbox"/> Phase II <input type="checkbox"/> Phase III <input type="checkbox"/> Phase IV <input type="checkbox"/>	
Post Marketing Observational Study	<input type="checkbox"/>	Others: (please specify in the column below)	<input type="checkbox"/>

Does the Proposal involve the use of any of the following? Check all that apply:

1. Drugs/ Device Use		
• An investigative/unapproved drug, supplement, chemical, biological products, or controlled substances	<input type="checkbox"/> Yes	<input type="checkbox"/> No
• A medical or non-medical device	<input type="checkbox"/> Yes	<input type="checkbox"/> No
• A proprietary product	<input type="checkbox"/> Yes	<input type="checkbox"/> No
• A placebo	<input type="checkbox"/> Yes	<input type="checkbox"/> No
If "Yes" to any of the previous points, please fill the REC forms #3 for the use of Devices; AND the REC form #4 for the use of drugs and/or biological products in research.		
2. Biological Samples		
Blood, Urine, Tissue, Saliva, etc. (Either banked or prospectively obtained)	<input type="checkbox"/> Yes	<input type="checkbox"/> No



If "Yes":		<input type="checkbox"/> Yes	<input type="checkbox"/> No
- Confirm that all relevant personnel have been trained and have an experience in dealing with biological samples.			
- Confirm that all relevant personnel have completed a "Blood borne pathogen training and immunization".		<input type="checkbox"/> Yes	<input type="checkbox"/> No
<b>3. Genetic Material Testing</b>			
Genetic testing of biological samples (Blood, Urine, Tissue, Saliva, etc. , or the use of recombinant DNA/Human gene transfer (including use of vectors)		<input type="checkbox"/> Yes	<input type="checkbox"/> No
If "Yes":			
A. Specify the genetic testing to be done on these samples.			
B. Will the genetic sample be sent outside the UAE?		<input type="checkbox"/> Yes	<input type="checkbox"/> No
If "Yes", approval from the ADHRTC and REC/IRB must be obtained before sending the genetic samples outside the UAE. Please attach the approval letter.			
C. Will results of genetic testing be reported to subjects?		<input type="checkbox"/> Yes	<input type="checkbox"/> No <input type="checkbox"/> NA
If "Yes", the following conditions must be met:			
1. A specific genetic test is being performed and subjects are notified at the time of the consent what the test is and how the results might affect them.			
2. Specify who will transmit the results of the study.			
3. Specify whether genetic counsellors will be available to subjects.			
<b>4. Stem Cells, Zygotes, Gametes and Fetuses</b>			
The Research project involves the use of stem cells, zygotes, gametes, or fetuses		<input type="checkbox"/> Yes	<input type="checkbox"/> No
If "Yes", please fill the REC form # REC # 009 for the use of Stem Cell, Zygotes, Gametes and Fetuses			
<b>5. Radiation or Radioisotopes</b>			
The research project involves the use of Radiation or Radioisotopes		<input type="checkbox"/> Yes	<input type="checkbox"/> No
If "Yes":			
- Please specify where the radiation will be used (Hospital, and building / room no.):			
- Please specify Name(s) of approved radioisotope permit holder, and the duration of permit:			
- Please specify methods of special handling and disposal of radioactive waste:			
<b>5. Experimental Animals</b>			



The research project involves the use of Experimental Animals?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
If “Yes”, approval from the Local Animal Facility and from the REC/IRB, Approval should be obtained before the use of experimental animals is initiated. Please fill the REC form #? for Experimental Animal Use in research.		

#### SECTION V: RESEARCH PROTOCOL AND SIGNIFICANCE

1. Please provide the proposed project abstract including the following subheadings: Background, objectives, and methods (not more than 300 words)

2. Please describe briefly how this study will contribute to existing knowledge in the field.

#### SECTION VI: RISKS AND BENEFITS OF THE PROPOSED RESEARCH

<b>1. POSSIBLE RISKS</b>		
<b>A. Indicate if the participants might experience any of the following risks:</b>		
i. Physical risk (including any bodily contact or administration of any substance)?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
ii. Psychological risks (including feeling demeaned, embarrassed, worried or upset)?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
iii. Social risks (including possible loss of status, legal risk, privacy and/or reputation as well as economic risks)?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
iv. Are any possible risks to participants greater than those the participants might encounter in their everyday life?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
<b>B. If you checked yes for any questions i – iv above, please describe the risk(s) in the space below</b>		
<b>C. Management of Risk: describe how each of the risks identified above will be managed or minimized. Please include an explanation regarding why alternative approaches cannot be used.</b>		





## SECTION VIII: CONSENT PROCESS

<b>1. Informed Consent:</b>	
<ul style="list-style-type: none"> <li>Will you use a written informed consent document?                     <ul style="list-style-type: none"> <li><input type="checkbox"/> Yes</li> <li><input type="checkbox"/> No, I am asking a waiver of written informed consent</li> <li><input type="checkbox"/> Not applicable</li> </ul> </li> </ul>	
<b>2. Written parental permission</b>	
<ul style="list-style-type: none"> <li>Will you obtain written parental or guardian permission for children, individuals under 18, prisoner and incompetent?                     <ul style="list-style-type: none"> <li><input type="checkbox"/> Yes</li> <li><input type="checkbox"/> No, I am asking a waiver of written informed consent</li> <li><input type="checkbox"/> Not applicable</li> </ul> </li> </ul>	
<b>3. Please attach/upload Arabic consent form using the forms provided by the facility REC/IRB</b> <b>An English consent form might also be attached/uploaded</b>	

## SECTION IX: CONFLICT OF INTEREST DISCLOSURE

The REC policy requires that members of the faculty conducting research involving human participants at the institute must disclose known significant financial interests that would reasonably appear to be affected by the research project and that if the interest is deemed to constitute a conflict of interest with the proposed research, the conflict has to be managed prior to the faculty member's engaged in the research with human participants.

<input type="checkbox"/> Yes	<input type="checkbox"/> No	Are you, a family member, or spouse the inventor of any products, novel treatment under evaluation, or technology used in the research?
<input type="checkbox"/> Yes	<input type="checkbox"/> No	Do you, or does a family member, or spouse have fiduciary role or have an ownership interest in any entity that provides materials, novel treatment under evaluation, products, technology, or services in the research?
<input type="checkbox"/> Yes	<input type="checkbox"/> No	Do you or does any family member, or spouse receives income/payments from an entity that provides materials, novel treatment under evaluation, products, technology, or services in the research?
<input type="checkbox"/> Yes	<input type="checkbox"/> No	Is the research sponsored by a company for which you, and/or a family member consult, serve on its scientific advisory board, data safety monitoring board, or board of directors or have a paid position?
<input type="checkbox"/> Yes	<input type="checkbox"/> No	Is the research sponsored by a company for which you (or your spouse or your children) hold any ownership interest (stock, not including stock owned through a mutual fund) or from which you are entitled to receive royalties from a licensing agreement?
<input type="checkbox"/> Yes	<input type="checkbox"/> No	Is the research sponsored by a company?
<input type="checkbox"/> Yes	<input type="checkbox"/> No	The value of my remuneration or financial interest exceeds DH 10000
<input type="checkbox"/> Yes	<input type="checkbox"/> No	Are you, a family member, or spouse receive other remuneration (trips, gifts... etc.)



