وزارة الصحة ووقاية المجتمع

MINISTRY OF HEALTH & PREVENTION

Guidelines for Conducting Clinical Trials with Investigational Products and Medical Devices

2017

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Section I General provisions

Subsection I-1. Clinical trials scope and definitions

Article 1. Scope

These Guidelines applies to all clinical trials conducted in the United Arab Emirates. It does apply to interventional, non-interventional studies including medical devices.

Article 2. Definitions

For the purposes of this Guidelines, the following definitions also apply:

Paragraph 2.1 Adverse event' means any untoward medical occurrence in a subject to whom a medicinal product is administered and which does not necessarily have a causal relationship with this treatment.

Paragraph 2.2 Adverse Device Effect (ADE) means an adverse event related to the use of an investigational medical device.

Paragraph 2.3 'Assent' means a child's affirmative agreement to participate in a clinical trial. Mere failure to object may not, absent affirmative agreement, be construed as assent.

Paragraph 2.4 'Authorized investigational product' means a medicinal product authorized in accordance with UAE Regulation, irrespective of changes to the labelling of the product, which is used as an investigational product.

Paragraph 2.5 'Auxiliary medicinal product' means a medicinal product used for the needs of a clinical trial as described in the protocol, but not as an investigational product.

Paragraph 2.6 'Clinical study/ trial' means any investigation in relation to humans intended:

a) to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more investigational products;
b) to identify any adverse reactions to one or more investigational products; or
c) to study the absorption, distribution, metabolism and excretion of one or more investigational products; with the objective of ascertaining the safety and/or efficacy of those investigational products. The terms clinical study and clinical trial are synonymous.

Paragraph 2.7 'Clinical study report' means a written description of a trial/study of any therapeutic, prophylactic, or diagnostic agent conducted in human subjects, in which the clinical and statistical description, presentations, and analyses are fully integrated into a single report.

Paragraph 2.8 'Clinical trial temporary on hold' means an interruption not provided in the protocol of the conduct of a clinical trial with the intention of resuming it at a later date

Paragraph 2.9 'Contract Research Organization' (CRO) a person or an organization (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial-related duties and functions.

Paragraph 2.10 ‘Early termination of a clinical trial’ means the premature end of a clinical trial due to any reason before the conditions specified in the protocol are complied with.

Paragraph 2.11 ‘End of a clinical trial’ means the last visit of the last subject, or at a later point in time as defined in the protocol.

Paragraph 2.12 ‘Good Clinical Practice (GCP)’ means a standard for design, conduct, performance, monitoring, auditing, recording, analyses, and reporting clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

Paragraph 2.13 Good Laboratory Practice (GLP) is a set of principles intended to assure the quality and integrity of non-clinical laboratory studies that are intended to support research or marketing permits for products regulated by government agencies.

Paragraph 2.14 Good Manufacturing Practice (GMP) is a system for ensuring that products are consistently produced and controlled according to quality standards. It is designed to minimize the risks involved in any pharmaceutical production that cannot be eliminated through testing the final product.

Paragraph 2.15 ‘Impartial Witness’ is a person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the subject or the subject’s legally acceptable representative cannot read, and who reads the informed consent form and any other written information supplied to the subject.

Paragraph 2.16 ‘Incapacitated subject’ means a subject who is, for reasons other than the age of legal competence to give informed consent, incapable of giving informed consent according to the law of the UAE.

Paragraph 2.17 ‘Independent Ethics Committee (EC)’ means an independent body constituted of medical, scientific, and nonscientific members, whose responsibility it is to ensure the protection of the rights, safety, and well-being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trials, of protocols and amendments, and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects. This body (ies) is established in the UAE in accordance with this Guidelines and empowered to give opinions for the purposes of this Guidelines, taking into account the views of laypersons, in particular patients or patients' organizations.

Paragraph 2.18 ‘Informed consent’ means a subject's free and voluntary expression of his or her willingness to participate in a particular clinical trial, after having been informed of all aspects of the clinical trial that are relevant to the subject's decision to participate or, in case of minors and of incapacitated subjects, an authorization or agreement from their legally designated representative to include them in the clinical trial.

Paragraph 2.19 'Inspection' means the act by a regulatory authority of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority to be related to the clinical trial and that may be located at the clinical trial site, at the sponsor's and/or contract research organization's (CRO's) facilities, or at other establishments deemed appropriate by regulatory authority.

Paragraph 2.20 'Investigator' means a person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.

Paragraph 2.21 'Investigational product' means a pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use. The terms investigational medicinal product (IMP) and investigational product (IP) are synonymous.

Paragraph 2.22 'Investigator's brochure' means a compilation of the clinical and non-clinical data on the investigational product or products which are relevant to the study of the product or products in humans.

Paragraph 2.23 'Legally acceptable representative' means an individual or juridical or other body authorized according to the law of the UAE, to consent, on behalf of a prospective subject, to the subject's participation in the clinical trial.

Paragraph 2.24 'Manufacturing' means total and partial manufacture, as well as the various processes of dividing up, packaging and labelling (including blinding).

Paragraph 2.25 'Medical device' means any instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific medical purpose(s) of:

a) diagnosis, prevention, monitoring, treatment or alleviation of disease,
b) diagnosis, monitoring, treatment, alleviation of or compensation for an injury,
c) investigation, replacement, modification, or support of the anatomy or of a physiological process,
d) supporting or sustaining life,
e) control of conception,
f) disinfection of medical devices
g) providing information by means of in vitro examination of specimens derived from the human body;

and does not achieve its primary intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its intended function by such means.

Paragraph 2.26 'Medical device incident' is any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labeling or the instructions for use which, directly or indirectly, might lead to or might have led to the death of a patient, or user or of other persons or to a serious deterioration in their state of health.

Paragraph 2.27 'Minor' means a subject who is, according to the law of the UAE, under the age of legal competence to give informed consent to treatments or procedure involved in clinical trials.

Paragraph 2.28 'Non-interventional study' is a study fulfilling cumulatively the following requirements:

a) The medicinal product is prescribed in the usual manner in accordance with the terms of the marketing authorization;
b) The assignment of the patient to a particular therapeutic strategy is not decided in advance by a trial protocol but falls within current practice and the prescription of the medicine is clearly separated from the decision to include the patient in the study;
c) No additional diagnostic or monitoring procedures are applied to the patients and epidemiological methods are used for the analysis of collected data.

The terms Non-interventional study (NIS) and observation study (OBS) are synonymous.

Paragraph 2.29 'Normal clinical practice' means the treatment regime typically followed to treat, prevent, or diagnose a disease or a disorder.

Paragraph 2.30 Post-Authorization Efficacy Study (PAES) is any study conducted where concerns relating to some aspects of the efficacy of the investigational product are identified and can only be resolved after the investigational product has been marketed.

Paragraph 2.31 Post-Authorization Safety Study (PASS) is any study relating to an authorized investigational product conducted with the aim of identifying, characterizing or quantifying a safety hazard, confirming the safety profile of the investigational product, or of measuring the effectiveness of risk management measures.

Paragraph 2.32 'Protocol' means a document that describes the objectives, design, methodology, statistical considerations and organization of a clinical trial. The term 'protocol' encompasses successive versions of the protocol and protocol modifications.

Paragraph 2.33 'Serious adverse event' means any untoward medical occurrence that at any dose requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability or incapacity, results in other important medical event, results in a congenital anomaly or birth defect, is life-threatening, or results in death.

Paragraph 2.34 'Serious deterioration in the state of health' can include:

a) life-threatening illness;
b) permanent impairment of a body function or permanent damage to a body structure;

c) a condition necessitating medical or surgical intervention to prevent a) or b); examples: - clinically relevant increase in the duration of a surgical procedure - a condition that requires hospitalization or significant prolongation of existing hospitalization;
d) any indirect harm as a consequence of an incorrect diagnostic or In-Vitro Diagnostic (IVD) test results when used within manufacturer's instructions for use;
e) fetal distress, fetal death or any congenital abnormality or birth defects.

Paragraph 2.35 'Start of a clinical trial' means the first act of recruitment of a potential subject for a specific clinical trial, unless defined differently in the protocol.

Paragraph 2.36 Standard Operating Procedures (SOPs) are a set of step-by-step instructions compiled by an organization to help workers carry out routine operations. SOPs aim to achieve efficiency, quality output and uniformity of performance, while reducing miscommunication and failure to comply with industry regulations.

