Policies, Regulations and Guidelines for Research Involving Human
Preface

There exist endless debates concerning the application of guidelines and policies for ethical conduct of research involving human subjects. These debates are likely to continue as new information becomes available. Researchers in biomedicine and the social and behavioral sciences confront the challenging task of adhering to national and international regulations in social and cultural environments in which ethical guidelines may not be easily translated or applied. This document is meant to outline ethical guidelines, policies and regulations that should be followed in Qatar in conducting research involving human subjects.

This document is reasonably comprehensive and is stated at a level that should assist scientists, subjects, reviewers and interested citizens to understand the ethics in research involving human subjects. These rules, regulations and policies should be followed since, generally, they provide guidance to resolve most ethical problems arising from research involving human subjects. However, since science is in a continuous state of flux and that specific advances may raise ethical issues, appendices will be added to this document as the need arises.

The Qatar Health Research Ethics Committee has unanimously approved this document. A law to legally enforce this document is in process.

In assembling this document, research ethics in various countries and international organizations were searched. The following publications were consulted and many were adapted or modified to meet the conditions in Qatar.

The Belmont Report.
http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm

World Medical Association, Declaration of Helsinki. Ethical Principles for Medical Research Involving Human Subjects
http://www.wma.net/e/policy/b3.htm

Council for International Organizations of Medical Sciences (CIOMS)- International Ethical Guidelines for Biomedical Research Involving Human Subjects.

US Health and Human Services Regulations for the Protection of Human Subjects
http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm

Ethical challenges in study design and informed consent for health research in resource-poor settings
http://www.who.int/tdr/publications/publications/seb_topic5.htm

Council for International Organizations of Medical Sciences
World Medical Association Declaration of Helsinki:
Ethical Principles for Medical Research Involving Human Subjects.
Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, and amended by the:
29th WMA General Assembly, Tokyo, Japan, October 1975
35th WMA General Assembly, Venice, Italy, October 1983
41st WMA General Assembly, Hong Kong, September 1989
48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996
52nd WMA General Assembly, Edinburgh, Scotland, October 2000
53rd WMA General Assembly, Washington 2002 (Note of Clarification on paragraph 29 added)
55th WMA General Assembly, Tokyo 2004 (Note of Clarification on Paragraph 30 added)
59th WMA General Assembly, Seoul, October 2008

Proceedings of the First Meeting of the Eastern Mediterranean and Arab Forum on Bioethics in Research held on August 12-14, 2008 in Cairo, Egypt and sponsored by World Health Organization, United Nations Educational, Scientific and Cultural Organization, ISESCO, and University of Maryland, USA

"Ethical Practices for Health Research in the Eastern Mediterranean Region of the World Health Organization: A Retrospective Data Analysis"

Medical Genetics Ethics, Islamic views and considerations in Iran

Kuwait Institute for Medical Specialization, the Ministry of Health, State of Kuwait

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Basic Policy for Protection of Human Research Subjects

This policy applies to all research involving human subjects conducted, privately or governmentally supported or otherwise subject to regulation by any department of research or research organization in Qatar. This includes research conducted or supported in collaboration with a non-Qatari institution.

This policy does not affect any local or foreign laws or regulations which may otherwise be applicable and which provide additional protections for human subjects involved in research.

Research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from this policy:

(1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

(2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless: (i) information obtained is recorded in such a manner that human subjects can be identified; and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

(3) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified.

(4) Research and demonstration projects which are designed to study, evaluate, or otherwise examine: (i) Public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in levels of payment for benefits or services under those programs.

(5) Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe.

When research covered by this policy takes place in foreign countries, procedures normally followed in the foreign countries to protect human subjects with guidelines consistent with the World Medical Assembly Declaration (Declaration of Helsinki amended 1989) may be reviewed and approved by the Institutional Review Board (IRB) of the Institution in Qatar.

Definitions: For the purpose of this policy:
(a) **Research** means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to general knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes.

(b) **Human subject** means a living individual about whom an investigator conducting research obtains: (1) Data through intervention or interaction with the individual or (2) Identifiable private information.

*Intervention* includes both physical procedures by which data are gathered (for example, vein puncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

*Interaction* includes communication or interpersonal contact between investigator and subject.

*Private information* includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

(c) **IRB** means an Institutional Review Board established in accord with and for the purposes expressed in this policy.

(d) **Minimal risk** means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

**Assuring compliance with this policy**

(a) Each institution engaged in research which is covered by this policy shall provide written assurance satisfactory to the Supreme Council of Health of Qatar that it will comply with the requirements set forth in this policy.

(b) Institutions will conduct or support research covered by this policy only if the institution has an assurance approved as provided in the attachments to this document, and only if the institution has certified to the Supreme Council of Health that the research has been reviewed and approved by an Institutional Review Board (IRB) and will be subject to continuing review by the IRB. Assurances applicable to conducted research shall include:

(1) A statement of principles governing the institution in the discharge of its responsibilities for protecting the rights and welfare of human subjects of research conducted at or sponsored by the institution. This requirement does not preempt provisions of this policy applicable to institution-supported or regulated research and need not be applicable to any research exempted or waived.
(2) Designation of one or more Institutional Review Boards (IRBs) established in accordance with the requirements of this policy, and for which provisions are made for meeting space and sufficient staff to support the IRB's review and recordkeeping duties.

(3) A list of IRB members identified by name; earned degrees; representative capacity; indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationship between each member and the institution. Changes in IRB membership shall be reported to the Institution head, and to the Department of Research, Supreme Council of Health, or any successor office.

(4) Written procedures which the IRB will follow (i) for conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution; (ii) for determining which projects require review more often than annually and which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review; and (iii) for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.

(5) Written procedures for ensuring prompt reporting to the IRB, and appropriate institutional officials of: (i) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB; and (ii) any suspension or termination of IRB approval.

(c) The assurance shall be executed by an individual authorized to act for the institution and to assume on behalf of the institution the obligations imposed by this policy and shall be filed in such form and manner as the institutional head prescribes.

(d) The Institutional head (the person who officially authorized to represent and speaks on behalf of the institution) will evaluate all assurances submitted in accordance with this policy through such officers and employees of the institution. The institutional head's evaluation will take into consideration the adequacy of the proposed IRB in light of the anticipated scope of the research activities and the types of subject populations likely to be involved, the appropriateness of the proposed initial and continuing review procedures in light of the probable risks, and the size and complexity of the institution.