What is (are) the name(s) of the company or entity for which you will be engaging in the external activity (if applicable)?

Please provide a brief description of the nature of your relationship with the entity, and the amount of your expected remuneration from, or the value of your financial interest in the outside company or entity; if applicable.

Investigators must declare to the REC of any change in circumstances during the development of, or in the course of a project that would mean that they or their spouse, or family members would receive or hold any of the declarable items described above. Please check the following box if applicable.

I have read the above statement on conflicts of interest. I have nothing to declare now and I will immediately declare in writing to the REC of any future conflicts of interest

#### SECTION X: PRINCIPAL INVESTIGATOR CERTIFICATION

I agree to:

Comply with the provision of the UAE federal law on the subject of medical liability, and its Implementing Regulations governing research on human subjects, any Ministerial terms, rules & procedures regulating research & medical trials protocol & standards issued by the DOH

I also understand the absolute need to:

1. Design the study with the standards set by the DOH and other sponsoring agencies.
2. Obtain prior approval from the REC before amending the research protocol or the approved consent form.
3. Report to the REC in accordance with REC policy, any adverse event(s) and/or unanticipated problem(s) involving risks to participants.
4. Submit a progress report both annually and whenever requested by the REC/DOH.
5. Submit the Re-Approval form/Completion Form as needed.
6. Ensure that each individual listed as study personnel in this application is knowledgeable of the study procedures described in the proposal.
7. Include the REC approval no. in any published paper coming out of this study.
8. Abide to the items and conditions listed in the attached files, including but not limited to the



researcher guide, study proposal, informed consent, etc.

9. Abide timely with all the requested reports or forms, as failure to do so will entitle the REC to terminate the approval already granted to the study under progress.

Furthermore, by signing below, I also attest that I have appropriate facilities and resources for conducting the study.

Principle Investigator (PI) Name

PI Signature

Date

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

Student Investigator Name\*

Student Investigator Signature

Date

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

Co-Investigator Name

Co-Investigator Signature

Date

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\*(Only for student, resident or fellow-initiated Research)

Please attach/upload the detailed (above) Research Proposal Form.

**Study protocols should be formatted using Times New Roman font, size 12, double-spaced.**

This section is to be completed by REC	
Research Proposal Number	
Date Received	
Date sent to ADHRTC (if applicable)	
Primary Reviewer	
Date Reviewed	
Date of Committee Review	



Decision	Approved <input type="checkbox"/>	Rejected <input type="checkbox"/>	Pending <input type="checkbox"/>
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This section is to be completed by ADHRTC			
Research Proposal Number			
Date Received from REC			
Date Reviewed			
Date of ADHRTC Committee Review			
Decision	Approved <input type="checkbox"/>	Rejected <input type="checkbox"/>	Pending <input type="checkbox"/>



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Devices Use Form # REC 003

The REC/IRB requires the fulfilment of the regulations below in all proposals involving the use of Devices (transponders, pumps, etc.):

Please respond to the following points:

A. Identify anatomical site where the device will be located:

B. Describe the device. Identify any active ingredients/chemicals (mercury, etc.) contained with the device:

C. What is the size (dimensions) of the device?

D. Describe the method by which the device will be implanted:

E. Will the device be recovered/retrieved? yes no

If yes, describe how the device will be recovered/retrieved:



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**USE OF DRUGS AND/OR BIOLOGICAL PRODUCTS IN RESEARCH # REC 04**

The REC/IRB requires the completion of the below form for all proposals involving the use of Drugs and/or Biological Products in Research:

Please respond to the following points:

A- Identify the drug(s) or biological products:

Trade name of Drug or Biological Product	Generic or Biological name	Manufacturer of the product	Recommended storage temperature*

B- \*If the Drug or Biological Product are to be stored at refrigerator or freezer temperature:

a. Is there a back-up power source in the event of power outage?

Yes

No

b. Is the refrigerator or freezer alarmed to alert staff in the event of power outage?

Yes

No

c. Confirm Drug or Biological Product will be stored in a dedicated medication storage refrigerator or freezer:

Yes

No

C- Is the Drug or Biological Product currently approved by MOHAP?

Yes

No

If Yes, please provide the package insert



If No, please provide the following:

Chemical Structure	
Pharmacology	
Form of Administration	
Maximum Tolerated Dose in Humans	
Toxicity Observed	
Pharmacokinetics Data	
Procedures for minimizing adverse events in humans	

D- If the Drug or Biological Product used in this research are not dispensed by a pharmacist, they can only be dispensed by a physician, or personnel in agreement with the physician. Examples of these personnel are physician's assistant and nurse. Only persons with legal authority to dispense the Drug or Biological Product, and those under their direct supervision, can have access to the Drug or Biological Product storage area.

List the person(s) and their degree, responsible for dispensing the drug or biological product to the project's subjects, and having access to the storage area.

E- Emergency Unbinding:

1- Please explain how the contents of a drug container will be identified in case of emergency. The names and contact information of the persons who will be responsible for the unbinding, and who are expected to be available 24 hours a day/7 days a week, in a timely manner should be listed.

2- Please confirm that the following information is on the labeling of the medication container dispensed to the study subjects.

- a. Name, address and telephone number of the clinic or physician's office
- b. Prescribing physician's name
- c. Subject's name or subject number
- d. Date of dispensing
- e. Direction for use
- f. Drug name or protocol name or number
- g. Manufacturer's name

Yes

No

3- If the study is registered as Clinical Trial, please indicate the Clinical Trial Identifier:



<div style="border: 1px solid black; padding: 5px; background-color: #f0f0f0;"><b>Institute logo</b></div>	<p><b>REC/Institutional Review Board</b> لجنة أخقيات بحوث لاغلمي</p>  <p>دائرة الصحة DEPARTMENT OF HEALTH</p>	<div style="border: 2px solid yellow; padding: 5px; background-color: #f0f0f0;"><p>For REC/IRB use only: For Review [    ] FOR ADHRTC [    ] Proposal No. _____</p></div>
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**USE OF STEM CELL, ZYGOTES, GAMETES AND FETUSES IN RESEARCH Form # REC 05**

Please respond to the following points:

A- Identify the Stem Cell source, and describe how you plan to acquire the bio-specimens (i.e. stem cells extracted from the umbilical cord or adult stem cells):

B- Please describe the specific use and the rationale for the use of the stem cells:

C- Do you plan to generate new Human embryonic stem cell (HESC) lines?