Paragraph 2.37 'Sponsor' means an individual, company, institution or organization which takes responsibility for the initiation, for the management and for setting up the financing of the clinical trial.

Paragraph 2.38 'Subject' means an individual who participates in a clinical trial, either as recipient of an investigational product or as a control. A subject may be either a healthy human or a patient.

Paragraph 2.39 'Substantial amendment' means any change to any aspect of the clinical trial which is made after notification of a decision referred to in Section IV (Amendments in clinical trials) and which is likely to have a substantial impact on the safety or rights of the subjects or on the reliability and robustness of the data generated in the clinical trial.

Paragraph 2.40 'Suspension of a clinical trial' means interruption of the conduct of a clinical trial by the UAE.

Paragraph 2.41 UAE Regulations is the legislation framework followed during marketing authorization process in the UAE.

Paragraph 2.42 'Vulnerable Subjects' are individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples are members of a group with a hierarchical structure, such as 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. Other vulnerable subjects include patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors, and those incapable of giving consent.

Subsection I-2. Clinical trials background

Article 3.
Paragraph 3.1 Clinical testing on humans shall be carried out subject to the fundamental principles of protection of human rights and dignity in each medico-biological study in accordance with the Declaration of Helsinki.
Paragraph 3.2 All clinical trials of medicinal products on humans, including trials of bioavailability and bioequivalence, shall be planned, carried out and reported in compliance with the rules of Good Clinical Practice, the requirements of this Guidelines, Joint Commission International (JCI) requirements and ISO 14155 for clinical investigation of medical devices for human subjects-Good Clinical Practice.
Paragraph 3.3 All considerations which are made in Federal Law No. (4) of 2016 (in respect of medical liability) should be taken into account during review and approval of any activities under this Guidelines.
Paragraph 3.4 The Declaration of Helsinki and the GCP guidelines are appended in Appendix 07 and 08 respectively.

Article 4.
Paragraph 4.1 The rights, safety and health of the subjects in a clinical trial shall be placed above the interests of science and the public.
Paragraph 4.2 Any available preclinical and/or clinical data about the medicinal product tested must be adequate to justify the clinical trial being carried out.

Article 5.
Paragraph 5.1 A clinical trial must be scientifically justified and described in a clear and detailed way in the testing protocol.
Paragraph 5.2 When developing the documentation and when carrying out the clinical trial for a medicinal product, the sponsor and the investigator shall take into account all available guidelines published by the US Food and Drug Administration, the European Medicines Agency, World Health Organization and the scientific committees attached to them.

Article 6.
Paragraph 6.1 Clinical testing of medicinal products on humans shall be carried out in conformity to the required procedures for assuring the quality of every aspect of clinical testing.
Paragraph 6.2 The entire information about clinical testing shall be recorded, monitored, processed and stored in a way that shall ensure its accurate reporting, interpretation and validation, the personal data of subjects being protected.

Subsection I-3 Suitability of individuals and sites involved in conducting the clinical trial

Article 7.
Paragraph 7.1 All persons conducting a clinical trial must have relevant professional qualification, training and experience, in order to undertake their delegated activities in compliance with Good Clinical Practice.

Paragraph 7.2 The investigator should be thoroughly familiar with the appropriate use of the investigational product(s), as described in the protocol, in the current Investigator's Brochure, in the product information, and in other information sources provided by the sponsor.
Paragraph 7.3 The Investigator should have sufficient time to conduct and complete the trial properly within the agreed time period.
Paragraph 7.4 The Investigator, for the foreseen duration of the trial, should have adequate staff and facilities available to conduct the trial properly and safely.
Paragraph 7.5 The clinical testing of a medicinal product shall take place under the supervision of a physician or a doctor of dental medicine with a recognized medical specialization in the respective area, who shall be aware of the available preclinical and/or clinical data about the product and the study risks and procedures.
Paragraph 7.6 A GCP certification, provided by an approved GCP training organization for investigator completed not later than three years with incorporated exam and final score more than 80%.
Paragraph 7.7 A physician or a doctor of dental medicine with suitable qualifications and UAE license from Ministry of Health and Prevention (MOHP), Dubai Health Authority (DHA), Health Authority Abu Dhabi (HAAD) shall be responsible for the medical or dental care provided to test subjects during the clinical trial, and for making medical or dental decisions.

Article 8.
Paragraph 8.1 Clinical study/ trial may be carried out in Out/in-patient care establishments/centers that have obtained an activities license under the terms and conditions of the relevant UAE accrediting authorities, both governmental and private.
Paragraph 8.2 In addition to the requirements under Paragraph 8.1, the study site should have adequate resources, staffing, and facilities to conduct the proposed clinical study/ trial
Paragraph 8.3 The Institution in which a medicinal product is to be tested shall give consent for the participation of the investigator and for the conducting of the trial.

Article 9.
Paragraph 9.1 Clinical study/ trial on humans shall be carried out after obtaining regulatory and ethical approval sfor:
9.1.1. medicinal products not authorized in the United Arab Emirates;
9.1.2. medicinal products that have been authorized in the UAE when tested for an unauthorized indication, for a pharmaceutical form other than the authorized one, in a group of patients who have not been studied so far or for obtaining additional information.
Paragraph 9.2 Medicinal products authorized in the UAE, within the meaning of Paragraph 9.1, item 9.1.2, shall be those that have obtained marketing authorization in compliance with the applicable UAE MOHP Regulations.

Article 10.
Paragraph 10.1 Clinical study/ trial on humans shall be carried out with medicinal products that have been manufactured, maintained and stored in accordance with the rules of Good Manufacturing Practice (GMP) for medicinal products under development and research.

Paragraph 10.2 An investigational product that has been subjected to pharmacological and toxicological studies in accordance with the requirements of Good Laboratory Practice (GLP) may be proposed for clinical study/ trial.
Paragraph 10.3 Adequate chemical and pharmaceutical information should be provided to ensure the proper identity, purity, quality & strength of the investigational product, the amount of information needed may vary with the Phase of clinical trials, proposed duration of trials, dosage forms and the amount of information otherwise available.

Article 11. A clinical trial may commence and shall be carried out where:

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

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

Article 13.
Paragraph 13.1 The sponsor shall be liable in case of health deterioration or of causing death during or on the occasion of clinical testing, where the trial is carried out in accordance with the requirements and procedures based on the protocol approved by the Ethics Committee.
Paragraph 13.2 The investigator shall be liable in case of health deterioration or of causing death during or on the occasion of clinical testing when the requirements and procedures based on the protocol approved by the Ethics Committee have not been observed.

Article 14.
Paragraph 14.1 The sponsor of a clinical trial shall be a person established on the territory of the UAE or his licensed legally authorized representative.
Paragraph 14.2 The sponsor and the investigator/institution may be the same person.
Paragraph 14.3 The Contract Research Organization involved in the clinical trial shall be registered and with valid license on the territory on the UAE.

Article 15. The sponsor shall ensure the tested medicinal product(s) and all articles required for its administration are free of charge for any case of interventional design.

Subsection I-4 Protection of subjects and informed consent

Article 16.
Paragraph 16.1 Clinical testing of medicinal products shall only be permitted on an individual who is:

16.1.1. informed, in a preliminary conference with a physician, i.e., a member of the research team, of the purposes, risks and inconveniencies of testing, and of the terms under which it is to be carried out;
16.1.2. informed of his right to withdraw from testing at any time, without any penalty for him and is being informed about no loss of treatment as a regular patient even after the withdrawal.
16.1.3. has personally given consent in writing to take part, having been made aware of the nature, significance, effects and possible risks of the clinical testing .
16.1.4. has been given adequate time and
16.1.5. a copy of the document (or the record) has been provided to the subject.

Paragraph 16.2 Where the individual is illiterate (that is cannot read or write), informed consent for the participation in a clinical trial shall be given orally in the presence of legally acceptable representative who shall certify in writing that the individual has personally given informed consent for taking part in the clinical trial.

Paragraph 16.3 A fully capacitated individual, understanding the nature, implications, significance and possible risks of the clinical trial, may only give informed consent under Paragraph 16.1, item 16.1.3 and Paragraph 16.2. The informed consent for participation in a clinical trial may be withdrawn at any time.

Paragraph 16.4

If a subject is unable to read or if a legally acceptable representative is unable to read, an impartial witness should be present during the entire informed consent discussion. After the written informed consent form and any other written information to be provided to subjects, is read and explained to the subject or the subject's legally acceptable representative, and after the subject or the subject's legally acceptable representative has orally consented to the subject's participation in the trial and, if capable of doing so, has signed and personally dated the informed consent form, the impartial witness should sign and personally date the consent form. By signing the consent form, the impartial witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject or the subject's legally acceptable representative, and that informed consent was freely given by the subject or the subject's legally acceptable representative.