(e) On the basis of this evaluation, the institutional head may approve or disapprove the assurance, or enter into negotiations to develop an approvable one. The institutional head may limit the period during which any particular approved assurance or class of approved assurances shall remain effective or otherwise condition or restrict approval.

(f) An institution with an approved assurance shall certify that each application or proposal for research covered by the assurance and by this Policy has been reviewed and approved by the IRB. Such certification should be submitted with the application or proposal or by such later date as may be prescribed by the institution to which the application or proposal is submitted. **Under no condition** shall research
covered by the Policy be supported or conducted prior to receipt of the certification that the research has been reviewed and approved by the IRB.

**Institutional Review Board (IRB) membership**

(a) Each IRB shall have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB shall be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of cultural backgrounds and sensitivity to such issues as religion, community attitudes, etc. to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable laws, and standards of professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas. If an IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these subjects.

(b) Every nondiscriminatory effort will be made to ensure that the composition of the IRB members is balanced, including the institution’s consideration of qualified persons of both sexes. No IRB may consist entirely of members of one profession.

(c) Each IRB shall include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas. A lay member may also be considered.

(d) Each IRB shall include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

(e) No IRB may have a member participate in the IRB’s initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.

(f) An IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues which require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB.

**Institutional Review Board (IRB) functions and operations**

In order to fulfill the requirements of this policy each IRB shall: (a) Follow written procedures in the same detail as described below and, to the extent required. (b) Except when an expedited review procedure is used, review proposed research at convened meetings at which a majority of the members of the IRB are present. In order for the research to be approved, it shall receive the approval of a majority of those members present at the meeting.
Institutional Review Board (IRB) review of research

(a) An IRB shall review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by this policy.

(b) An IRB shall require that information given to subjects as part of informed consent. The IRB may require that information be given to the subjects when in the IRB’s judgment the information would meaningfully add to the protection of the rights and welfare of subject. This information must be in the language that patient / parents / guardians can read and understands.

(c) An IRB shall require documentation of informed consent or may waive documentation with appropriate justification.

(d) Within two weeks of its meeting, an IRB shall notify investigators and the institution in writing of its decision to approve or disapprove the proposed research activity or of modifications required to secure IRB approval of the research activity. If the IRB decides to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing.

(e) An IRB shall conduct continuing review of research covered by this policy at intervals appropriate to the degree of risk, but not less than once per year, and shall have authority to observe or have a third party observe the consent process and the research.

Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research

(a) Research that may be reviewed by the IRB through an expedited review procedure may include research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories: 1) Clinical studies of drugs and medical devices only when cleared/approved for marketing and the medical use; (2) Collection of blood samples by finger stick, heel stick, ear stick, or vein puncture; 3) Prospective collection of biological specimens for research purposes by noninvasive means; 4) Collection of data through noninvasive procedures; 5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes; 6) Collection of data from voice, video, digital, or image recordings made for research purposes; 7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

(b) An IRB may use the expedited review procedure to review minor changes in previously approved research during the period (of one year or less) for which approval is authorized.

(c) For multicenter, multinational research projects which have been approved by the IRBs in their relevant countries, the institutional Qatari IRB may carry an expedited
review provided that a copy of relevant research ethics information as approved by the other IRBs is submitted.

Under an expedited review procedure, the review may be carried out by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB. In reviewing the research, the reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with the non-expedited procedure.

(d) Each IRB which uses an expedited review procedure shall adopt a method for keeping all members advised of research proposals which have been approved under the procedure.

(e) The institutional head may restrict, suspend, terminate, or choose not to authorize an institution's or IRB's use of the expedited review procedure.

Criteria for Institutional Review Board (IRB) approval of research

(a) In order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied:

(1) Risks to subjects are minimized: (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

(2) Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

(3) Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

(4) Informed consent will be sought and appropriately documented from each prospective subject or the subject's legally authorized representative.

(5) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

(6) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
(b) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

**Review by institution**

Depending on individual institutional policies, research covered by this policy that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials (e.g. board of governors, chancellor, CEOs) of the institution. However, those officials may not approve the research if it has not been approved by an IRB.

**Suspension or termination of Institutional Review Board (IRB) approval of research**

An IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be reported promptly to the investigator, appropriate institutional officials, funding agency, as well as the Supreme Council of Health.

**Cooperative research**

Cooperative research projects are those projects covered by this policy which involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with this policy. With the approval of the department or institutional head, an institution participating in a cooperative project may enter into a joint review arrangement, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort. Research collaboration with foreign institutions must provide IRB approval from the foreign institution as well as IRB approval from the Qatari institution to the funding body.

**Institutional Review Board (IRB) Records**

(a) An institution, or when appropriate an IRB shall prepare and maintain adequate documentation of IRB activities, including the following:

(1) Copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample of consent documents, progress reports submitted by investigators, and reports of injuries to subjects. (2) Minutes of IRB meetings which shall be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving of research; and a written summary of the discussion of controversial issues and their resolution. (3) Records of continuing review activities. (4) Copies of all correspondence between the IRB and the investigators. (5) A list of IRB members in detail as described above. (6) Written procedures for the IRB in the same detail as described above. (7) Statements of significant new findings provided to subjects.
(b) The records required by this policy shall be retained for at least 3 years, and records relating to research which is conducted shall be retained for at least 3 years after completion of the research. All records shall be accessible for inspection and copying by authorized representatives of the Supreme Council of Health at reasonable times and in a reasonable manner.

**General requirements for informed consent**

Except as provided elsewhere in this policy, no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject’s legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in a language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject’s legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

(a) **Basic elements of informed consent:** In seeking informed consent the following information shall be provided to each subject: (1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental; (2) A description of any reasonably foreseeable risks or discomforts to the subject; (3) A description of any benefits to the subject or to others which may reasonably be expected from the research; (4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject; (5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained; (6) An explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained; (7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and (8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

(b) **Additional elements of informed consent:** When appropriate, one or more of the following elements of information shall also be provided to each subject: (1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable; (2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent; (3) Any additional costs to the subject that may result from participation in the research; (4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject; (5) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; and (6) The approximate number of subjects involved in the study.
(c) **An IRB may approve a consent procedure** which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided the IRB finds and documents that: (1) The research project is to be conducted by or subject to the approval of the Supreme Council of Health officials and is designed to study, evaluate, or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs; (2) The research involves no more than minimal risk to the subjects; (3) The waiver or alteration will not adversely affect the rights and welfare of the subjects; (4) The research could not practicably be carried out without the waiver or alteration; and (5) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

(d) **The informed consent requirements** in this policy are not intended to preempt any applicable laws which require additional information to be disclosed in order for informed consent to be legally effective.