Yes

No

If “Yes”, please explain the scientific rationale for generating new Human embryonic stem cell (HESC) lines:

D- Where will the research take place? Identify all space where the research will be performed. This includes ancillary support rooms such as tissue culture rooms and freezer storage areas (Indicate institute, and building, floor, and room number):



E- Please provide a list of all individuals involved in the design, conduct, or reporting of the research:

Name	Department/Division	For renewals, is this individual new since the last submission?

I, the principal investigator, confirm that I shall abide by the regulations set by the Department of Health regarding research on stem cells, zygotes, gametes and fetuses. I understand that no research may be conducted for the purpose of human cloning. I will abide by the prohibitions determined by medical liability law, regulations & resolutions in implementation thereof, and ethical principles, where harms and dangers to humanity outweigh the expected benefits. I certify that the research proposal is fulfilling the aforesaid law & regulations & the following conditions:

- 1- Cloning of humans for the purpose of obtaining and using stem cells in research or for any other use is strictly prohibited.
- 2- Excess fertilized eggs from in vitro fertilization procedures performed for medical indications shall not be used for therapeutic purposes or in stem cell research.
- 3- Male or female gametes taken from sperms or eggs may not be donated to produce fertilized eggs that can grow into a fetus for the purpose of generating stem cells therefrom.
- 4- Embryonic stem cells derived from fetuses aborted in accordance with the provisions of the medical liability law & its implementing regulations, or from miscarried fetuses without any signs of life yet may be used whether in research or in scientific and laboratory experiments in accordance with applicable UAE federals and local rules.
- 5- In case of stillborn fetuses, embryonic stem cells may be transferred and used in research in accordance with the law.
- 6- Stem cells of an adult human may be used, provided said human is not subject to any harm, and such stem cells can be used to treat a patient, and the expected benefit outweighs the possible harm.
- 7- Research objectives shall be clearly and accurately defined, and the research is preceded by sufficient experiments on animals if the nature of the research so requires, subject to the decision of the REC/IRB.
- 8- Assessing the expected benefit for the human subject and the extent to which it outweighs the possible harm shall be through a clear and thorough scientific assessment conducted by the investigator and submitted to the REC/IRB.



- 9- If the REC/IRB finds that the potential harm for the human subject outweighs the expected benefit, it shall not approve the research project;
- 10- The REC/IRB shall review periodic reports submitted by the investigator to ensure that the expected benefit continues to outweigh the possible harm.
- 11- The investigator or research team conducting the research shall be specialized and shall have sufficient scientific expertise and scientific competence.
- 12- The "Informed Consent" shall be obtained from the human subject prior to conducting the research and the information provided shall contain a full explanation of expected benefits and potential risks of the research.
- 13- The investigator shall keep detailed records of the source of stem cells and results of their use in the research, and shall submit periodic research reports to the REC/IRB. The institution may set up its own bank to store stem cells for research purposes subject to the approval of the ADHRTC.
- 14- Stem cells stored in stem cell banks may not be used for research purposes without the prior permission of the REC/IRB and the owner's consent, and upon obtaining the "Informed Consent" from the donor.
- 15- Each sample shall be given a permanent label indicating to whom it belongs. Information included in said label shall be updated by the principal investigator under the supervision of the REC/IRB.
- 16- The institution shall set up a special record for research conducted on the sample under the supervision and monitoring of the REC/IRB.
- 17- The institution shall safeguard the sample and shall destroy it under the supervision of the REC/IRB when it is no longer needed or if the donor so requests.
- 18- The institution shall prepare a periodic report on research conducted on the sample for submission to the REC/IRB.
- 19- The investigator shall submit, along with the research proposal, a description of the mechanism of safeguarding samples and records thereof.
- 20- All personal data resulting from the research conducted on the sample shall be part of the rights of the donor, and they may not be used or published without his consent, taking confidentiality and privacy into consideration.
- 21- The REC/IRB may, when necessary, add or amend conditions for use of stem cells.



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**Final Report (Study Completion or Termination) Form # REC 06**

1. Date:			
2. Study Title:			
3. Study Design:			
4. Principal Investigator (PI):			
College/Department:		PI Title:	
Phone:			Email:
Fax:			Mailing address:
Sponsor/Funding agent (NA: <input type="checkbox"/> ):			
5. Total number of subjects:			
Note: The numbers below should reflect activity for the entire length of the project:			
Number of subjects planned:		Number enrolled:	
Number of subjects completed:		Number of subjects discontinued:	
Number of signed informed consent forms in your study file: <input type="text"/>			
6. Briefly summarize your project (an attached report/reprint will not replace this summary):			



7. If study was terminated, specify reason (NA: ):

**Report prepared by:**

Printed Name

Signature

Date

**I have reviewed this report:**

Principal Investigator Name:

Signature

Date



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Proposal No.

Request to Amend a Currently Approved Project Form # REC 07

Part 1 – Administrative Information:

Proposal Information	
REC approval (study) #	
Study Title:	
Contact Information	
Principle Investigator name	
Principle Investigator Address:	
Email address:	
Hospital/Department:	

Part 2 – Amendment Information

1. Please select ALL the categories of amendment(s) you are requesting:

- Change in Study Title.
- Change in Principal Investigator.
- Addition of/change in research personnel.
- Addition of/change in funding source.
- Change to research/study design.

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- Addition of/change to study population.
- Addition of/change to survey(s), questionnaire(s), or other research tools (Please attach the original & the revised tool(s)).
- Addition of/change to the identifiers collected in the study, or any others that would impact the privacy and confidentiality of the study participants.
- Addition of/change to informed consent and/or procedures (Please attach the original & the revised documents).
- Other changes (specify) .....

1. For each category you have selected above, please describe the changes you are proposing:
  
2. Please state the reasons you are making amendments to the study:
  
3. Are any of these changes the result of something that occurred during human participant interaction or an unexpected event?  Yes  No
  
4. Will the proposed changes affect the risks or benefits to research participants?  
 Yes  No  
If Yes, please explain:
  
5. Do these changes involve information that might relate to a subject's willingness to take part in the research?  
 Yes  No

Signature

**Principal Investigator**

I certify that the information I provide in this application is correct and complete. I also pledge that I will not change any of the procedures, forms, or protocols used in this study without first seeking review and approval from the REC.

