In the Name of God

Ethical Guidance for Clinical Trials in the Islamic Republic of Iran

۲۰۱۳

Introduction

Clinical trials are recognized to be the most efficient method for collecting evidential data for clinical purposes, and play a crucial and significant role in advancing medical sciences. However, unlike other studies, clinical trials entail intentional interventions in the parameters being tried, and thus involve a greater degree of ethical concerns and considerations than other modes and types of research.

This guidance addresses the most important ethical considerations to be regarded and observed for clinical trials. Researchers and participants in clinical trials should know and follow the provisions of this guidance, the "General Ethical Guidance for Medical Research", special domestic guidances for research ethics in different disciplines, and any other related regulations or requirements. This issue is particularly emphasized in regard to the provisions of the "Ethical Guidance for Research on Vulnerable Groups".

Chapter ١ – Assessing Advantages and Disadvantages

١ Clinical trials shall be designed and executed fully based on a written protocol and proposal, which shall include ethical considerations, information regarding research funding, sponsors, professional affiliations, any possible conflict of interests, and designated measures to encourage participation in the research project.

٢ A clinical trial may commence only after the consideration and approval of the related proposal and protocol by a research ethics committee, entitled to supervise clinical trials being executed in its jurisdiction. The researcher(s) shall submit all the information and documents required for such supervision to the related committee.

٣ The researcher(s) shall immediately inform the related research ethics committee and other relevant authorities of any serious adverse development or accident that can be attributed to the research project.

٤ The ethics committee shall hold permanent responsibility for supervision over the ethical execution of the research project, and the researcher(s) shall thus inform the committee of any alterations in the research protocol or serious adverse developments. Moreover, the committee shall be informed of any new piece of information that may affect or jeopardize the participants' safety or research execution.

٥ A clinical trial may only be conducted by experts with relevant professional authority and sufficient scientific competence.

٦ Executing clinical trials may be justified only when the population encompassing the participants can benefit from the results and findings.

٧ All precautions shall be taken to safeguard the participants' privacy, guarantee the confidentiality of their information, and minimize possible adverse impacts of the trial on their physical and mental health.

٨ When designing a clinical trial, follow-up procedures after the trial and appropriate measures shall be considered for the participants' access to the best methods of prevention, diagnosis, treatment or other suitable medical

services, if required. Access in this respect shall not necessarily mean providing services free of charge.

٩ In case of any adverse event or side effects attributed to the trial, during or after its execution, the researcher(s) shall guarantee suitable treatment and care for the affected participant(s) without any charges. Financial measures for fulfilling this obligation, such as insuring the participants, shall be considered when designing the research protocol.

١٠ In case a disease or special health condition is diagnosed in a participant, during or after the trial, the researcher(s) or the sponsoring institute shall inform the participants.

١١ When agreed by the participants, the researcher(s) shall inform their family physician of their participation in the trial.

١٢ All data for the clinical trial shall be recorded, utilized and stored in a manner that provides for their accurate identification, reporting and interpretation.

١٣ Any financial transaction with the participants shall be limited to compensating the expenses resulting from or associated to their participation in the trial, or expressing the researchers' gratitude. Any unusual payments that may jeopardize the participants' liberty for accepting or continuing participation in the trial shall be seriously avoided.

١٤ Double-blind trials shall be designed in a manner that clarifies the individual(s) authorized to break the code, and the method for doing so, in case an event occurs for one or more participants that justifies breaking the code. Details in this respect shall be specified in the research protocol.

١٥ An intervention not yet approved by firm medical evidence shall not be exempted from passing through a complete standard process of evaluation and trial for reasons such as being herbal, traditional, or the like.

١٦ If female participants are required for a clinical trial at phase one, the chosen participants shall be either outside the fertility age, or using certain contraceptive methods.

۱۷ In trials including radiation, the intervention type and dosage shall be approved by the related research ethics committee. Such approvals shall be based on expert consultative opinions.

۱۸ Healthy participants in trials including radiation shall be over ۵۰ years old, and younger participants may be chosen only if the trial targets their specific age group. The number of participants shall be kept at a minimum that satisfies the trial objective(s) and required accuracy.

۱۹ For trials including medical interventions, where the drug in question is neither available nor registered in the Iranian drug inventory, the Iranian Food and Drug Administration (FDA) may proceed to approve the clinical trial and import the desired drug in accordance with relevant regulations and legislations.

Chapter ٢ – Informed Consent

١ Participants in clinical trials shall always express their informed consent in written form. The informed consent document shall include all information needed by the participants to decide whether or not to participate in the trial, as mentioned in the following paragraphs.

٢ The informed consent document shall be signed by the participants (or their legal representatives) and the lead researcher (or another member of the research team with sufficient knowledge and capacity, instead of the lead researcher). The document shall be prepared and signed in two copies, one provided to the participant and researcher each.

٣ In cases where the participant is unable to read the informed consent document for any reason, a third person with no mutual interest with either side shall read and explain the provisions of the document to the participant, and answer any questions. In such cases, the form shall be signed by the mentioned third person, in addition to the participant (by signature or fingerprint) and researcher.

٤ The template informed consent document designed for the trial shall be attached to the proposal submitted to the research ethics committee for approval. Ethical consideration of the proposal for a clinical trial without considering the related informed consent document would lack any legal validity.

٥ The informed consent document shall be prepared in a language comprehensible for the participant(s), and the participants or their legal representatives shall be allowed sufficient time to investigate about the trial details. It shall be clarified that the trial is a research process, participated in voluntarily, and refusing or terminating participation at any time would not affect the participant's health, rights or the care provided.