(e) **Nothing in this policy is intended to limit the authority of a physician** to provide emergency medical care, to the extent the physician is permitted to do so under applicable laws.

**Documentation of informed consent**

(a) Informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative. A copy shall be given to the person signing the form.

(b) The consent form may be either of the following: (1) A written consent document that embodies the elements of informed consent as described above. This form may be read to the subject or the subject's legally authorized representative, but in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed; or (2) A short form written consent document stating that the elements of informed consent as described above have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative, in addition to a copy of the short form.

(c) An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either: (1) that the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or (2) that the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.
Cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

**Applications and proposals lacking definite plans for involvement of human subjects**

Certain types of research applications are submitted to departments or institutions with the knowledge that subjects may be involved within the period of support, but definite plans would not normally be set forth in the application or proposal. These include projects in which human subjects' involvement will depend upon completion of instruments, prior animal studies, or purification of compounds. **These applications need not be reviewed by an IRB before an award may be made.** However, except for research exempted or waived, **no human subjects may be involved** and no human research can be supported until the project has been reviewed and approved by the IRB, as provided in this policy, and certification are submitted by the institution to the funding body.

**Research undertaken without the intention of involving human subjects**

In the event research is undertaken without the intention of involving human subjects, but it is later proposed to involve human subjects in the research, the research shall first be reviewed and approved by an IRB, as provided in this policy, a certification submitted, by the institution, to the funding body, and final approval given to the proposed change by the funding body.

**Evaluation and disposition of applications and proposals for research to be conducted or supported by Intramural staff of a Department or an Institution**

(a) All applications and proposals involving human subjects submitted by the intramural officers and employees of a department or an institution must be reviewed by an approved IRB that is not necessarily residing in the same Department or Institution. (b) On the basis of this evaluation, the Department or Institution head may approve or disapprove the submission of the application or proposal, or enter into negotiations to develop an approvable one.

**Use of Research funds**

Research funds administered by a department or institution may not be expended for research involving human subjects unless the requirements of this policy have been satisfied.

**Early termination of research support: Evaluation of applications and proposals**

(a) The institutional head as well as the Department of Research at the Qatar Supreme Council of Health may require the funding body that research support for any project be terminated or suspended in the manner prescribed in applicable program requirements, when the institution has materially failed to comply with the terms of this policy. (b) In making decisions about supporting or approving applications or proposals covered by this policy the institutional head may take into
account, in addition to all other eligibility requirements and program criteria, factors such as whether the applicant or the person or persons who would direct or has/have directed the scientific and technical aspects of an activity has/have materially failed to discharge responsibility for the protection of the rights and welfare of human subjects.

**Additional Conditions**

With respect to any research project or any class of research projects the institutional head may impose additional conditions prior to or at the time of approval when in his/her judgment additional conditions are necessary for the protection of human subjects.

**ADDITIONAL PROTECTIONS FOR PREGNANT WOMEN, HUMAN FETUSES AND NEONATES INVOLVED IN RESEARCH**

This section applies to all research involving pregnant women, human fetuses, neonates of uncertain viability, or nonviable neonates. This includes all research conducted by any person in any facility in Qatar.

**Definitions**

For the purpose of this policy, the following applies:

- **Dead fetus**: means a fetus that does not exhibit heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, or pulsation of the umbilical cord.
- **Delivery**: means complete separation of the fetus from the woman by expulsion or extraction or any other means.
- **Fetus**: means the product of conception from implantation until delivery.
- **Neonate**: means a newborn.
- **Nonviable**: neonate means a neonate after delivery that, although living is not viable.
- **Pregnancy**: encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery.
- **Viable**: as it pertains to the neonate, means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration.

**Duties of IRBs in connection with research involving pregnant women, fetuses, and neonates**

In addition to other responsibilities assigned to IRBs, each IRB shall review research and approve only research which satisfies the conditions of all applicable sections of this policy.

**Research involving pregnant women or fetuses**

Pregnant women or fetuses may be involved in research if all of the following conditions are met:

- (a) Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been
conducted and provide data for assessing potential risks to pregnant women and fetuses;

(b) The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;

(c) Any risk is the least possible for achieving the objectives of the research;

(d) If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions described above;

(e) If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions described above except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.

(f) Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;

(g) For children as defined above, who are pregnant, assent and permission are obtained in accord with the provisions of (d) above;

(h) No inducements, monetary or otherwise, will be offered to terminate a pregnancy;

(i) Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; except as a part of an approved randomized clinical trials in which decision about timing, method or procedure of delivery will be made by randomization, and

(j) Individuals engaged in the research will have no part in determining the viability of a neonate, except as a part of RCT in which the decision will be made by randomization.

**Research involving neonates**

(a) **Neonates of uncertain viability and nonviable neonates** may be involved in research if all of the following conditions are met:

1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates; 2. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate; 3. Individuals engaged in the research will have no part in determining the viability of a neonate; 4. The requirements of paragraph (b) or (c) of this section have been met as applicable.
(b) **Neonates of uncertain viability.** Until it has been ascertained whether or not a neonate is viable, a neonate **may not** be involved in research covered by this subpart **unless** the following additional conditions have been met:

(1) The IRB determines that: (i) The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or (ii) The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and, (2) When the neonate survives as a result of any research intervention, he will be at a very high risk of adverse neuro-developmental outcome later in his life. This must be clearly explained to the parents at the time of taking their consent. (3) The legally effective informed consent as described above is obtained, and it is suggested that the individual researcher, IRB and the institution should have indemnity against the legal consequences of this outcome.

(c) **Nonviable neonates.** After delivery, nonviable neonate may not be involved in research covered by this subpart unless all of the following additional conditions are met:

(1) Vital functions of the neonate will not be artificially maintained; (2) The research will not terminate the heartbeat or respiration of the neonate; (3) There will be no added risk to the neonate resulting from the research; (4) The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and (5) The legally effective informed consent has been obtained.

(d) **Viable neonates.** A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of this policy.

**Research involving, after delivery, the placenta, the dead fetus or fetal material**

(a) Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable laws and regulations regarding such activities.

(b) If information associated with material described above is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent subparts of this policy are applicable.