\_\_\_\_\_  
Name/Signature of Principal Investigator

\_\_\_\_\_  
Date



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Proposal No.

ADHRTC Risk Assessment Form # REC 08

All applications should have attached: REC application to their institution's REC, consent form sample, REC evaluation letter from the investigator's institution and a copy of the proposal.

Institution:	
Principal Investigator	
Project ID#	
Project Title	

Summary of the project, to include its significance (max 300 words):

1. Pharmaceutical sponsor trial  Yes  No (If not, go to #2)

a. The trial is:

- Funded  
 Non-funded (e.g. material transfer, material loan, service support)

b. If funded, payment is made to:

- Institution  
 Principal Investigator  
 Not Applicable

c. Team members who declare Conflict of Interest:



- Nobody in the research team has a conflict of interest
- Principal Investigator
- Co-investigators
- Other study team members

d. Intervention & MOH importation license status (if needed):

- Drug
- Device
- Other

- Public website listing, reference and data results (e.g. [www.clinicaltrials.gov](http://www.clinicaltrials.gov) identifier NCT number).

Locations:

- Single center
- Multicenter (list centers or attach listing)

2. Multicenter clinical research  Yes  No (If not, go to #3)

a. Who is the record holder of the research?

b. Consenting process:

- Face-to-face
- Online
- Waiver of Inform Consent Form

c. Describe the Database used to store information, and its location:

d. Systems of Electronic Data collection

e. List participation sites. You may attach separate sheets if needed.

f. Contract/Agreement between parties



- a. An agreement is in place  Yes  No
- b. There are other UAE sites already involved  Yes  No
- c. Data use agreement
- Material transfer
  - Material loan
  - Non-Disclosure Agreement
  - Other

- g. Data source for the records shared among the centers:
- Medical records
  - Online Case Report Forms & tests/results
  - PHI (protected health information) shared with 3<sup>rd</sup> parties: tick all types applicable:
    - Name collected
    - Street address, PO Box, city collected
    - Date of birth collected
    - Date of death collected
    - Phone numbers collected
    - Fax number collected
    - Email address collected
    - Emirates ID # collected
    - Passport # collected
    - Medical record #
    - Account numbers (bank, credit cards, hospital) collected
    - Certificate/license numbers (DOH, professional, driver's) collected
    - Vehicle license, plate numbers collected
    - Device identifiers (IP, Web URLs) collected
    - Biometric identifier collected
    - Full face photo or comparable images
    - Unique identifying number, characteristic or code collected

List your reason for collecting the PHI indicated (ticked) above:

**3. Genetics medical testing & genomics or genetics research utilizing non-commercially purchased DNA/RNA**

Yes  No

- a. Patient Genetics tests are proposed:
- Not Applicable, no patient genetics testing
  - Single tests
  - Multiple tests



b. In either medical testing or research, are vulnerable population involved as subjects or patients:

- Mental disabilities or cognitive impairments
- Terminally ill, or illiterate
- Non-English and non-Arabic speaking
- Minors
- Other

c. For research, indicate source of the participants: where you recruit

d. Are there agreements in process with the collaborating sites, or individual consultants?

- Yes       No

e. The Consent of participants:

- Includes only present research
- Includes future research
- Includes approval to release data into public database
- There is action plan in the consent for participants to withdraw consent

f. Where is Genomics research Information stored?

List all locations including cloud options (cloud storage is not permissible for medical care information, but it is for research)

g. Is the documentation of test/research stored in the medical record?  Yes       No

h. Sample identifiers to be used:

- A code is assigned
- Protected Health Information (PHI) is used as identifier

i) The samples are destroyed after use.  Yes       No

There is language in the agreement with collaborating institutions about sample destruction

- Yes       No       Not Applicable

j) Permission is granted in the consent for future tests, including future research use of samples:

- At the applicant site
- At the 3<sup>rd</sup> party's site



- k) Is there genetic counselling available once results are available?  
 Yes  No  Not Applicable
- l) Is there available psychological support in the case of genetics testing?  
 Yes  No  Not Applicable
- m) For Medical genetic testing analysis, are there external entities involved?  
 Yes  No  Not Applicable

If yes, list the information they receive

If yes, explain the method of sharing information

- n) For Genomics or genetics research are there co-investigators, consultants or mentors residing outside UAE?  
 Yes  No  Not Applicable

If yes, list the information or samples they receive

If yes, explain the method of sharing information

The co-investigator residing abroad is a solo consultant.

- Yes  No  Not Applicable





## APPENDIX 5: Recommended Information for the REC Committee Roster

It is recommended that the following information be provided for REC members:

- 1) First and Last Name.
- 2) Earned Degrees.
- 3) Phone Number.
- 4) E-mail Address.
- 5) Term Start Date.
- 6) Term End Date.
- 7) Research output Status (last 5 years).
- 8) Affiliation Status (if any with other medical or academic institutes).
- 9) Area of Specialty.
- 10) Narrative Description of Area of Expertise (e.g. brief description of all relevant experiences that describe each member's expected contributions to the REC).
- 11) REC Office prior expertise (e.g. Chair, Vice-chair, member, If any).
- 12) Representative capacity (indicate which, if any, vulnerable populations are being represented by this member, e.g. children, pregnant women, or prisoners, etc.; or if the member represents the perspectives of research participants).

## APPENDIX 6: Guideline on the Informed Consent Form

(Also refer to Appendix 11 for Guidance on Risks and Benefits)

### 1. Consent Form Checklist

Ethically and legally, consent is not considered to be informed unless the investigator(s) discloses all those facts, risks, and discomforts that might be expected to influence an individual's decision to willingly participate as a volunteer in a research project.

### 2. This checklist is for the investigator's own use; it should not be submitted to the REC

This checklist should be used to ensure that ALL of the required elements are included in the study's consent form:

- a. Study Title has been included.
- b. Name(s) of funding agency/agencies (if applicable).
- c. Investigator(s) are listed, and their designation, department & address.

### 3. Purpose of this Research Project (does the consent document include):

- a. A clear Statement: that the study involves research.
- b. Nature of the study.
- c. Purpose for conducting the research.
- d. Total number of subjects involved.
- e. Investigational products (pharmaceutical/medical device) details with comparator(s)/placebo.

### 4. Procedures (does the consent document include):

- a. Step-by-step explanation of what will be expected from study participants.
- b. Identification of any procedures that are experimental.
- c. Identification of surgical/invasive procedures with the type of anaesthesia involved.
- d. Identification and purposes of any procedures for genetic testing with details of its regulations.
- e. Identification of subject's bio samples collection and detail of their transportation abroad.
- f. Length and frequency of each study procedure and total time commitment for the subject.
- g. Location of the research.
- h. The instruments / documents that will be used and conditions involved (include an explanation of the instruments in appropriate language).