Paragraph 16.5 Incapacitated adults shall be provided with information about the trial, the possible risks and benefits, which shall correspond to their ability of understanding.

Paragraph 16.6 The declared wish of an incapacitated adult to refuse taking part or to withdraw at any time from the clinical trial must be respected by the physician.

Article 17.

Paragraph 17.1 Clinical trial on a minor shall be carried out after obtaining written informed consent from both parents or from the legal guardians of the individual, subject to Article 16, Paragraphs 16.1 and 16.3. They should be involved in the process if they are able to "assent" by having a study explained to them and/or by reading a simple form about the study, and then giving their verbal choice about whether they want to participate or not.

Paragraph 17.2 The consent of the parents and legal guardians must represent the presumed will of the minor and may be withdrawn at any time without any penalty for him.

Paragraph 17.3 The declared wish of the minors to refuse taking part or to withdraw at any time from the clinical trial must be taken into account by the investigator.

Paragraph 17.4 Clinical trials on a minor shall be carried out after obtaining written informed consent from the individual and from both parents, or from the legally acceptable representative, subject to Article 16, Paragraphs 16.1 and 16.3. Where one of the parents is unknown, deceased or deprived of parental rights or, in case of divorce no such rights have been given to him/her, the written informed consent shall be given by the minor and by the parent exercising parental rights.
Paragraph 17.5 The consent of the minor, of the parents or of the legally acceptable representative may be withdrawn at any time without any penalty for the minor.
Paragraph 17.6 The declare wish of the minor to withdraw at any time from the clinical trial must be taken into account by the investigator.
Paragraph 17.7 The minor shall be given information about the trial and about the possible risks and benefits in a way that will ensure understanding by a physician who has experience with minors.

Article 18. Information given to the subject or, where the subject is not able to give informed consent, his or her legally acceptable representative for the purposes of obtaining his or her informed consent shall:
Paragraph 18.1 enable the subject or his or her legally acceptable representative to understand:
18.1.1. the nature, objectives, benefits, implications, risks and inconveniences of the clinical trial;
18.1.2. the subject's rights and measures regarding his or her protection, in particular his or her right to refuse to participate and the right to withdraw from the clinical trial at any time without any resulting penalty and without having to provide any justification;
18.1.3. the conditions under which the clinical trial is to be conducted, including the expected duration of the subject's participation in the clinical trial; and (iv) the possible treatment alternatives, including the follow-up measures if the participation of the subject in the clinical trial is discontinued;
Paragraph 18.2 be kept comprehensive, concise, clear, relevant, and understandable to a layperson and should be in or her vernacular language.
Paragraph 18.3. be provided in a prior interview with a member of the investigating team who is a physician and appropriately qualified.

Article 19.
Paragraph 19.1 If immediate use of the investigational product is, in the investigator's opinion, required to preserve the life of the subject.
19.1.1 the decision shall be made and documented by at least two physicians not involved in the research team.
19.1.2 and if the time is not sufficient to obtain the independent determination required in item 19.1.1 of this article in advance of using the investigational product, the determinations of the clinical investigator shall be made and, within 5 working days after the use of the product, be reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.
Paragraph 19.2 The documentation required in Paragraph 19.1, 19.1.1 or 19.1.2 of this article shall be submitted to the EC within 5 working days after the use of the investigational product.

Article 20.
Paragraph 20.1 During the trial, the subject shall receive at his request additional information from a person independent from the sponsor.
Paragraph 20.2 Written information provided to subjects of clinical trials of a medicinal product shall contain contact details of the independent person (member of Ethics Committee, but not part of the study team) for additional information.

Subsection I-5 Clinical trials with vulnerable groups of patients

Article 21. Clinical trials on minors may be undertaken provided that:
Paragraph 21.1 the protocol has been approved by the relevant Ethics Committee after discussion of the clinical, moral and psycho-social aspects of childhood, in which at least two pediatricians have taken part;
Paragraph 21.2 a direct benefit is expected from the clinical trial for the group of patients that will be included in it;
Paragraph 21.3 the clinical trial is directly related to the clinical condition of the suffering minor;
Paragraph 21.4 the medicinal product tested is intended to be used for diagnosis, treatment or prevention of diseases that are specific to minors;
Paragraph 21.5 the trial is intended to be carried out on minors;
Paragraph 21.6 the purpose of the trial is to verify data obtained from clinical trials on individuals that are able to give informed consent or data obtained through other research methods;
Paragraph 21.7 the results obtained from clinical trials on adults and their interpretation may not also be considered valid for minors and young persons;
Paragraph 21.8 the trial is planned in a way to minimize pain, inconvenience, fear and other foreseeable risks associated with the disease, and the level of risk and physical pain have been predefined and are constantly controlled during testing;
Paragraph 21.9 no financial or other incentives are provided, other than compensation.

Article 22.
Paragraph 22.1 Clinical trials on individuals under Article 16, Paragraphs 16.4 and 16.5, who are not able to give informed consent, shall be carried out in accordance with the requirements of Article 11.
Paragraph 22.2 Other than the requirements under Paragraph 22.1, the participation of adults who are not able to give informed consent in clinical trials shall be allowed, provided that:
22.2.1. the respective Ethics Committee, involving specialists with competence in respect to the disease concerned or to the group of patients, has approved the protocol after discussing the clinical, moral and psycho-social aspects of relevance to the particular disease and to the group of patients;
22.2.2. it may be expected that taking the medicinal product tested would bring benefits exceeding the risks or that risks have been fully eliminated;
22.2.3. the purpose of the trial is to check data obtained through clinical trials on humans who are able to give informed consent or of data obtained through other research methods;
22.2.4. the trial is directly connected to a life-threatening or disabling disease of which the adult person concerned who is not able to give informed consent suffers;

22.2.5. the clinical trials have been planned so that pain, inconvenience, fear and other foreseeable risks associated with the disease have been reduced to a minimum and the level of risk and the degree of physical pain have been set in advance and are constantly monitored during the trial;
22.2.6. no financial and other incentives are provided, except for compensation.

Article 23. No clinical trials of a medicinal product may be conducted on pregnant and breast-feeding women, unless the medicinal product concerned is required for their treatment and may not be tested on any other group of patients.

Section II Ethics and Research Committees

Article 24. Clinical trial scope, purpose, type and design determine the appropriate body or bodies which shall be involved in the assessment of the application. This includes the involvement of Ethics and Regulatory Committees within the timelines for the authorization of that clinical trial as set out in this Guidelines. When determining the appropriate body or bodies, the UAE should ensure that the necessary expertise is available to assess the application. In accordance with international guidelines, the assessment should be done jointly by a quorum (as stipulated in the Committees Standard Operating Procedures (SOPs)). Members shall collectively have the necessary qualifications, experience and represent a quorum of membership list. The Committees should be independent of the sponsor, the clinical trial site, and the investigators involved, as well as free from any other undue influence.

Subsection II-1 Higher Committee of Ethics (HCE)

Article 25. The composition of the Higher Committee of Ethics (HCE) shall be stipulated by decision of the Council of Ministers at the proposal of the Minister of Health.

Article 26. Scope of activities and responsibilities
Paragraph 26.1 The Higher Committee of Ethics shall set-up and oversee the Regulatory Committee at Ministry of Health and Prevention (RCMOHP).
Paragraph 26.2 The Higher Committee of Ethics shall establish a clear process for accreditation of the Central Ethics Committees, working under Subsection II-3 of this Guidelines.
Paragraph 26.3 The Higher Committee of Ethics shall perform an independent audit to both Central Ethics Committees and Investigator's sites.
Paragraph 26.4 The Higher Committee of Ethics shall provide an opinion on deontological and ethical issues in the area of clinical trials when it has been approached by the Central Ethics Committees, by the Ministry of Health and Prevention or by the investigator.
Paragraph 26.5 The Higher Committee of Ethics shall keep and maintain a register of the Central Ethics Committees.
Paragraph 26.6 The register of the treatment establishments with which Central Ethics Committees have been set up shall be posted on the Ministry of Health and Prevention website.