**Add ional Protections Pertaining To Biomedical And Behavioral Research Involving Vulnerable Subjects**

**Applicability**

(a) The regulations in this subpart are applicable to all biomedical and behavioral research conducted involving vulnerable subjects (e.g. prisoners) in addition to those imposed above; and (b) Nothing in this subpart shall be construed as indicating that compliance with the procedures set forth herein will authorize research involving
vulnerable subjects such as prisoners, to the extent such research is limited or barred by applicable laws.

**Purpose**

The purpose of this subpart is to provide additional safeguards for the protection of vulnerable subjects such as prisoners since they may be under constraints because of their circumstances (e.g., incarceration, for prisoners) which could affect their ability to make a truly voluntary and un-coerced decision whether or not to participate as subjects in research.

**Composition of Institutional Review Boards where vulnerable subjects are involved**

In addition to satisfying the above requirements, an Institutional Review Board shall also meet the following specific requirements:

(a) A majority of the Board (exclusive of prisoner members for example) shall have no association with the prison involved, apart from their membership on the Board; and (b) At least one member of the Board shall be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by more than one Board; only one Board needs satisfy this requirement.

**Additional duties of the Institutional Review Boards where prisoners are involved**

(a) In addition to all other responsibilities prescribed above for Institutional Review Boards, the Board shall review and approve such research only if it finds that:

1. The research under review represents one of the categories of research permissible;
2. Any possible advantages accruing to the prisoner through his or her participation in the research are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages is impaired; (3) The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers; (4) Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the Board justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project; (5) The consent form information is presented in language which is understandable to the subject population; (6) Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and (7) Where the Board finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.

(b) The IRB shall carry out such other duties as may be assigned, and
(c) The institution shall certify to the funding body and the Supreme Council of Health that the duties of the IRB under this section have been fulfilled.

**Permitted research involving prisoners**

(a) Biomedical or behavioral research may involve prisoners as subjects only if:

(1) The institution responsible for the conduct of the research has certified that the IRB has approved the research; and (2) In the judgment of the funding body and the Supreme Council of Health, the proposed research involves solely the following:

(i) Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects; (ii) Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects; (iii) Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Supreme Council of Health has consulted with appropriate experts; or (iv) Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Supreme Council of Health has consulted with appropriate experts, of the intent to approve such research.

**Additional Protections For Children Involved As Subjects In Research**

(a) This subpart applies to all research involving children as subjects either in Qatar or in collaboration with foreign institutions. Institutional heads may adopt non-substantive procedural modifications as may be appropriate from an administrative standpoint.

(b) Exemptions applicable to this subpart include those mentioned above involving research conducted in established or commonly accepted educational settings; involving the use of educational tests; the collection or study of existing data; research and demonstration projects; and taste and food quality evaluation and consumer acceptance studies. Exemption regarding educational tests is also applicable to this subpart. However, exemption for research involving survey or interview procedures or observations of public behavior does not apply to research covered by this subpart, except for research involving observation of public behavior when the investigator(s) do not participate in the activities being observed.

(c) The exceptions, additions, and provisions for waiver as they appear above are applicable to this subpart.

**Definitions.**

The definitions described above shall be applicable to this subpart as well. In addition, as used in this subpart:
(a) *Children* are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the State of Qatar. (i.e. less than 18 years of age).

(b) *Assent* means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

(c) *Permission* means the agreement of parent(s) or guardian to the participation of their child in research.

**IRB duties.**

In addition to other responsibilities assigned to IRBs, each IRB shall review research covered by this subpart and approve only research which satisfies the conditions of all applicable sections of this subpart.

**Research not involving greater than minimal risk**

Institutions will conduct or fund research in which the IRB finds that no greater than minimal risk to children is presented, and only if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in this policy.

**Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects**

Institutions will conduct or fund research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being, only if the IRB finds that:

(a) The risk is justified by the anticipated benefit to the subjects;

(b) The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and

(c) Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians.

**Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition**

Institutions will conduct or fund research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure which is not likely to contribute to the well-being of the subject, only if the IRB finds that:

(a) The risk represents a minor increase over minimal risk;
(b) The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;

(c) The intervention or procedure is likely to yield generalizable knowledge about the subjects’ disorder or condition which is of vital importance for the understanding or amelioration of the subjects’ disorder or condition; and

(d) Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians.

Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children

Institutions will conduct or fund research that the IRB does not believe meets the requirements only if:

(a) the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and

(b) the Supreme Council of Health, after consultation with a panel of experts has determined either:

1. that the research in fact satisfies the conditions applicable in this policy, or
2. the following: (i) the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; (ii) the research will be conducted in accordance with sound ethical principles; (iii) adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians.

Requirements for permission by parents or guardians and for assent by children

(a) In addition to the determinations required under other applicable sections of this subpart, the IRB shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate. If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived as described above.

(b) In addition to the determinations required under other applicable sections of this subpart, the IRB shall determine, in accordance with and to the extent that consent is
required, that adequate provisions are made for soliciting the permission of each child's parents or guardian. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research to be conducted.

(c) In addition to the provisions for waiver contained above, if the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements, provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with current laws. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

(d) Permission by parents or guardians shall be documented in accordance with and to the extent required by this policy.

(e) When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

(f) If the research requires making videos or photographs of Women and / or children, the IRB should strictly scrutinize this and eliminate every possibility of any misuse of these videos or photographs for any purpose.

### Ethical Conduct of Clinical Trials

**I. SCH statement**

The Supreme Council of Health recognizes the standards of the International Conference on Harmonization’s E6 “Good Clinical Practice” (E6 GCP). This guidance reflects the consolidated guidance for clinical trials and the current requirements of the regulatory body of the State of Qatar presented by the Supreme Council of Health, the regulatory bodies from the European Union, Japan, Australia, Canada, the Nordic countries, World Health Organization (WHO) and the United States of America. E6 GCP is an international ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety, and wellbeing of trial subjects are protected; consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data are credible. This guidance should be followed when conducting clinical trials in the State of Qatar. The principles established in this guidance may also be applied to other clinical investigations that may have an impact on the safety and well-being of human subjects.

Institutional Review Boards, Sponsors and Investigators involved in clinical trials conducted within the State of Qatar must comply with the principles of International Conference of Harmonization (ICH) - Good Clinical Practice (GCP).

Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety and well-being of trial subjects are protected; consistent with the principles
that have their origin in the Declaration of Helsinki, and that the clinical trial data are credible.