### 5. Risks (does the consent document include a description of):

- a. All potential risks described (mental, social, financial, legal, dignity, or physical. The use of survey questions of a sensitive nature may pose emotional distress caused by remembering unpleasant experiences).
- b. Safeguards that are to be employed to reduce or minimize risks.
- c. Safeguards in the genetic testing.
- d. Safeguard in the subject's bio samples being sent abroad.
- e. All the investigational product (pharmaceutical or medical device) side effects, including serious, rare, and/or fatal.

### 6. Benefits (does the consent document include):



- a. All direct or indirect benefits that may be reasonably expected from the research.
- b. Statement “No promise or guarantee of benefits have been made to encourage you to participate”.

**7. Extent of Anonymity and Confidentiality** (does the consent document include):

- a. Extent to which subjects will be identifiable
- b. Explanation of how the study will provide the utmost confidentiality or anonymity [confidentiality = individual can be identified directly or through identifiers, but the researchers promise not to divulge that information; anonymity = individuals cannot be identified by anyone, including researchers]
- c. Optional: Statement: “At no time will the researchers release the results of the study to anyone other than individuals working on the project without your written consent”.
- d. Explanation of who will have access to the data.
- e. Statement “It is possible that the REC may view this study’s collected data for auditing purposes. The REC is responsible for the oversight of the protection of human subjects involved in research”.
- f. Description of when data will be destroyed or will be retained for any future (secondary) research purpose, or could be archived at the physician’s record for any future registry development.
- g. Description of when the bio samples will be destroyed or will be kept retained for any further (secondary) research purposes and/or by other investigator.

**8. Compensation** (does the consent document include):

- a. Subjects informed whether compensated or not for the portion of their time spent in the study.
- b. Amount of compensation.

**9. Freedom to Withdraw** (does the consent document include):

- a. Statement that participation is voluntary; subjects are free to withdraw from the study at any time without penalty or loss of benefits to which the subjects are otherwise entitled.
- b. Statement that participants are free not to answer any questions or respond to experimental situations that they choose without penalty.
- c. Statement that participants are free not to provide or donate their bio-samples, in case they have concern especially for sending samples abroad for research purposes.
- d. Statement that the participants are free to refuse the genetic testing on their bio-samples.
- e. Statement describing that there may be circumstances under which the investigator may determine that a subject should not continue as a subject.

**10. Subject’s Responsibilities** (does the consent document include):

- a. Statement “I voluntarily agree and consent to participate in this study. I have the following responsibilities:” List of subject’s responsibilities, with the significant limits of subject’s study compliance and adherence, detailed visits, restrictions (if any), not disclosing about the study [to discuss only to the family.

**11. Subject’s Permission** (does the consent document include):

- a. Statement “I have read the Consent Form and conditions of this project.
- b. I have had all my questions answered. I hereby acknowledge the above and give my voluntary consent.
- c. Signature line for the participant (or the responsible guardian, if the participant is not able or legally unfit to give informed consent).



- d. Signature line for an impartial witness (not connected with the research), affirming that the participant was informed & he/she has given consent, either verbally (if illiterate) or in writing.
- e. Contact information of investigators (24-hour/7 days, contact no. of the PI).
- f. Contact information of REC Research Coordinator listed as follows:
- g. "If I should have any questions about the protection of human research participants regarding this study, I may contact the REC office." Current contact numbers of the REC Research coordinator should be listed.
- h. Translator section should be added as one of the signatory options in the Informed Consent form, provided that some patients might need one at the time of consenting.
- i. Structure of Consent Document.
- j. Language of the consent form is directed toward the individual signing the form (avoiding use of jargon, scientific terms, and concepts not readily comprehended by the non-scientist public)
- k. The text and readability of consent form is appropriate for the age, mental capacity and maturity of the individual signing the form.
- l. The consent form does not contain any exculpatory language in which the subject is made to waive or appear to waive any of the subject's rights.
- m. The final draft of the consent document has been reviewed for grammatical and typographical errors.

**Please note that:**

1. The consent form should not ask patients to waive any of their legal rights, nor should they be asked to release the investigator, sponsor, or hospital from liability for negligence.
2. In cases where persons who are legally incapable of giving informed consent, the investigators nevertheless should (1) provide an appropriate explanation, (2) obtain the participant's assent, and (3) obtain appropriate permission from a legally authorized person.
3. Translator section should be added as one of the signatory options in the Informed Consent form, provided that some patients might need one at the time of consenting.



## APPENDIX 7: Guideline on Reporting Suspected Adverse Reaction (SAE)/ Suspected Unexpected Serious Adverse Reaction (SUSAR)

The following provides guidance on the reporting for SAEs, SUSAR(s) and other unanticipated events (see Appendix 8 on the Description of Unanticipated Events).

All adverse drug reactions (ADRs) that are both serious and unexpected should be reported in the following defined way:

1. **What to report:** The sponsor of a clinical trial (Phase I-IV) with at least one investigator site must report SUSARs according to the following scenarios:
  - a. All suspected adverse reactions related to an investigational medicinal product or medical device (the tested investigational medicinal products, devices, and comparators) which occur in the concerned trial, and that are both unexpected and serious (SUSARs) are subject to expedited reporting, with stringent timeline if they are fatal and life threatening.
  - b. In some studies, like, Post Marketed Trials Safety Studies, sponsor may require the reporting of all such 'otherwise non-reportable Adverse Events (AEs)', as in case of 'Events of (Clinical) Interests'. The investigator will have to report to the sponsor and REC, all such Adverse Events as per the sponsor's guidelines. Otherwise, these should only be documented and filed in the Investigator Site File, for the purpose of compliance monitoring check.
2. **What not to report:** Expedited reporting is not usually required:
  - a. For reactions which are serious but expected.
  - b. For non-serious adverse reactions whether expected or not. However, in some trials, the unexpected 'non-serious' and expected 'serious' adverse events may require reporting within the sponsor's and REC timelines.
  - c. It is generally not necessary to report events that are considered **unrelated** to the investigational medicinal product.
3. **Who should report to whom:**
  - a. The PI and/or the sponsor should report all the relevant safety information previously described to the regulatory authority and to the REC/IRB concerned. The sponsor shall inform all investigators concerned of relevant information about SUSARs that could adversely affect the safety of subjects. When required, the REC report to the DOH or relevant authority within the given timelines.
4. **When to report**
  - a. **Fatal or Life threatening and/or Unexpected SAEs/SUSARs:** For local events (**research site /on site**), the sponsor, regulatory authority and REC should be notified immediately after the PI has first knowledge of the event with the minimum criteria for expedited reporting.
  - b. The relevant follow-up information should be sought and a report completed as soon as possible.