Subsection II-2 Regulatory Committee at the Ministry of Health and Prevention (RCMOHP)

Article 27. Composition
Paragraph 27.1 The Regulatory Committee at the Ministry of Health and Prevention (RCMOHP) shall be set up by the Minister of Health and its composition shall be specified by an order of the Minister.
Paragraph 27.2 The RCMOHP shall be headed and represented by a Chairperson.
Paragraph 27.3 The Regulatory Committee at the Ministry of Health and Prevention (RCMOHP), shall be composed of 5 to 7 members, having the qualifications, experience and training required to examine and evaluate the proposed clinical trial.

Article 28. Scope of activities and responsibilities

Paragraph 28.1 The Regulatory Committee at the Ministry of Health and Prevention (RCMOHP) shall be a specialized body of the Ministry of Health and Prevention that supervises the quality, safety and efficacy during conduct of clinical trials.

Paragraph 28.2 The Regulatory Committee at the Ministry of Health and Prevention (RCMOHP) shall:

28.2.1. issue permission for conducting clinical trials with interventional design on medicinal products and/or devices;

28.2.2. exercise control on the conduction of clinical trials through annual and safety reporting process;

28.2.3. be notified of all clinical trials with non-interventional design conducted in the UAE;

28.2.4. keep record of all ongoing and completed clinical trials on the territory of the UAE;

28.2.5. carry out the functions of a consultative body on issues of quality, efficacy and safety of medicinal products;

28.2.6. carry out consultancy, scientific, information and publishing activities in the drugs sector;

28.2.7. take part in activities in the area of medicinal products development and patients' safety of international bodies and organizations, as well as the enforcement of international treaties to which the UAE is a party;

28.2.8. participate in the international harmonization and standardization of the technical measures related to conducting of clinical trials;

28.2.9. create and maintain a national internet portal for clinical trials;

28.2.10 to regulate and authorize through license process various contract research organization in the country to conduct clinical trials on behalf of the sponsor as per the regulation set forth by the Ministry of Health and prevention;

28.2.11 to conduct clinical investigator/site inspection to determine if the clinical investigators/site are conducting clinical studies in compliance with applicable statutory and regulatory requirements;

28.1.12 periodically updating and initiating the training programs to develop awareness.

Article 29. Functions and operations

Paragraph 29.1 The structure, functions and organization of the work of the RCMOHP shall be specified in Rules adopted by the Minister of Health.

Paragraph 29.2 The sessions of the RCMOHP shall be conducted in closed sessions. Where necessary, the chairperson of the Committee may invite the sponsor or investigator to take part therein.

Subsection II-3 Central Ethics Committee (CEC)

Article 30. Composition

Paragraph 30.1 The Central Ethics Committees, shall be set up of minimum 5 members, having the qualifications and experience required to examine and evaluate the scientific, medical and ethical aspects of the proposed clinical trial.

Paragraph 30.2 A Central Ethics Committee shall be set up within:

30.2.1. Abu Dhabi Department of Health
30.2.2. Dubai Health Authority (DHA)
30.2.3. Dubai Healthcare City Authority (DHCA)
30.2.4. Ministry of Health and Prevention (MOHP)
30.2.5. Governmental Universities
Paragraph 30.3 The Central Ethics Committees composition shall be specified by an order of the Institution Head.
Paragraph 30.4 The committee shall comprise:
30.4.1. at least one member whose primary area of interest is in a nonscientific area and
30.4.2. at least one member who is independent of the institution/trial site
30.4.3. representative of both genders and being financially and administratively independent of the treatment establishment in which the clinical trial takes place.
Paragraph 30.5 The Central Ethics Committees may use the services of external experts for the needs of their work.
Paragraph 30.6 While conducting clinical trials on minors, the Central Ethics Committees shall ensure involvement of pediatrician as regular member or external experts.
Paragraph 30.7 The term of office as well as the rules of renewing the members of the Central Ethics Committees shall be clearly determined in writing.

Article 31. Scope of activities and responsibilities
Paragraph 31.1 The Central Ethics Committee shall give an opinion for all clinical trials with interventional and non-interventional design.
Paragraph 31.2 Each Central Ethics Committee shall establish a clear process for accreditation of the Local Ethics Committees, working under Subsection II-4 of this Guidelines and being under their jurisdiction.

Article 32. Functions and operations
Paragraph 32.1 The Central Ethics Committees shall produce written standard operational procedures in compliance with the rules of Good Clinical Practice within a month of being set up, thereby fixing the terms and conditions of their work. These standard operational procedures shall be approved by the Higher Committee of Ethics as part of an accreditation process.
Paragraph 32.2 The sessions of the Central Ethics Committees shall be conducted in closed sessions. Where necessary, the chairperson of the Central Ethics Committee may invite the sponsor or investigator to take part therein.
Paragraph 32.3 Only those members of the Central Ethics Committees who do not participate directly in a specific trial and are administratively and financially independent of the sponsor and investigator may vote and take part in deliberations.
Paragraph 32.4 In order to certify the circumstances under Paragraph 32.3, members of the Central Ethics Committees shall sign a statement of conflict of interests.

Subsection II-4 Local Ethics Committee (LEC)

Article 33. Composition

Paragraph 33.1 The Local Ethics Committees, shall be set up of minimum 5 members, having the qualifications and experience required to examine and evaluate the scientific, medical and ethical aspects of the proposed clinical trial.

Paragraph 33.2 A Local Ethics Committee shall be set up within one single clinical establishment and its composition shall be specified by an order of the Institution Head.

Paragraph 33.3 The committee shall comprise:

33.3.1. at least one member whose primary area of interest is in a nonscientific area and

33.3.2. at least one member who is independent of the institution/trial site

33.3.3. representing both genders and being financially and administratively independent of the treatment establishment in which the clinical trial takes place.

Paragraph 33.4 The Local Ethics Committees may use the services of external experts for the needs of their work.

Paragraph 33.5 While conducting clinical trials on minors, the Local Ethics Committees shall ensure involvement of pediatrician as regular member or external experts.

Paragraph 33.6 The term of office as well as the rules of renewing the members of the Local Ethics Committees shall be clearly determined in writing.

Article 34. Scope of activities and responsibilities

The Local Ethics Committee shall give an opinion for all clinical trials with interventional and non-interventional design when this is requested by the relevant Central Ethics Committee and when it is involving only one investigational site.

Article 35. Functions and operations

Paragraph 35.1 The Local Ethics Committees shall produce written standard operational procedures in compliance with the rules of Good Clinical Practice within a month of being set up, thereby fixing the terms and conditions of their work. These standard operational procedures shall be approved by the respective Central Ethics Committee as part of an accreditation process.

Paragraph 35.2 The sessions of the Local Ethics Committees shall be conducted in closed sessions. Where necessary, the chairperson of the Local Ethics Committee may invite the sponsor or investigator to take part therein.

Paragraph 35.3 Only those members of the Local Ethics Committees who do not participate directly in a specific trial and are administratively and financially independent of the sponsor and investigator may vote and take part in deliberations.

Paragraph 35.4 In order to certify the circumstances under Paragraph 35.3, members of the Local Ethics Committees shall sign a statement of conflict of interests.

Section III Authorization to conduct clinical trials

Sub-section III-1. Submission process

Article 36. Clinical trials with interventional design, may begin when the following conditions are fulfilled:
1. the Ethics Committee (REC or LEC) has given a positive opinion,
2. the Regulatory Committee at the Ministry of Health and Prevention (RCMOHP) has issued a written approval and
3. Drug Control Department at the Ministry of Health and Prevention (DCD) has issued an import license.

Article 37. For clinical trials with non-interventional design, may begin when the following conditions are fulfilled:
1. the Ethics Committee (REC or LEC) has given a positive opinion, and
2. the Regulatory Committee at the Ministry of Health and Prevention (RCMOHP) has been notified in writing prior to the first subject being enrolled.

Article 38. Procedures at the Ethics Committee (REC or LEC) and the RCMOHP may take place simultaneously, at the sponsor's choice.

Article 39. The granted opinion of the REC shall be valid for all centers within the assigned territory to the committee and only those included in the application. A gained decision shall be considered as a Single Opinion EC.

Article 40. A clinical trial shall be conducted in compliance with the protocol that has obtained a positive opinion from the Ethics Committee (REC or LEC), and subject to the terms specified in the documentation filed.

Article 41. The EC and RCMOHP shall collect a fee for the submission of applications requesting an opinion. The fee shall be in the amount determined in the tariff.