This Guidance also contains procedures and requirements for the submission to, and review by, the Supreme Council of Health. In order to provide multiple layers of protection for human subjects involved in clinical trials, a designated clinical trial study must be reviewed by a registered IRB committee and a Data Safety Monitoring Board. A sponsor or an institution conducting clinical trials in Qatar shall submit all the clinical trial documents to the Supreme Council of Health if the sponsor or the institution intends to conduct a clinical investigation involving a drug (e.g. new drug; or an approved drug used for a different indication) or combination of drugs, or a device, or a therapeutic intervention. If the project involves a new drug that is not approved for human use, and is part of a multicenter trial the correspondence from the regulatory agency of jurisdiction [e.g. Food and Drug Administration (FDA), European Medicines Agency (EMA)] must be also submitted to the SCH for review.

A sponsor or an institution conducting clinical trials in Qatar shall not begin a clinical investigation subject to the Supreme Council of Health review and approval until the Supreme Council of Health will provide the sponsor or institution in Qatar with a written determination, within 30 days after the Supreme Council of Health receives all the required documents.

II. Definitions

**Investigator:** an individual who actually conducts a clinical investigation (i.e., under whose immediate direction the drug is administered or dispensed to a subject). In the event an investigation is conducted by a team of individuals, the principle investigator is the responsible leader of the team. "Sub/co-investigator" includes any other individual member of that team.

**Sponsor:** An individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial. The sponsor may be a pharmaceutical company, governmental agency, academic institution, or other organization. The sponsor does not actually conduct the investigation.

**Subject:** a human who participates in an investigation, either as a recipient of the investigational new drug or as a control. A subject may be a healthy human or a patient with a disease.

**Clinical Research:** Clinical Research is research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. All Clinical Trials are a subset of Clinical Research.

**Clinical investigation:** means any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects. For the purposes of this guidance, an experiment is any use of a drug except for the use of a marketed drug in the course of medical practice.

**Clinical Trial:** A Clinical Trial is a prospective biomedical or behavioral research study
of human subjects that is designed to answer specific questions about biomedical or behavioral interventions such as: drugs, treatments, devices, or new ways of using known drugs, treatments, or device.

III. Conducting Clinical Trials and the Supreme Council of Health Review

An investigational new drug/device/therapeutic intervention may be used in a clinical investigation if the following conditions are met:

(1) The sponsor of the investigation submits all the required documentation to the Supreme Council of Health for review and approval; and the sponsor complies with all applicable requirements in this Guidance and with E6 GCP Guidance with respect to the conduct of the clinical investigations; and

(2) The participating investigator in Qatar conducts his or her investigation in compliance with the requirements set forth under paragraph (1).

The clinical trial may commence:

(1) Only after the Supreme Council of Health receives all the required documentation and a written determination is issued by the Supreme Council of Health; or

(2) On earlier notification by the Supreme Council of Health that the clinical investigations may begin. The Supreme Council of Health will notify the research team in Qatar in writing of the date it receives the required documents for its review.

(c) A sponsor of a multi-center clinical trial may ship an investigational new drug to participating institutions/investigators in Qatar:

(1) Once the institution/investigator in Qatar has the written Supreme Council of Health written approval;

(d) An investigator may not administer an investigational new drug to human subjects until the Supreme Council of Health written permission is obtained.

IV. E6 Good Clinical Practice “CLINICAL TRIAL PROTOCOL AND PROTOCOL”

The contents of a trial protocol should generally include the following topics. However, site specific information may be provided on separate protocol page(s), or addressed in a separate agreement, and some of the information listed below may be contained in other protocol referenced documents, such as an Investigator’s Brochure [see also section 7 of the E6 GCP, at http://www.fda.gov/downloads/Drugs/Guidances/ucm073122.pdf]

6.1. General Information
6.1.1 Protocol title, protocol identifying number, and date. Any amendment(s) should also bear the amendment number(s) and date(s).
6.1.2 Name and address of the sponsor and monitor (if other than the sponsor).
6.1.3 Name and title of the person(s) authorized to sign the protocol and the protocol amendment(s) for the sponsor.
6.1.4 Name, title, address, and telephone number(s) of the sponsor's medical expert (or
dentist when appropriate) for the trial.
6.1.5 Name and title of the investigator(s) who is (are) responsible for conducting the trial, and the address and telephone number(s) of the trial site(s).
6.1.6 Name, title, address, and telephone number(s) of the qualified physician (or dentist, if applicable) who is responsible for all trial-site related medical (or dental) decisions (if other than investigator).
6.1.7 Name(s) and address of the clinical laboratory and other medical and/or technical department(s) and/or institutions involved in the trial.

6.2. Background Information
6.2.1 Name and description of the investigational product(s).
6.2.2 A summary of findings from nonclinical studies that potentially have clinical significance and from clinical trials that are relevant to the trial.
6.2.3 Summary of the known and potential risks and benefits, if any, to human subjects.
6.2.4 Description of and justification for the route of administration, dosage, dosage regimen, and treatment period(s).
6.2.5 A statement that the trial will be conducted in compliance with the protocol, GCP, and the applicable regulatory requirement(s).
6.2.6 Description of the population to be studied.
6.2.7 References to literature and data that are relevant to the trial, and that provide background for the trial.

6.3. Trial Objectives and Purpose
A detailed description of the objectives and the purpose of the trial:
6.4 Trial Design The scientific integrity of the trial and the credibility of the data from the trial depend substantially on the trial design.
A description of the trial design should include:
6.4.1 A specific statement of the primary endpoints and the secondary endpoints, if any, to be measured during the trial.
6.4.2 A description of the type/design of trial to be conducted (e.g., double-blind, placebo-controlled, parallel design) and a schematic diagram of trial design, procedures, and stages.
6.4.3 A description of the measures taken to minimize/avoid bias, including (for example): (a) Randomization. (b) Blinding
6.4.4 A description of the trial treatment(s) and the dosage and dosage regimen of the investigational product(s). Also include a description of the dosage form, packaging, and labeling of the investigational product(s).
6.4.5 The expected duration of subject participation, and a description of the sequence and duration of all trial periods, including follow-up, if any.
6.4.6 A description of the "stopping rules" or "discontinuation criteria" for individual subjects, parts of trial, and entire trial.
6.4.7 Accountability procedures for the investigational product(s), including the placebo(s) and comparator(s), if any.
6.4.8 Maintenance of trial treatment randomization codes and procedures for breaking codes.
6.4.9 The identification of any data to be recorded directly on the CRFs (i.e., no prior written or electronic record of data), and to be considered to be source data.