- c. **Non-Fatal/non-life threatening, Unexpected SAEs/SUSARs.** All other Unexpected SAEs/SUSARs and safety issues must be reported to the regulatory authority and REC of the facility participating in the study as soon as possible after the PI and/or sponsor has first knowledge.
- d. **Expected Serious Adverse Events (SAEs)** are required to be reported to the REC, only, if indicated in the Investigator Brochure as reportable, or, causality related to study product, or occurring more frequently than expected. Sponsor will report these expected events to the REC Only, if, and, as, indicated in the study protocol at specified timeline. These all expected SAEs will be documented in the Adverse Event log at study site provided by the sponsor, or Investigator designed AE log.
- e. Generally Expected Serious Adverse Events (SAEs), and Non-Serious Adverse Events (both expected and unexpected) do not require the reporting to the REC (non-reportable); only collection, documentation and filing in the Investigator Site File (ISF) is required. This information could be asked by the compliance monitor at the time of monitoring, to ensure that no safety information of the subjects is missed in documentation, and if required, reviewed by the REC.

## 5. How to Report

- a. Minimum criteria for initial expedited reporting of SUSARs: Information on the final description and evaluation of an adverse reaction report may not be available within the required time frames for reporting.
- b. For reporting purposes, initial expedited reports should be submitted within the time limits as soon as the minimum following criteria defining a valid case report are met:
  - i. A suspected investigational medicinal product;
  - ii. Identifiable subject (e.g. study subject code number);
  - iii. An adverse event assessed as serious and unexpected, and for which there are a reasonable suspected causal relationship;
  - iv. An identifiable reporting source;
  - v. The mandatory administrative information for guidance on clinical safety data management. E.g. the unique case identifier (i.e. sponsor's case identification number) where applicable, a study protocol number e.g. European Union Drug Regulating Authorities Clinical Trials Database (EudraCT) number or the sponsor's trial protocol code number where applicable.

## 6. Follow-up reports of SUSARs:

- a. In case of incomplete information at the time of initial reporting, all the appropriate information for an adequate analysis of causality should be actively sought from the reporter or other available sources. The sponsor should report further relevant information after receipt as follow-up reports.
- b. In certain cases, it may be appropriate to conduct follow-up of the long-term outcome of a particular reaction.



## APPENDIX 8: Description of Unanticipated Events

1. Event (including on-site and off-site adverse event reports, injuries, side effects, breaches of confidentiality, or other problems) – occurs any time during or after the research study, which in the opinion of the Principal Investigator (PI):
  - a. Involved harm to one or more participants or others, or placed one or more participants or others at increased risk of harm.
  - b. Is unexpected (an event is “unexpected” when it is not described with specificity in the protocol and informed consent document; or if described with specificity, it occurs beyond the expected frequency and/or severity identified); and
  - c. Is related to the research procedures (an event is “related to the research procedures” if, in the opinion of the principal investigator, it was more likely than not to be caused by the research procedures).
2. Information that indicates a change to the risk to benefit ratio of the research. For example:
  - a) An interim analysis indicates that participants have a lower rate of response to treatment than initially expected; or
  - b) A paper is published from another study that shows that an arm of the research study is of no therapeutic value.
  - c) . 2a and 2b (‘low’ or ‘no’ efficacy response) could be counted as Efficacy Failure, for which, if the study therapeutic area/product indication is Life Threatening disease, event needs to be reported immediately as in expedited reporting.
  - d) Safety monitoring indicates that a particular side effect is more severe, or more frequent than initially expected.
3. Change(s) in FDA and other international agency such as European medicine agency or withdrawal from marketing of a “test article” (a drug, device, or biologic) used in a research protocol.
4. Change(s) to the protocol taken without prior REC review to eliminate an apparent immediate hazard to a research participant.
5. Incarceration of a participant.
6. Event that requires prompt reporting to the sponsor.
7. Complaint of a participant when the complaint indicates unexpected risks or the complaint cannot be resolved by the research team.
8. Protocol violation, a term meaning an accidental or unintentional change to the REC approved protocol) that placed one or more participants at increased risk, or has the potential to occur again.
9. An unanticipated adverse device effect.
10. New information that may affect adversely the safety of the participants or the conduct of the clinical trial; and
11. Any changes significantly affecting the conduct of the clinical trial or increasing the risk to participants.



## APPENDIX 9: Guideline on Amendments: Types and Actions

1. **Minor (Non-Substantial):** Of relatively little importance and, therefore, not considered as substantial. They are changes to the details of research that have no significant implications for participants or for the conduct, management or scientific value of the study and can be regarded as non-substantial or minor amendments. Examples might be as follows:
  - a. Correction of typographical errors in the research protocol or other study documentation
  - b. Other minor clarifications of the research protocol
  - c. Changes to the Principal Investigator's research team (other than appointment of key collaborators)
  - d. Changes to the research team at particular trial sites (other than appointment of a new Principal Investigator)
  - e. Changes in funding arrangements
  - f. Changes in the documentation used by the research team for recording study data
  - g. Changes in the logistical arrangements for storing or transporting samples
  - h. Extension of the study beyond the period specified in the application form
  - i. Issue of an updated Investigator's Brochure or Summary of Product Characteristics relating to an investigational medicinal product.
  
2. **Major (Substantial):** Whatever procedural changes alter the risk, which participants are exposed to, or the potential benefit, constitutes a major amendment. The following changes shall normally be regarded as substantial:
  - a. A change in the primary purpose or objective of the research, such as Introduction of additional genetic studies;
  - b. Changes to the design or methodology of the study, or to background information affecting its scientific value;
  - c. Changes to the procedures undertaken by participants;
  - d. Any change relating to the safety or physical or mental integrity of participants, or to the risk/benefit assessment for the study;
  - e. Introduction of new classes of investigations or other interventions (rather than simply re-scheduling or modifying those already approved)
  - f. Recruitment of a new type of participant (especially if these would be regarded as being from vulnerable groups)
  - g. Changes to study documentation such as participant information sheets, consent forms, questionnaires, letters of invitation, letters to GPs or other clinicians, information sheets for relatives or caregivers;
  - h. Change in the use of biological samples
  - i. A change of sponsor(s) or sponsor's legal representative;
  - j. Appointment of a new PI or key collaborator or temporary arrangements to cover the absence of a PI;
  - k. A change to the responsibility and liability insurance coverage for the study;
  - l. A significant change to the definition of a research site;
  - m. A change to the definition of the end of the study;
  - n. Any other significant change to the protocol or the terms of the original REC application;