Subsection III-2. Ethics Committee Application for a clinical trial

Article 42.
Paragraph 42.1. In order to obtain an opinion, the investigator shall submit to the Ethics Committee (Central or Local):
42.1.1. administrative documentation;
42.1.2. information about subjects;
42.1.3. documentation concerning the trial protocol;
42.1.4. documentation about the medicinal product tested;
42.1.5. documentation about the technical requirements and the staff;
42.1.6. data about funding and the administrative organization of trials.

Paragraph 42.2. The content, the format and the requirements to the documentation under Paragraph 42.1 are specified in the Appendix 02 to this Guidelines.

Article 43.

Paragraph 43.1. The Ethics Committee (Central or Local) shall provide an opinion, taking the following into account:

43.1.1. the significance of the clinical trial;

43.1.2. the positive evaluation of the ratio between the expected benefits and the risks in accordance with Article 11, item 1, and the extent to which the conclusions are justified;

43.1.3. the clinical trial protocol;

43.1.4. the extent to which the investigator and the research team are suitable to conduct the clinical trial;

43.1.5. the Investigator's brochure;

43.1.6. the consistency and completeness of written information to be provided and the procedure for obtaining informed consent, as well as the extent to which the trial on humans incapable of giving informed consent is justified in the cases under Articles 21 and 22;

43.1.7. the foreseen compensation or restitution in case of damages or death that may result from the clinical trial;

43.1.8. the insurance covering investigator and sponsor liability;

43.1.9. where necessary, the terms and conditions of remunerating or compensating investigators and subjects in the clinical trial and the elements of the contract between the sponsor and the institution;

43.1.10. the terms and conditions of recruiting subjects.

Paragraph 43.2 The Ethics Committee (Central or Local) shall:

43.2.1. give a positive opinion;

43.2.2. provide justification for refusal, or

43.2.3. request some modification as a condition for obtaining a positive opinion.

Article 44.

Paragraph 44.1 When evaluating the documentation, the Ethics Committee (Central or Local) may require, on a one-off basis, the applicant to provide additional documentation. The periods under Section III, Subsection 4 shall be suspended until the requested documentation has been submitted.

Paragraph 44.2 The procedure for examination of the study shall terminate where, within 60 calendar days of receiving a request for additional information, the sponsor fails to submit the documentation requested by the committee.

Article 45.

Paragraph 45.1 Where the opinion of the Central Ethics Committee is negative, the investigator may, within a period of 90 calendar days of the date of notification, appeal its decision to the Higher Committee of Ethics.

Paragraph 45.2 The opinion of the Higher Committee of Ethics shall be final and binding.

Article 46.

Paragraph 46.1 Where the opinion of the Local Ethics Committee is negative, the Investigator may, within a period of 60 calendar days of the date of notification, appeal its decision before the respective Central Ethics Committee.
Paragraph 46.2 The opinion of the respective Central Ethics Committee shall be final and binding.

Sub-section III-3. Clinical Trial Application to the Regulatory Committee at the Ministry of Health and Prevention

Article 47.
Paragraph 47.1 The sponsor shall submit to the Regulatory Committee at the Ministry of Health and Prevention (RCMOHP) a model-based application for the conducting of a clinical trial.
Paragraph 47.2 Where the applicant for a clinical trial is not a sponsor, the application shall be accompanied by documentation certifying that the person has been legally authorized by the sponsor.
Paragraph 47.3 Where the sponsor is not registered in the territory of the UAE, the application shall be accompanied by a document specifying the data about his authorized representative on the territory of the UAE.
Paragraph 47.4 The following shall be attached to the application:
1. administrative documents;
2. information about subjects;
3. documentation about the trial protocol;
4. documentation about a tested medicinal product(s);
5. documentation about the technical requirements and about the staff;
6. documentation about the funding and the administrative organization of the trial.

Paragraph 47.5 The content, the format and the requirements to the documentation under Paragraph 47.4 are specified in the Appendix 02 to this Guidelines.

Article 48. The sponsor shall declare that the documentation filed with regulatory committee at the Ministry of Health and Prevention and with the Ethics Committee (REC or LEC) contains the same information.

Article 49. The Ministry of Health and Prevention Executive Director shall refuse to issue an authorization for conducting a clinical trial of medicinal products for gene therapy where a risk exists that the genome of the reproductive cells of the trial subject could be modified.

Sub-section III-4. Issuing of an Import License by Drug Control Department at the Ministry of Health and Prevention

Article 50.
Paragraph 50.1 Only the sponsor or an authorized representative can import into the territory of the UAE from third countries all types of medicinal products and investigational products intended for clinical trials.

Paragraph 50.2 In order to obtain import authorization (license), the person under Paragraph 50.1 shall file with the Drug Control Department at the MOHP:
50.2.1 an application based on a model approved by the MOHP.
50.2.2 a list of the medicinal products and forms to be imported.
50.2.3 a copy of the manufacturing authorization issued by the regulatory body of the exporting state and a certificate verifying the compliance of the conditions for the manufacturing, control and storage with standards that are at least equivalent to the standards of Good Manufacturing Practice.
50.2.4 certificate of analysis of the batches intended to be used in the clinical trial.
50.2.5 copy of the positive opinion of the EC (REC or LEC) and RCMOHP (if applicable).
50.2.6 a document evidencing the payment of a fee specified in the Tariff.
50.2.7 a justification of calculation of the quantity of the investigational product required as per the study protocol.

Sub-section III-5. Issuing of an Export License for Bio-samples by Drug Control Department at the Ministry of Health and Prevention

Article 51.
Paragraph 51.1 Only the sponsor or an authorized representative can export from the territory of the UAE to third countries all types of biological samples from clinical trials.
Paragraph 51.2 In order to obtain export authorization (license), the person under Paragraph 51.1 shall file with the Drug Control Department at the MOHP:
51.2.1 an application based on a model approved by the MOHP.
51.2.2 a list of the samples and types to be exported.
51.2.3 copy of the positive opinion of the EC (REC or LEC) and RCMOHP (if applicable).
51.2.4 a document evidencing the payment of a fee specified in the Tariff.

Sub-section III-6. Timeliness for review

Article 52. Interventional Clinical Trial reviewed by Central EC
Within a period of 90 calendar days of filing an application, the REC concerned shall rule, issuing an opinion, which it shall send to the applicant and to the RCMOHP.

Article 53. Non-interventional Clinical Trial reviewed by Central EC
Within a period of 45 calendar days of filing an application, the REC concerned shall rule, issuing an opinion, which it shall send to the applicant.

Article 54. Clinical Trial Application review by Regulatory Committee at the Ministry of Health and Prevention (RCMOHP)
Paragraph 54.1 Within 90 calendar days of the date of submission of the application for a clinical trial of medicinal products and/or device with interventional design, the Ministry of Health and Prevention shall notify the applicant in writing that the trial:
54.1.1. may be conducted on the territory of the UAE,

54.1.2. require some modification as a condition for obtaining a positive opinion, or
54.1.3. the clinical trial to be conducted has been refused, stating the reasons for this.
Paragraph 54.2 When evaluating the documentation, the Ministry of Health and Prevention may obtain, on a one-off basis, additional documentation from the applicant within 15 calendar from the submission.
Paragraph 54.3 The periods under Paragraph 54.1 shall be suspended until the requested documentation has been submitted.
Paragraph 54.4 If the applicant fails to submit an application under item 54.1.2 within the specified period of 60 calendar days, the procedure shall terminate and the clinical trial shall not take place.

Article 55. Interventional Clinical Trial reviewed by Local EC
Within a period of 60 calendar days of filing an application, the LEC concerned shall rule, issuing an opinion, which it shall send to the applicant and to the RCMOHP.