6.5. Selection and Withdrawal of Subjects
6.5.1 Subject inclusion criteria.
6.5.2 Subject exclusion criteria.
6.5.3 Subject withdrawal criteria (i.e., terminating investigational product treatment/trial treatment) and procedures specifying:
(a) When and how to withdraw subjects from the trial/ investigational product treatment.
(b) The type and timing of the data to be collected for withdrawn subjects.
(c) Whether and how subjects are to be replaced.
(d) The follow-up for subjects withdrawn from investigational product treatment/trial treatment.

6.6. Treatment of Subjects
6.6.1 The treatment(s) to be administered, including the name(s) of all the product(s), the dose(s), the dosing schedule(s), the route/mode(s) of administration, and the treatment period(s), including the follow-up period(s) for subjects for each investigational product treatment/trial treatment group/arm of the trial.
6.6.2 Medication(s)/treatment(s) permitted (including rescue medication) and not permitted before and/or during the trial.
6.6.3 Procedures for monitoring subject compliance.

6.7. Assessment of Efficacy
6.7.1 Specification of the efficacy parameters.
6.7.2 Methods and timing for assessing, recording, and analyzing efficacy parameters.

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

6.9. Statistics
6.9.1 A description of the statistical methods to be employed, including timing of any planned interim analysis.
6.9.2 The number of subjects planned to be enrolled. In multicenter trials, the number of enrolled subjects projected for each trial site should be specified. The justification of sample size with reflections on the calculations of the power of the trial must be indicated.
6.9.3 The level of significance to be used.
6.9.4 Criteria for the termination of the trial.
6.9.5 Procedure for accounting for missing, unused, and spurious data.
6.9.6 Procedures for reporting any deviation(s) from the original statistical plan (any deviation(s) from the original statistical plan should be described and justified in the protocol and/or in the final report, as appropriate).
6.9.7 The selection of subjects to be included in the analyses (e.g., all randomized subjects, all dosed subjects, all eligible subjects, evaluative subjects).

6.10. Direct Access to Source Data/Documents
The sponsor should ensure that it is specified in the protocol or other written agreement that the investigator(s)/institution(s) will permit trial-related monitoring, audits, IRB/IEC review, and regulatory inspection(s) by providing direct access to source data/documents.

6.11. Quality Control and Quality Assurance

6.12. Ethics Description of ethical considerations relating to the trial

6.13. Data Handling and Recordkeeping

6.14. Financing [and Insurance Financing and insurance, if applicable] if not addressed in a separate agreement.

6.15. Publication Policy, if not addressed in a separate agreement.
CLINICAL TRIAL MONITORING & DATA SAFETY MONITORING BOARD

Institutional Review Boards, Sponsors/Funding Bodies and Investigators involved in clinical trials conducted within the State of Qatar must comply with the principles of International Conference of Harmonization (ICH) - Good Clinical Practice (GCP).


CLINICAL TRIAL MONITORING

Clinical Trial Monitoring is the act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, standard operating procedures (SOPs), GCP, and the applicable regulatory requirements. Refer to part 5.8 of the Principles of International Conference of Harmonization (ICH) - Good Clinical Practice (GCP) E6.

The purpose of trial monitoring is to verify that:

1 - The rights and well-being of human subjects are protected.

2 - The reported trial data are accurate, complete, and verifiable from source documents.

3 - The conduct of the trial is in compliance with the currently approved protocol/amendment(s), with GCP, and with applicable regulatory requirement(s).

In order to perform these tasks, Sponsor/Funding Body has the flexibility to hire a Contract Research Organization (CRO) or use Sponsor Clinical Research Support Unit when it is applicable. Clinical Research Support Unit should consist of trained and experimented members including Clinical Trial Managers, Clinical Trial Coordinators, Clinical Data Managers, Clinical Research Associates, and Biostatisticians.

The fund allocated by Sponsor/Funding Body for clinical trial must include a specific budget for the clinical trial monitoring.

DATA SAFETY MONITORING BOARD

All human subjects’ research requires ongoing monitoring of subject safety. For some clinical trials and large observational studies, a Data Safety Monitoring Board (DSMB), shall be required to monitor the research. The purpose of the DSMB is to ensure the safety of subjects and to preserve the validity and integrity of the research data through ongoing monitoring and assessment. DSMB make recommendations concerning the continuation, modification or termination of the trial.

SCH Regulations:

- Roles and Responsibilities
The Principal Investigator shall report regularly on the safety of subjects to the institution's Institutional Review Board (IRB). When no DSMB is established, the Principal Investigator shall prepare a Data and Safety Monitoring Plan (DSMP) for review and approval by the Institution's IRB.

A DSMP shall include steps for identifying and assessing risks to subjects, a description of a mechanism for reporting adverse events to all relevant oversight bodies, a description of the consent process and what information should be included in the consent form, plans for protecting the confidentiality of subjects data, and procedures for assuring data quality and protocol compliance.

A DSMB shall be required for all Phase III clinical trials. Phase I and Phase II clinical trials that pose greater than minimal risk shall also require a DSMB. For observational studies, decisions on whether a DSMB (or some equivalent) is required shall be made on a case-by-case basis by the IRB and/or the Qatar Supreme Council of Health (SCH).

- **Membership**

DSMB members must be totally independent from the study they monitor and must maintain a constant neutral position in order to avoid undue bias and shall be appointed by either the Principal Investigator (in consultation with his/her institution) and/or the Sponsor. DSMB membership is reviewed and approved by the Qatar SCH. The membership of the DSMB shall reflect the disciplines and medical specialties necessary to interpret the data from the clinical trial and to fully evaluate participant safety. The number of DSMB members depends on range of medical issues, complexity in design and analysis, and potential level of risk but generally consists of three to seven members including, at a minimum:

1. - Expert(s) in the clinical aspects of the disease/patient population being studied;
2. - One or more skilled statisticians;
3. - Investigator(s) with expertise in current clinical trials conduct and methodology.

Where the study involves especially vulnerable populations, and therefore at higher risk, and/or has broad public health or policy implications, consideration should be given to adding experts in ethics, law and public health as well someone with experience in the vulnerabilities represented by the study subjects. Any compensation to DSMB members for their work shall be provided by the Qatar SCH.