٦ The participants shall have access to information regarding insurance or any other measures designed to compensate damages resulting from participation in the trial. Moreover, participants shall be informed about the medical

services provided to them in case they are injured or disabled in the trial process, or afterwards.

٧ An informed consent document shall be valid for the whole length of researcher-participant interaction. Any newly achieved information that might affect the participants' decision to accept or continue participation in the trial shall be provided to them in written form.

٨ At the time of signing the informed consent document, it shall be ensured that the participant has not agreed to participation under any pressure, or due to medical, institutional or other affiliations. If the probability for that exists, the consent document shall be obtained by a third person with full knowledge about the trial, and yet no relation to the related participants.

٩ Participants shall accept or continue their participation in the trial voluntarily. Therefore, no member of the research team may force, encourage, deceive, threaten or coerce participants to do so.

١٠ Since all side effects or damages attributed to the trial shall be compensated for the participants, clearance of obligations shall not be possible for clinical trials, and no clause for that shall be stipulated in the informed consent document. This issue differentiates between informed consent for research and treatment purposes.

١١ The informed consent document provided for signature to the participant shall include the following items about the clinical trial:

١١.١ Title;

١١.٢ Nature;

١١.٣ Objective(s);

١١.٤ Treatment (or intervention) involved, and probability of random designation for treatment (or intervention);

١١.٥ Follow-up methods, including invasive and non-invasive methods;

١١.٦ Participants' obligations;

١١.٧ Research aspects of the trial;

١١.٨ Predictable risks for the participants;

١١.٩ Expected benefits for participants (the participants shall be informed if no benefits can be conceived for participants);

١١.١٠ In case placebos are used, the meaning of placebo drugs, probability of being assigned to the placebo group, and possible benefits or risks of being assigned to the placebo group;

١١.١١ Alternative treatment methods available to the participants, along with their potential benefits and risks;

١١.١٢ Free-of-charge nature of research interventions for the participants;

١١.١٣ Compensation and/or treatment of problems resulting from the trial;

١١.١٤ Amount and method of payment, if applicable, to the participants in return for their cooperation;

١١.١٥ Reimbursement of expenses imposed on the participants during and as a result of the trial;

١١.١٦ Voluntary nature of participation in the trial, and clarification that participants are entitled to terminate their cooperation at any stage of the trial, without having to pay fines or damages, or having their normal treatment process affected;

١١.١٧ Confidentiality of the participants' personal information, and clarification that the results will be published statistically without divulging their personal information;

١١.١٨ Persons or authorities that have access to trial information, including research ethics committees;

١١.١٩ Clarification that the participants or their legal representatives will be immediately informed if new information was achieved in regard to the participants' health conditions, or influential on their continued participation;

١١.٢٠ Name and contact information of individual(s) to contact for further information about the trial, or if unexpected side effects occurred;

١١.٢١ Prediction and description of conditions that might terminate participants' cooperation in the trial;

١١.٢٢ Expected period of participation in the trial; and

١١.٢٣ Possible conflict of interests of researchers and their professional affiliations.

١٢ In case the trial is terminated or suspended for any reason before the designated time, the researcher or research institute shall inform and assure the participants of proper treatment and follow-up as required.

Chapter ٣ – Placebo

١ Benefits, risks, side effects and efficiency of the method(s) under trial shall be compared against the best available methods for prevention, diagnosis or treatment.

٢ Using placebos in clinical trials shall be unacceptable when standard treatments or interventions exist, except when

٣.١ no evidence exists for higher efficacy of standard treatments than placebos;

٣.٢ standard treatments are not accessible due to their unstable provision or financial limitations (in terms of cost payment within the public health system, so this does not include conditions where efficient standard treatment is affordable for the wealthy, but not for people with low incomes);

٣.٣ the patient population under study is resistant to one standard treatment, and no alternative standard treatment exists for them;

٣.٤ the trial aims at investigating the efficacy of a treatment together with a standard treatment, and the patient population under study has undergone the standard treatment for some reason;

٣.٥ the patient population under study is intolerant of standard treatments, and continuing them would cause irreversible damage of any extent or side effects associated with the treatment, without any alternative standard treatments; and

٣.٦ a prevention, diagnosis or treatment method is considered for a slight disease condition, and patients receiving the placebo would not be exposed to higher or irreversible risks.

٣ Using placebo surgeries shall not be acceptable as a placebo, except when all the following conditions are fulfilled:

٣.١ The assessed consequence is subjective, such as pain or living quality;

٣.٢ A comparable real surgery does not exist and the only way for accurate investigation of intervention efficacy is a placebo surgery;

٣.٣ The risk of a placebo surgery is acceptably low;

٣.٤ The patient has signed an informed consent document at full liberty, and awareness that s/he might undergo a placebo surgery without any treatment benefit; and

٣.٥ The related research ethics committee approves conducting placebo surgeries for the desired intervention, with full compliance with the submitted protocol.

Chapter ٤ – Damage Compensation

١ Any damage to the participants resulting from the trial, which would have not occurred without their participation in the trial, shall be properly compensated.

٢ The individual(s) or institute(s) responsible for compensating for damages shall be specified in the trial protocol and inform consent document.

٣ Damages to the participants resulting from clinical trials shall be compensated under any conditions, and does not require proof of researchers' misconduct.

٤ The following cases shall not require compensation:

٤.١ Slight damages, such as negligible or curable pain or discomfort;

٤.٢ Cases where the product or drug under study fails to produce the predicted impact;

٤.٣ The disease aggravates during taking placebos;

٤.٤ Damages resulting from the participants' own fault; and

٤.٥ Phase ٤ of the clinical trial.

٥ In case of disputes between the participant(s) and researcher(s) on the necessity or method of damage compensation, the issue shall be referred to, and decided upon by the research ethics committee approving the related clinical trial.