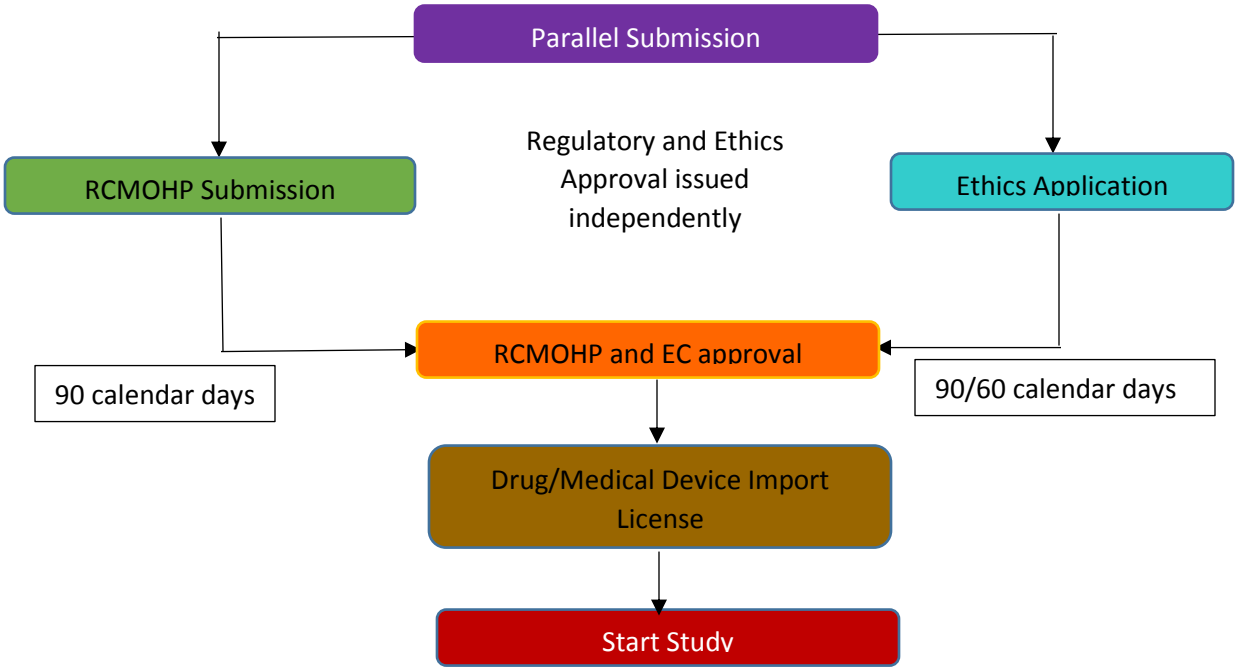
Article 56. Non-interventional Clinical Trial reviewed by Local EC
Within a period of 30 calendar days of filing an application, the LEC concerned shall rule, issuing an opinion, which it shall send to the applicant.

Article 57. Import License by DCD at MOHP
Within a period of 7 calendar days of filing an application, the DCD shall issuing an import license, which it shall send to the applicant.

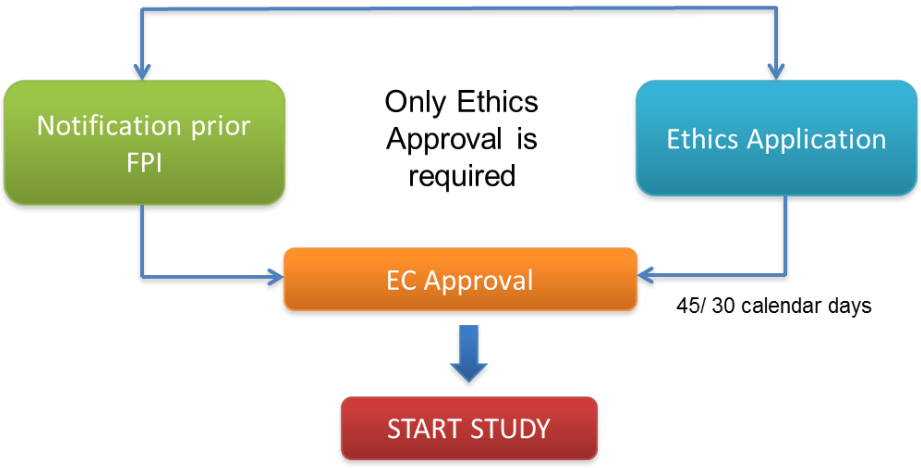
Article 58. Export License by DCD at MOHP
Within a period of 7 calendar days of filing an application, the DCD shall issuing an export license, which it shall send to the applicant.

Appendix 01 Flow chart of Authorization process

1. Regulatory Process for Interventional Clinical Trial approved by RCMOHP and CEC/LEC



2. Regulatory Process for Non-Interventional Clinical Trial, approved by Central or Local EC



Appendix 02 The content, format and requirements of submitted documents

1. The content, format and requirements to the documentation submitted to Ethics Committee (Central or Local)

Article 1. Administrative documentation

Paragraph 1.1 Ethics Committee Application (ECA): an electronic pre-defined form on an official portal contains mandatory and optional fields and allowing embedding additional files.

Paragraph1.2 Cover Letter: The applicant shall 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.

Paragraph 1.3 List of Regulatory Authorities and Ethics Committees apart from UAE ones, to which the application has been submitted and information about their decisions.

Paragraph 1.4 List of all study centers and investigators planned to participate in the UAE.

Paragraph 1.5 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.

Paragraph 1.6 Statement, according to Article 48

Paragraph 1.7 Evidence of registration of the clinical trial on the ClinicalTrials.gov website.

Paragraph 1.8 Certified copy of the CRO license granted by the RCMOHP.

Article 2. Information about subjects

Paragraph 2.1 Information for the patient/ subject and Informed Consent Form (in English; in Arabic and any other language that will be used).

Paragraph 2.2 Description of the procedures for obtaining informed consent from a legal representative, where applicable.

Paragraph 2.3 Ethical grounds for enrolling participants incapable to give informed consent, in accordance with Section I, Subsection 5, Articles 21 and 22 of the Guidelines, where applicable.

Paragraph 2.4 Any other information that will be used for subject enrollment 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:

- 2.4.1 Patient diary.
- 2.4.2 Patient card.
- 2.4.3 Adverse Events diary.
- 2.4.4 Instructions for medication application or for handling medical device;
- 2.4.5 Scales and Questionnaires (including Quality of Life questionnaires);
- 2.4.6 Calendar(s).
- 2.4.7 Patient advertisement.
- 2.4.8 Additional trial information given in writing & / or multimedia technology to the subject.
- 2.4.9 Copies or pictures of any materials intended to be given to the patient.

Article 3. Documentation concerning the trial protocol;

Paragraph 3.1 Study Protocol and all current amendments, developed in accordance with ICH-GCP requirements and Article 3 and 5 of the Guidelines and contains as minimum:

3.1.1 Clear justification of the known and potential risks and benefits, if any, to human subjects.

3.1.2 Selection of Subjects – inclusion and exclusion criteria.

3.1.3 Description of and justification for the selected subject population, especially in case of vulnerable subject group.

3.1.4 Withdrawal of Subjects.

3.1.5 Description of informed consent process in case of enrollment of subject temporary or permanent enable to be consented.

3.1.6 The trial procedures to be followed, including all invasive procedures and all criteria for assessment and decisions.

3.1.7 Planned monitoring and other control.

3.1.8 Statistical, safety and ethical considerations.

Paragraph 3.2 Study Protocol summary in English.

Paragraph 3.3 Peer review of the scientific value of the trial, where available.

Paragraph 3.4 Protocol pages signed by the sponsor and by the Investigator from each study site participating in the trial.

Paragraph 3.5 Case Report form.

Article 4. Documentation about the medicinal product tested

Paragraph 4.1 Investigator's brochure (issued not later than one year before application submission).

Paragraph 4.2 Summary of Product Characteristics, when applicable.

Paragraph 4.3 Outline/ summary of all currently active clinical trials with the investigated product.

Article 5. Documentation about the technical requirements and the staff

Paragraph 5.1 Description of the equipment and/ or the technical requirements necessary to perform the Protocol procedures.

Paragraph 5.2 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.

Paragraph 5.3 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 Section I, Article 7 of the Guidelines.

Paragraph 5.4 GCP training certificates of all study staff members.

Paragraph 5.5 Financial Disclosure of Principal Investigator.

Paragraph 5.6 Confidentiality agreement of Principal Investigator.

Paragraph 5.5 Documents, confirming the circumstances in accordance with Section I, Article 8, of the Guidelines – Accreditation of the Institution.

Article 6. Data about funding and the administrative organization of trials

Paragraph 6.1 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.

Paragraph 6.2 Provision for compensation or a sample agreement between Sponsor and study subjects, when such compensation is considered.

Paragraph 6.3 Sample Agreement between Sponsor, Institution and investigator, defining terms and conditions of conducting the clinical trial.

Paragraph 6.4 Written approval according to Section I, Article 8, Paragraph 8.2 of the Guidelines – Statement by the Director of the Institution regarding permission for conducting the study (if applicable).

Paragraph 6.5 Information about a clinical trial finance resource in case the Sponsor is a not-profit organization.

Paragraph 6.6 Pre site assessment report signed by the sponsor or its representative.

Paragraph 6.7 Evidence for payment of the required fee.