- **DSMB Chair**

Members of the DSMB will look to the chair for leadership on administrative as well as scientific issues. The chair shall be capable of

1. - Facilitating discussion,
2. - Integrating differing points of view, and
3. - Moving toward consensus on recommendations to be provided to the sponsors.

The chair shall confirm his/her commitment to participate for the duration of the trial (or for the term of the appointment, for chairs of DSMB monitoring multiple trials).

- **Confidentiality**

Confidentiality must always be maintained during all phases of DSMB review and deliberations. Usually, only voting members of the DSMB shall have access to interim
analyses of outcome data by treatment group. Exceptions may be made when the DSMB deems it appropriate. The reason and to whom the exceptions for access to interim analyses is granted will be documented in the Closed Session Report. DSMB members must maintain strict confidentiality concerning all privileged trial results ever provided to them. The DSMB shall review data only by masked study group (such as X vs. Y rather than experimental vs. control) unless or until the DSMB determines that the identities of the groups are necessary for their decision-making. Whenever masked data are presented to the DSMB, the key to the group coding must be available for immediate unmasking.

• DSMB Meeting Procedures

The initial DSMB meeting occurs after the IRB approval and before the start of the trial. This initial meeting is a scientific and statistical review of the research protocol in order to realize an assessment of the study. The conclusion of this initial meeting is the followings:
- Approval for the conduct of the Clinical Trial, or
- Disapproval for the conduct of the Clinical Trial, or
- Request protocol modifications for conducting the Clinical Trial.

When the Sponsor has obtained the final approval for conducting the Clinical Trial, the agenda for each meeting is developed jointly by the Sponsor, the Principal Investigator (regardless of whether a contract, cooperative agreement, or grant), the study statistician, and DSMB Chair.

A. Open Session: Issues relating to the general conduct and progress of the study are discussed including adverse events and toxicity issues, accrual, demographic characteristics of enrollees, disease status of enrollees (if relevant), comparability of groups with respect to baseline factors, protocol compliance, site performance, quality control, and timeliness and completeness of follow-up. Any data provided must be presented without grouping by treatment assignment or otherwise by preserving the masking of all subjects. Outcome results must not be discussed during this session. DSMB members, voting and ex officio members, Sponsor and ad hoc experts attend this session. The lead investigator and the study biostatistician should be in attendance in order to present results and respond to questions. This session is open to study investigators, coordinating center staff, representatives for industrial collaborators, representatives from the Qatar SCH and representatives from the funding body.

B. Closed Session: Grouped safety data and, if appropriate, efficacy data are presented by the study statistician(s) at this session. Grouped data should be presented by coded treatment arm. This session is normally attended only by voting members, study statisticians, and invited ex officio members. The DSMB may invite the participation of other individuals for all or part of the session.

C. Closed Executive Session: This final session involves only DSMB voting members to ensure complete objectivity as they discuss outcome results, make decisions, and formulate recommendations regarding the study. If treatment codes have been made accessible to the DSMB, then the DSMB may unmask the data based on procedures identified in advance.

• Voting
A quorum, as defined by the DSMB in the initial meeting, must be present either in person or by conference call. After a thorough discussion of DSMB members' opinions and rationale and an attempt to reach clarity regarding individual recommendations, the
final recommendations of each DSMB member should be solicited in Closed Executive Session (ex officio members shall not vote and shall not be present at this voting session). A consensus opinion or recommendation among members is not required; each member may have individual opinions. The final recommendations are recorded and either identified as majority or minority positions or are accompanied by actual vote tallies for each divergent recommendation, i.e., as number of votes for or against a particular action, such as continuing or terminating a study, etc.

DSMB decisions to modify a research protocol, impose a temporary hold on the study, or recommend its termination shall be accompanied by a clear rationale, including relevant data from the study or relevant external factors, for its decision/recommendation. These DSMB decisions must be submitted to the Principal Investigator, the institution’s IRB, the funding body and the Qatar SCH.

Where a study’s Principal Investigator, institution, or the funding body disagrees with the DSMB’s proposed modifications or recommendations, the Qatar SCH shall establish procedures for resolving such disputes in a timely manner.

**SCH Guidelines**

When determining whether a DSMB is required, the following factors should be considered:

1. **The risks to subjects.** This should include, but not be limited to, consideration of the toxicity and dosage of a drug, frequency of exposure to a drug, subject's total time on a drug, the invasiveness of the intervention, and the subjects’ disease status.

2. **The nature of the subject populations.** This should include, but not be limited to, consideration of a study population's (or subset of the population) vulnerability to such matters as the disease being treated, the likelihood and severity of any treatment side effects, the release of confidential information about subjects, the ability of subjects to fully understand the nature of the study, and the study’s recruitment, enrollment and retention plans.

3. **The complexity of the study.** This should include, but not be limited to, consideration of the number of research sites that comprise the study, its duration, the number of subjects involved, and the difficulty in determining treatment effects in the presence of other factors related to co-morbidity.

**Conflict of Interest**

Procedures should be in place to determine that members of a DSMB have no conflict of interest that would impair their judgment to assess the study objectively, or could be perceived by others to have such a conflict in ways that would erode trust in the work of the DSMB. When a DSMB member possesses special expertise critical to the work of the Board and is not readily replaceable, the conflict(s) should be managed in order to preserve the integrity of the monitoring function.

Conflicts of interest that may affect possible DSMB members are as follows:

- Financial conflict of interest;
- Investigators entering subjects into the trial (because of their knowledge of interim results);
"Intellectual" conflicts: individuals known to have strong views on the relative merits of the intervention(s) under study.

The research team, in consultation with the funding agency program, should have selection procedures for DSMB members that include:

- Assessing potential conflicts of interest and ensure that those with serious conflicts of interest are not included;
- Provide disclosure to all DSMB members of any potential conflicts that are not considered to impede objectivity and thus would not preclude service on the DSMB;
- Identify and disclose any concurrent service of any DSMB member on other DSMBs of the same, related or competing products.

**Meeting schedule and format**

The initial frequency of DSMB meetings will depend on the expected rate of accrual and event occurrence at the time the trial is designed as well as the perceived risk of the experimental and/or control interventions; annual or more frequent review may be needed. The study protocol will generally describe the schedule of interim analyses to be considered by the DSMB, or the considerations that will determine the timing of meetings (e.g., a plan for interim analysis after a certain number of primary outcomes have been reported). The study protocol will also typically describe the statistical approach to the interim analysis of trial data. To minimize the potential for bias, these descriptions should be complete before the conduct of any unblinded interim analyses.