3. **Updating of the Investigator's Brochure for the IMP:** should not be regarded as a substantial amendment unless there is a change to the risk/benefit assessment for the trial.
  - a. Amendments normally requiring authorization only:
    - i. Amendments related to the quality of the IMP;
    - ii. Changes to non-clinical pharmacology and toxicology data;
    - iii. Changes to clinical trial and human experience data.
  - b. Amendments normally requiring a favourable ethical opinion only:
    - i. Amendments to the patient information sheets, consent forms, letters to their primary physicians or clinicians, letters to relatives/carers, etc (whether generic to the whole study or specific to a particular trial site);
    - ii. Change of insurance or indemnity arrangements for the trial;
    - iii. Change of the Principal Investigator or appointment of a key collaborator;
    - iv. Change of Principal Investigator at a trial site;
    - v. Change to the definition of a trial site;
    - vi. Any other significant change to the conduct or management of the trial at particular trial sites;
    - vii. Any other amendments to the terms of the REC application.
  - c. Amendments normally requiring both authorization and a favourable ethical opinion:
    - i. Amendments related to the research protocol (except those relating only to patient information sheets, consent forms, etc.);
    - ii. Amendments related to the safety of the IMP;
    - iii. Any other amendments related to the safety or physical or mental integrity of trial participants, or change to the risk/benefit assessment;
    - iv. Change of the sponsor or sponsor's legal representative;
  - d. Change of the Clinical Research Organization (CRO) assigned significant tasks;
    - i. Change of the definition of the end of the trial.
4. Where the amendment requires authorization or ethical opinion only, the notice of amendment form should be sent to the REC/IRB for information.



## APPENDIX 10: Guideline on Protocol Deviations

### 1. Important Protocol Deviation

- a. Important protocol deviations are a subset of protocol deviations that may significantly impact the completeness, accuracy, and/or reliability of the study data or that may significantly affect a subject's rights, safety, or well-being. For example, important protocol deviations may include enrolling subjects in violation of key eligibility criteria designed to ensure a specific subject population or failing to collect data necessary to interpret primary endpoints, as this may compromise the scientific value of the trial. These deviations are changes that the REC must approve before the proposed change is implemented (via submission of a substantial amendment).

#### Examples.

- i. Enrolling subjects from outside the eligibility criteria.
- ii. Changes in the text, nature and manner of obtaining the Informed Consent.
- iii. Study activity with the subjects without or prior to the informed consent is signed
- iv. Significant deviation in the schedule of administration of an investigational product (affecting the risk/benefit ratio and safety of subjects).
- v. Failing to collect necessary data to interpret the primary endpoints
- vi. Improper unbinding of study medication or procedure

### 2. Emergency Protocol Deviations

- a. These are the deviations occurring in an emergency situation, such as when a departure from the protocol is required immediately to protect the life or physical well-being of a participant. In such cases there is no time to prospectively seek the approval of the REC. The sponsor and the REC of deviation record should be notified as soon as possible, but not later than 7 days after the emergency situation occurred

### 3. Minor Protocol Deviation

- a. A minor protocol deviation is in the investigator's judgment a deviation that does not adversely affect the risk/benefit ratio of the study, the rights, safety, or welfare of the participants or others, or the integrity of the study.

#### Examples.

- i. Study procedure conducted out of timeframe (Applicable if it does not affect risk/benefit ratio & safety of the subjects, and not repeatedly);
- ii. Study visit out of timeframe (Applicable if it does not affect risk/benefit ratio & safety of the subjects, and not repeatedly);
- iii. Participant failure to initial every page of the consent form;
- iv. Copy of consent form not given to subjects during informed consent process;
- v. Site over-enrolment;
- vi. Participant failure to return patient diary (given to subjects to record study elements at home);
- vii. Missing original signed consent, but have a copy of the subject's signed consent;
- viii. Repeated minor deviations may be considered as non-compliance.



#### 4. Reporting of the Protocol deviations

- a. Investigator should report all the protocol deviations, occurring during the study on a timely (quarterly) manner to the REC.
- b. However, the investigator should report all major protocol deviations as soon as possible.
- c. All the protocol deviations should be documented in the Protocol Deviation Log. The Investigator has to ensure the presence of updated and signed deviation log at his/her site.
- d. For minor protocol deviations, the investigator should document the corrective and preventive actions taken by him/her, to avoid their recurrence.
- e. For repeated minor deviations, or major deviations with risk, safety or compliance elements, the investigator should make Corrective and Preventive Action.
- f. In case of unnoticed (undocumented) deviations from the protocol detected at a later point in time (e.g. during Clinical Research Organization (CRO) monitoring action(s) of the trial), these deviations should be reported on a quarterly basis to the REC. The REC will then decide on the required actions (if any) according to the procedure outlined in SOP of Protocol deviation.
- g. On finding of changes, increasing the risk to subjects and/or affecting significantly the conduct of the trial (apart from Emergency protocol deviations), the REC will assess and may produce its Corrective and Preventive Action in order to resolve any future non-compliance and safety of the subjects. The investigator has to practice the Corrective and Preventive Action and notify the REC on it through a report.
- h. The REC compliance Monitor may be requested to have a re-monitoring visit to check the report validity on Corrective and Preventive Action and if necessary, may initiate or request a re-training of the study investigators.



## APPENDIX 11: Guideline on Risks and Benefits

### 1. Risks

- a. Levels of Risk: In general, the higher the risk involved in the project, the more detailed the explanation, precautions, and informed consent must be. The nature and type of informed consent is determined by the level of risk. Accordingly, the following broad guidelines for degrees of risk may be of assistance in making a necessary determination:
  - i. **No greater than minimal risk:** the risk of psychological, social, or physical harm or discomfort is no greater than what would ordinarily be experienced in daily life or during routine physical or psychological tests. (This would generally, although not always, correspond to Exempt Review.)
  - ii. **Greater than minimal risk:** the risk of psychological, social, or physical harm or discomfort exceeds what would ordinarily be experienced in daily life or during routine physical or psychological tests; see examples below. (This will generally require either Expedited or Full Board Review.)