2. The content, format and requirements to the documentation submitted to Regulatory Committee at the Ministry of Health and Prevention (RCMOHP)

Article 7.

Paragraph 7.1 For clinical trial with interventional design the sponsor or an authorized representative shall submit to the Ministry of Health and Prevention a specific electronic application and all listed documents in Article 1, 2, 3, 4, 5 and 6 of the Appendix 02 (The content, format and requirements of submitted documents) of the Guidelines.

Paragraph 7.2 In addition the following documents shall be presented:

- 7.2.1 Investigational Product Dossier (IPD).
- 7.2.2 Statement from the manufacturer, in all cases when the investigational product has a market authorization.
- 7.2.3 Copy of the manufacturing authorization for medicinal products that are in the process of research and development, if the investigational product does not have a marketing authorization.
- 7.2.4 Document to certify the conformity of the manufacturing conditions of the active substances of biological origin, control and storage standards to be equivalent to the requirements of the GMP for medicinal products in a process of research and development.
- 7.2.5 Results/ reports from viral safety studies, where applicable.
- 7.2.6 Examples of drug labels in English & Arabic, according to the requirements to the information on the packaging of medicinal products used in clinical trials.

Section IV Amendments in clinical trials

Article 59.

Paragraph 59.1 A change in the way a clinical trial is conducted could be requested by the regulatory committee at the Ministry of Health and Prevention and/or respective Ethics Committee (CEC or LEC) whenever necessary, in order to ensure the safety of subjects, the scientific value of the trial and/or compliance with Good Clinical Practice.

Paragraph 59.2 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 Articles 42 and 47 that affects:

59.2.1. the safety or the physical and mental integrity of the subjects;

59.2.2. the scientific value of the study;

59.2.3. the conduct or the organization of the study;

59.2.4. the quality or the safety of one of the medicinal products tested.

Article 60.

Paragraph 60.1 The sponsor through the PI may introduce changes, other than significant ones under Article 59, Paragraph 59.2, to the clinical trial protocol at any time.

Paragraph 60.2 In the cases under Paragraph 59.1, the sponsor shall keep the documentation related to the changes and shall submit it to the Regulatory Committee at the Ministry of Health and Prevention (RCMOHP) and Investigator will keep documentation to the respective Ethics Committee upon request.

Article 61.

Paragraph 61.1 The sponsor through the PI may apply planned substantial amendments in the trial protocol and in the documentation under Articles 42 and 47, where:

61.1.1. the respective Ethics Committee has given a written positive opinion;

61.1.2. the RCMOHP has issued a written approval for this in respect to interventional clinical trials.

Paragraph 61.2 The provision of Paragraph 58.1 shall not apply to changes in the approved protocol which are required in order to protect the subjects from imminent danger when new information is discovered pertaining to the conduct of the trial, or to the development of the tested medicinal product.

Paragraph 61.3 In the cases under Paragraph 61.2, the investigator shall immediately notify the respective Ethics Committee, while sponsor notify the regulatory committee at the Ministry of Health and Prevention of the available new information, of the measures taken and of the changes introduced in the protocol.

Article 62.

Paragraph 62.1 When planning substantial amendments in the clinical trial and in the documentation under Articles 42 and 47, the sponsor shall file a written application, based on a model, with the Ministry of Health and Prevention and with the respective Ethics Committee.

Paragraph 62.2 The application shall be accompanied by documentation required to justify the changes and certifying that after applying the change, the evaluation of the ratio between the benefits and the risks under Article 11 shall be kept.
Paragraph 62.3 Substantial amendment is considered whenever there is a change in the information pointed in the Appendix 03 (Example list of information changes considered as substantial).
Paragraph 62.4 The requirements to the application and the documentation about the amendments is specified in the Appendix 04 (The requirements to the application and the documentation about the amendments).

Article 63. Within a period of up to 30 calendar days of receiving an application for amendment, the respective Ethics Committee and RCMOHP, if applicable shall notify the applicant of its resolution, issuing:
1. a positive opinion on the requested changes and issuing an approval, or
2. a motivated refusal of changes in the clinical trial.

Article 64
Paragraph 64.1 In the cases under Article 63, item 2, the sponsor may submit a modification of the proposed amendment, in line with the reasons, within 14 calendar days after receiving a rejection.
Paragraph 64.2 Within a period of 14 calendar days of the date of receiving the changed documentation under Paragraph 64.1, the body initially issuing a refusal shall issue a change to the authorization for a clinical trial involving medicinal products, or a refusal.
Paragraph 64.3 A refusal under Paragraph 64.2 shall not be subject to appeal.

Appendix 03 List of information changes considered as substantial

1. Changes related to the study protocol
1.1. Change in the study endpoint/ objective.
1.2. Change in the study design and/or methodology or background scientific information, based on which the study is conducted.
1.3. Changes in the following study subject documents:
1.3.1. Subject/ patient information sheet and Informed Consent Form;
1.3.2. Information related to a legal representative;
1.3.3. Questionnaires, invitation letters, notification letters to the treatment or other physicians.
1.4. Change in the schedule/ methodology of biological sampling related to the study.
1.5. Adding or removing of examination and/or testing.
1.6. Change in the subject aging limits.
1.7. Change in the inclusion and/or exclusion criteria.
1.8. Change in the safety following procedure.
1.9. Change in the prolongation of using the investigational product.
1.10. Change in the route or the dose of investigational product administration.
1.11. Change in the drug comparator.
1.12. Any change related to safety and physical and/or intellectual integrity of subjects or study risk/ benefit rationality.
1.13. Change in the study end schedule.

2. Changes related to the administrative organization of the study:
2.1. Change in the study sponsor and/or his legal representative.
2.2. Change in the approved investigational site.
2.3. New investigator.
2.4. Including a new clinical site.
2.5. Change of investigator in the approved investigational site.
2.6. Change in the insurance or the way of subject compensation.
2.7. Other significant changes in the protocol and/ or other supplementary documents part of initial application.

3. Changes related to quality of the investigational product:
3.1. Change in the investigational product name from sponsor code into international nonproprietary name (INN).
3.2. Change in the materials in the primary package.
3.3. Change in the investigational product manufacture.
3.4. Change in the specification of investigational product, when includes extension of permitted limits and/or tests drop out.
3.5. Change in the specification of additional supplements, when this could interfere the final product.
3.6. Significant change in the manufacturing process.
3.7. Limitation in the IP storage condition.

3.8. Decreasing of expiration period of the investigational product after opening or diluting.
3.9. Change in the procedures for active substance testing, including additional method.
3.10. Change in the procedures for non-pharmacopeia ingredients, including adding a new method.

4. All amendments in non-clinical data for investigational product, which could lead to change of the ratio risk/ benefit.

5. All amendments in clinical data for investigational product, which could lead to change of the ratio risk/ benefit.

Appendix 04 The requirements to the application and the documentation about the amendments

Article 1. Ethics Committee (CEC or LEC)

Paragraph 1.1 In case of planned substantial amendments in a clinical trial, the PI or his authorized representative shall 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.

Paragraph 1.2 The application should be accompanied by the following documents:

1.2.1. Cover Letter.

1.2.2. Summary of the proposed amendment.

1.2.3. List of modified documents with their effective dates and version numbers.

1.2.4. Pages from the amended documents according to Appendix 02 (Initial submission) with previous and new wording.

1.2.5. Comments of any novel aspect of the amendment (if any).

1.2.6. Document for paid fee.

Article 2. Regulatory Committee at the Ministry of Health and Prevention (RCMOHP)

Paragraph 2.1 In case of planned substantial amendments in a clinical trial, the sponsor or his authorized representative shall submit a Clinical Trial Application (CTA) to the Research Committee at the Ministry of Health and Prevention an electronic pre-defined form on an official portal that contains mandatory and optional fields and allowing embedding additional files.

Paragraph 1.2 The application should be accompanied by the documentation as described in the Article 1, Paragraph 1.2 of the Appendix 04 (The requirements to the application and the documentation about the amendments).

Section V Suspension of the clinical trial

Article 65.
Paragraph 65.1 The sponsor or the investigator may undertake urgent measures in order to protect the subjects of the clinical trial against any suddenly appearing risks to their safety and health.
Paragraph 65.2 In the cases under Paragraph 65.1, the sponsor shall immediately notify the Ministry of Health and Prevention and the respective Ethics Committee of the action undertaken and of their causes.