**Monitoring for effectiveness**

In studies with serious outcomes, all parties would wish that any major treatment advance be identified and made available as soon as possible. It is critical, however, that the study yields a valid and definitive result. Thus, tensions between ethical and scientific considerations may arise. A DSMB, guided by a pre-specified statistical monitoring plan acceptable to both the DSMB and the research team leadership, will generally be charged with recommending early termination on the basis of a positive result only when the data are truly compelling and the risk of a false positive conclusion is acceptably low.

In studies where there are doubts that the hypothesized benefit is likely to be achieved, a DSMB may consider that the study continuation is futile and recommend early termination, if the interim data suggest that the research investigation is of no benefit (no trend indicating superiority of the new product, for example). In this case, false negative conclusions are of concern and statistical procedures guide such determinations.

**Monitoring for safety**

In long term outcome studies the DSMB is monitoring the following:

**Primary efficacy endpoint:** the DSMB may recommend early termination for safety
reasons, if the study participants group receiving the investigational intervention is found to be at higher risk for the outcome of interest sooner than the control group. Such assessments have potential implications for falsely concluding that there is an adverse effect, just as regular assessments of efficacy have the potential to lead to false positive conclusions about benefit. It is appropriate to demand less rigorous proof of harm to justify early termination than would be appropriate for a finding of benefit.

**Comparison of adverse event rates** in each treatment arm: particular attention will be given to monitoring adverse events of particular concern that can be identified in advance, before study initiation. The DSMB should be provided with interim summaries by treatment arm, of adverse events observed, not only those identified in advance. The rates of adverse events in treatment and control groups should be compared to detect adverse events.

**Review of individual adverse events of particular concern:** the research team may ask the DSMB to review any individual event thought to be of a major significance by the research team; such events would generally include deaths or other serious outcomes for which a causal connection with the intervention is plausible. Review of individual cases by the DSMB does not relieve the research team of the regulatory responsibilities, i.e. to report the serious adverse events to the IRB that would include deaths or other serious outcomes for which a causal connection with the intervention is plausible.

The DSMB may recommend early termination for safety reasons, or may recommend the following:

- Changing the eligibility criteria if the risks are concentrated in a particular population;
- Altering the dosage and/or the schedule;
- Screening procedures that could identify the study participants at increased risk;
- Disclosing the newly identified risks to current and future participants.

**Monitoring study conduct**

The DSMB shares responsibility for assessment of data related to study conduct with the research team, and, to some extent, with the IRB, and reviews this data in addition to data on effectiveness and safety. The data on study conduct may include:

- Rates of recruitment, ineligibility, noncompliance, protocol violations and dropouts, overall and by study site;
- Completeness and timeliness of data;
- Degree of concordance between site evaluation of events and centralized review;
- Balance between study arms on important prognostic variables;
- Accrual within important subsets.

The DSMB issues recommendations when there are safety concerns.

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1 The quality of the study and its ultimate ability to address the scientific questions of interest
• Consideration of external data

The DSMB may be asked to consider the impact of external information on the monitored study, when unexpected safety issues arise in related study and the research team may bring the data to the DSMB attention, or when the new data is publicly reported.

The DSMB may decide to recommend changes to the study design, including changes to the informed consent form, or sending letters to the study participants to disclose the new results, and DSMB’s access to unblinded data is essential to making the best decision.

The external data and DSMB’s access to unblinded data may have undesirable results, because DSMB is aware of the interim results and severely damage the credibility of the study and interpretation of final results.

The principle that interim protocol changes should not be influenced by emerging results has implications for the research team, who would initiate requests for protocol changes, the funding agency program and the Qatar SCH staff, who would need to evaluate any such requests for protocol changes. Research teams who wish to have the ability to request interim protocol changes without raising concerns about biasing the study should establish procedures to minimize bias, such as ensuring that they are completely unaware of unblinded comparative data. If the study is performed with blinded treatment allocation, and access to unblinded data is limited to the DSMB, making such changes as requested by the research team is straightforward.

If treatment allocation is not blinded, it is more difficult to maintain confidentiality of interim comparative results, as funding agency program will be reviewing data on each case. In such circumstances it may be very advantageous for the research team to set up a "firewall" to ensure that those who would be proposing interim protocol changes based on external data are insulated from knowledge of interim comparative results. To avoid any influence of interim data on consideration of protocol changes, SCH staff will also generally remain blinded to the interim results.

• Making recommendations to the research team

The DSMB can make recommendations in writing or orally and it should offer the study team the opportunity to ask questions and discuss the recommendations.

Recommendations for modifications are best accompanied by the minimum amount of data required for the research team to make a reasoned decision about the recommendation, and the rationale for such recommendations should be as clear and precise as possible. Research teams may wish to develop internal procedures to limit the interim data released by a DSMB after a recommendation until a decision is made regarding acceptance or rejection of the recommendation, to facilitate maintaining confidentiality of the interim results should the trial continue. A DSMB should document its recommendations, and the rationale for such recommendations, in a form that can be reviewed by the research team and then circulated, if and as appropriate, to IRBs, funding agency program, the Qatar SCH, and/or other interested parties.
DSMB recommendations and reporting requirements

All clinical trials conducted in Qatar are subject to safety reporting requirements. These requirements include prompt reporting to the Qatar SCH of certain serious and unexpected events. The research team, through its institutional official, is responsible for notifying the Qatar SCH in case of a serious adverse event potentially related to the research study.

When both the research team and the DSMB conclude that the increased rate of serious unanticipated adverse events is associated with the study, the finding, and support for the finding (which could include the DSMB report, any analysis, and pertinent data) would need to be submitted as a serious unexpected adverse experience.

Findings conveyed to research team by a DSMB as part of a recommendation to modify the trial could therefore mean that serious and unexpected events were occurring, and the research team would consequently be required to report an analysis of these events to the Qatar SCH and to all interested parties, including the funding agency program. The research team is generally responsible for reporting such findings to the approving IRB.

The research team should inform the Qatar SCH, the IRB and the funding agency program about all recommendations related to the safety of the study participants.

Acknowledgments:

Adapted from US Food and Drug Administration Guidance for Clinical Trial Sponsor - Establishment and Operation of Clinical trial Data Monitoring Committees; clinicaltrial.gov; and NIH Guide: Policy for Data and Safety Monitoring.