### 2. Types of Risk to Subjects

There is a variety of potential risk to subjects of which the researcher should be aware, including the following:

- a. Psychological Risk
  - i. The experience of participating in a study may cause a subject more, or persistent, psychological disturbance (anxiety, depression, stress, feeling of guilt, feeling of embarrassment or shame, or loss of self-esteem) than the subject would ordinarily experience in daily life or during routine physical or psychological tests.
  - ii. Most psychological risks are minimal and transitory, but the investigator and REC must be aware of the potential for serious psychological harm, particularly for fragile or especially sensitive individuals. To complicate matters further, different subjects may experience different types or levels of risk from the same research procedure.
  - iii. Researchers should word survey or interview questions to cause as little psychological disturbance as possible. It is often helpful to also provide referral information (e.g. a list of local self-help groups).
- b. Physical Risk
  - i. The most obvious sort of risk that could result from research is physical risk. Researchers should have appropriate safety and/or emergency training to enable study procedures to be carried out as safely as possible.
- c. Legal, Economic, Academic, Professional, or Social Risk
  - i. The disclosure of the subject's information may cause civil or criminal liability, or damage the subject's financial standing, academic standing, employability, or reputation; or may result in embarrassment within one's business or social group, loss of employment, or sanctions.
  - ii. Research subjects who are being interviewed about illegal or undesirable activities need to be informed about the limits of confidentiality before the interview begins.
- d. Personal/Familial Risk:



- i. Research studies involving the genetic testing of the subjects may affect their familial or personal life, disclosing the inherited disorders.
- ii. Genetic testing may reveal some unknown disease or possibility of disease in off springs, affecting the marital or future personal life of the subject.
- e. Special Risk for Vulnerable Populations
  - i. Institutional REC should be concerned with the protection of children, pregnant women, fetuses and prisoners. Other potentially vulnerable populations include persons with mental disabilities, residents of long-term care facilities, patients in health-care facilities, and “economically or educationally disadvantaged persons.” Such vulnerable persons may be at greater risk of psychological, social, economic, or physical harm from a research project that would impose only minimal risk upon other participants. Investigators are expected to include in their study design “additional safeguards to protect the rights and welfare of these subjects.
- f. Breach of Confidentiality/Lack of Respect for Participants
  - i. Confidentiality is of supreme importance in respecting human subjects. In addition to the potential harms discussed earlier, a breach of confidentiality (for example, when private information about a subject is shared with another party without the consent of the subject) can result in a variety of harms.
  - ii. Accordingly, investigator should take greater measures to protect the subjects' confidentiality. In virtually all studies in which information about subjects is collected, the investigator must guarantee that the information will remain confidential. This means that:
    - 1) To every extent possible, identifying information is completely separated from data;
    - 2) If it is necessary to link subjects to their data (e.g. in longitudinal studies), identifiers (names, etc.) are separated and masked through coding. The investigator must clearly specify how this will be accomplished (i.e. how the “crosswalk” documents linking identifiers to subject information will be kept secure, and who will have access to the “crosswalk” documents);
    - 3) In the rare instance it is necessary to maintain links between the subjects' identity and their data (i.e. the subjects' information includes identifiers and anyone with access to the raw data will be able to link subject information with subject identity), the investigator must explicitly describe how the data will be kept secure and who will have access to the data. In this case, this information must be stipulated in the subject’s informed consent form.

### 3. Benefits

- a. Types of Benefits to Subjects
 

There are two types of benefit that may accrue from a project: benefits to society (or to a specific community within the broader society), and benefits to the subjects themselves.

  - i. Typically, societal or community benefits are defined in terms of the knowledge or understanding the project is intended to produce, which may lead to improved health, safety, satisfaction, economic security, etc.
  - ii. Sometimes participation in a project conveys benefits to the subjects themselves beyond the knowledge that the project as a whole is intended to generate. For example, a thought-provoking questionnaire may be intellectually stimulating to the survey respondents, or may enhance self-understanding, or may make the respondents aware of services or resources with which they were previously unfamiliar.
  - iii. However, a number of research projects provide no direct benefits to subjects, and it may be many years before the results of the research are promulgated and useful to society or to



- groups of people. Thus, promises of a benefit to science or society are not adequate descriptions of benefit.
- iv. Regardless of whether or not there is a direct benefit to subjects, they must be told what the investigator is trying to learn and why (except when deception is a necessary element of the design).
  - v. Compensation to subjects is not considered a benefit in the risk/benefit analysis, nor is the fact that the participants may find it rewarding to be helpful.
- b. Compensation is NOT a benefit
- i. Investigators may pay research subjects for their participation or offer gift certificates or vouchers.
  - ii. However, it is important that payments or gifts not be so ample as to coerce participation from those who might otherwise decline to be a part of the study. Payment should not encourage subjects to participate or continue to participate against their better judgment.
  - iii. Subjects should receive partial payment if they withdraw from a study.
  - iv. Withholding all payment until participation is complete is coercive. A modest lump sum can be paid after a subject's " participation is complete if the arrangement is thoroughly documented in the consent form.



## APPENDIX 12: Links to References and Relevant Websites for Clinical Research

### Links to International References and Relevant Websites on Clinical Research

1. Declaration of Helsinki:
2. <https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/>
3. International Council of Harmonisation-Good Clinical Practice (ICH-GCP):
4. <http://www.ich.org/home.html>
5. World Medical Association (WMA): <http://www.wma.net/>
6. Belmont Report: <http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html>
7. Common Rule: <http://www.hhs.gov/ohrp/humansubjects/commonrule/>
8. And: <https://www.nsf.gov/bfa/dias/policy/docs/45cfr690.pdf>
9. USA Food and Drug Administration (FDA): <http://www.fda.gov/>
10. Council for International Organizations of Medical Sciences (CIOMS): <http://www.cioms.ch/>
11. Office of Human Research Protection (OHRP): <http://www.hhs.gov/ohrp/index.html>
12. International Medical Device Regulators Forum: <http://www.imdrf.org/>
13. Suspected Unexpected Serious Adverse Reactions (SUSAR) reporting:  
[http://ec.europa.eu/health/files/eudralex/vol-10/21\\_susar\\_rev2\\_2006\\_04\\_11\\_en.pdf](http://ec.europa.eu/health/files/eudralex/vol-10/21_susar_rev2_2006_04_11_en.pdf)
14. Vancouver Authorship Protocol: <http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html>

### Main Documents for International References on Research Ethics

1. Nuremberg Code- 1947 (Nuremberg, Germany)
2. Declaration of Helsinki-1964-2000-2014 (Helsinki, Finland)
3. Belmont report-1979 (Belmont Conference Center, Maryland, USA)
4. CIOMS- (Council of International Organizations of Medical Sciences), 1982-2002-2015 (Geneva, Switzerland)
5. Good Clinical Practice (GCP)-US FDA-1978
6. GCP-Europe-1991
7. International Council of Harmonization (ICH)-GCP-1990-1996
8. Common Rule-1991 (FDA-USA)
9. Consolidated Guidelines ICH-E6. (International Council of Harmonization-Good Clinical Practices), Sep 1997

**Note:** Documents on National Ethical rules & regulations are mandatory to be read, understood and followed by the local Ethics Committees and the Investigator Researcher