Article 66.
Paragraph 66.1 When the trial is conducted under terms other than those specified upon issuance of the authorization, or information is available that the scientific validity of the study is discredited, or there is a risk to the safety of the subjects, or any serious concerns about the protection of rights and wellbeing of the trial subject, the Ministry of Health and Prevention may provisionally suspend the trial or terminate it.
Paragraph 66.2 The termination may be imposed on a particular center or on all centers, for a multicenter clinical trial on the territory of the UAE.
Paragraph 66.3 In case of termination of the clinical trial in all centers on the territory of the UAE, the Regulatory Committee at the Ministry of Health and Prevention, prior to taking action under Paragraph 66.1, shall notify in writing the sponsor and the investigator.
Paragraph 66.4 Within 7 calendar days of receiving the notification, the sponsor and/or the investigator may give an opinion on the measures taken by the Ministry of Health and Prevention.
Paragraph 66.5 The provision of Paragraph 66.3 shall not apply where there is immediate risk to the health and safety of trial subjects.

Article 67. In the cases under Article 66, Paragraph 66.1, the Ministry of Health and Prevention shall immediately notify the respective Ethics Committees of the measures taken and the reasons for this.

Section VI Safety Follow-up and reporting as part of clinical trial

Article 68.
Paragraph 68.1 The investigator shall immediately notify the sponsors in writing, of any serious adverse event that has occurred in the course of the clinical trial with a subject in the center of which he is in charge as per the protocol. The required information is provided in Appendix 05.
Paragraph 68.2 After the notification under Paragraph 68.1, a detailed report in writing shall be submitted to the sponsor.
Paragraph 68.3 When a notification under Paragraph 68.1 or a report under Paragraph 68.2 is made, the trial subject shall be identified by a unique code specified in the trial protocol.
Paragraph 68.4 The investigator shall report to the sponsor and the ethics committee all adverse events (Adverse Event of Special Interest – AESI) or laboratory deviations specified in the protocol as critical to safety, within the period and in the format compliant to the requirements of the protocol.

Article 69. When the outcome of an adverse event during the conducting of a clinical trial is fatal, the investigator shall be obligated to provide the sponsor and the Ethics Committee with all additional information requested.

Article 70. The sponsor shall keep detailed records of all serious adverse events that have been provided to him by investigators, and shall make these available to the Regulatory Committee at the Ministry of Health and Prevention (RCMOHP).

Article 71.
Paragraph 71.1 The sponsor shall notify the RCMOHP and PI notifies the Ethics Committee, respectively, of any suspected unexpected serious adverse reaction that has occurred in the course of a clinical trial on the territory of the UAE and has resulted in death or has proven to be life-threatening, within 7 calendar days at the latest of receiving the information about it.
Paragraph 71.2 The sponsor and PI respectively shall provide the bodies under Paragraph 71.1 with additional information about the case within 7 calendar days of the date on which a notification was sent.
Paragraph 71.3 The sponsor and PI respectively shall notify the bodies under Paragraph 71.1 of all suspected unexpected serious adverse reactions other than those specified in Paragraph 71.1 that have occurred in the course of the clinical trial on the territory of the UAE, 15 calendar days at the latest from receiving the information about their occurrence.
Paragraph 71.4 When some information is not available at the time of report e.g. causality assessment by medical monitor of Sponsor/ CRO, compensation provided for study related injury or death, the same has to be provided as a follow-up report.

Article 72.
Paragraph 72.1 The format and the content of the notifications of SUSARs (both initial as well as follow-up reports) should be submitted along with a covering letter (printed on the company's/ CRO's letter head). A template of covering letter is specified in Appendix 06.

Paragraph 72.2 The sponsor shall inform the investigators carrying out the clinical trial with an investigational product of any suspected unexpected adverse reaction associated with the tested medicinal product, irrespective of its origin.

Article 73.
Paragraph 73.1 Once a year the sponsor shall submit to the RCMOHP and to the respective Ethics Committee a list of all suspected serious adverse reactions that have occurred within the past period and a report on the safety of trial subjects.
Paragraph 73.2 Once a year the sponsor shall submit to the RCMOHP and to the respective Ethics Committee an update of Investigator's brochure or other relevant information concerning the safety profile of the investigational product.

Article 74.
The RCMOHP shall record all information provided in compliance with Article 68, Paragraphs 68.1 and 68.3, about the suspected unexpected serious adverse reactions caused by investigational products tested.

Section VII Notification of completion of the clinical trial

Article 75.
Paragraph 75.1 The sponsor shall notify the Regulatory Committee at the Ministry of Health and Prevention (RCMOHP) and the respective Ethics Committee in writing of the termination or completion of the trial on the territory of the UAE.
Paragraph 75.2 The notification shall be filed within 90 calendar days of the completion of the study.
Paragraph 75.3 Unless otherwise specified in the protocol approved by the respective Ethics Committee, the last visit of a subject shall be considered as the completion of the trial.
Paragraph 75.4 Where a trial terminates early, the sponsor shall notify the RCMOHP and the respective Ethics Committee within up to 15 calendar days of making a decision, stating the reasons for it.

Article 76.
Notification under Article 75 shall contains:

1. Full name and study protocol number.
2. Name and contact details of the PI and its authorized representative.
3.
4. Name and contact details of the sponsor and its authorized representative.
5. Name and contact details of the Contract Research Organization, if any.
6. Details about initial and all subsequent approvals with reference number and authorizing body.
7. Details about exact initiation of the study.
8. Number and name of all approved sites on the territory of the UAE participated in the study.
9. Number of subject participate in the study (screened, enrolled, and completed).
10. Number of occurred serious adverse events per site.
11. Details of compensations provided for injury or death. In case no compensation has been paid, reason for the same.
12. 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.

Article 77. The sponsor shall present the RCMOHP and PI to the respective Ethics Committee with a final report on the clinical trial within one year from the end of the trial

Appendix 05 Data elements for reporting SAE occurring in a clinical trial

1. Subject details
   i. Subject initials & identifier
   ii. Country
   iii. Gender
   iv. Age and/or date of birth
2. Suspected Drug(s)
   i. Generic name of the suspect drug
   ii. Indication(s) for which suspect drug was prescribed or tested
   iii. Dosage form and strength
   iv. Daily dose and regimen (specify units - e.g., mg, ml, mg/kg)
   v. Route of administration
   vi. Starting date and time of day
   vii. Stopping date and time, or duration of treatment
3. Other Treatment(s) Provide the same information for concomitant drugs (including non-prescription/ OTC drugs) and non-drug therapies, as for the suspected drug(s).
4. Details of Serious Adverse Event (s)
   i. Start date (and time) of onset of event
   ii. Stop date (and time) or duration of event
   iii. Dechallenge and rechallenge information
   iv. Results of specific tests and/or treatment that may have been conducted
5. Outcome
   Information on recovery and any sequelae; for a fatal outcome, cause of death and a comment on its relationship to the suspected reaction; any post-mortem findings other information: anything relevant to facilitate assessment of the case, such as medical history including allergy, drug or alcohol abuse; family history; findings from special investigations etc.
   Details of compensations provided for injury or death. In case no compensation has been paid, reason for the same should be submitted. It is pertinent to mention that in case of study related injury or death, complete medical care as well as compensation for the injury or death should be provided.
6. Details about the Investigator
   i. Name, Address & Telephone number
   ii. Date of receipt by the investigator
   iii. Date of reporting the event to Licensing Authority
   iv. Date of reporting the event to Ethics Committee overseeing the site:
   v. Signature of the Investigator

Appendix 06 Covering letter elements for reporting SUSAR reporting in a clinical trial to the RCMOHP and the Ethics Committee

a) RCMOHP CT receipt number
b) Complete address of Sponsor and CRO (if any) including phone & e-mail address
c) Phase of clinical trial
d) Protocol or Study No. / Code / ID and the study title
e) Adverse event term / diagnosis (Whenever possible provide a „preferred term")
f) A brief narrative of the event, not exceeding 10 lines. A detailed narrative may be enclosed, if available.
g) Causality assessment by investigator and the medical monitor of Sponsor/CRO. The assessment report should clearly mention whether the SAE occurred is related or not related (Situations like unlikely, possibly, suspected, doubtful etc should not be used).
h) Whether the outcome is fatal
i) Details of compensations provided for injury or death. In case no compensation has been paid, reason for the same should be submitted. It is pertinent to mention that in case of study related injury or death, complete medical care as well as compensation for the injury or death should be provided.

Appendix 07 Declaration of Helsinki

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Appendix 08 Good Clinical Practice Guidelines

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