HANDBOOK
for
Research Ethical Rules and Regulations

Spring 2009

Acknowledgement

The Ethical policies and procedures at Qatar University have been developed by the QU Research Ethics Committee (REC) members. The current Research Ethics Handbook, however, has been compiled by Dr. Bahaa Darwish (Professor of Human Sciences and a member of Research Ethics Committee).We would like to extend our deep appreciation for Dr. Darwish and for all committee members and we would like to thank them for their hard work without which finalizing this handbook would not have been possible.

QU Research Ethics Committee (REC) members :

Dr. Khaled Al-Ali	Chair
Dr. Bahaa Darwish	Member
Dr. Hamda Al Naimi	Member
Dr. Sayed Goda	Member
Dr. Mariam Al-Ali	Member

Preface

Qatar University, represented by its Office of Research, has set, as part of its mission, to promote and strengthen research activity in the University to achieve excellence in research. Such research, as set in the QU Research Policies drafted by the Research Policies Committee, should serve a legitimate purpose and be consistent with the university's mission and the national requirements. Achieving such goals requires, in addition to research policies, ethical rules and regulations to ensure that researchers comply to generally accepted scientific principles and refrain from unacceptable practices, and that all proposed research is carried out safely and ethically in accordance with national and international standards.

This document, entitled “Handbook for Ethical Rules and Regulations for Research”, is a briefing of the original text: "Ethical Rules and Regulations for Research", that aims at formulating such regulations that apply to all researchers within Qatar University. This handbook gives a briefing of each of the five main parts of the original text: the generally accepted common scientific principles that researchers in all branches of, social and natural, sciences are expected to comply with, the guidelines for research involving human subjects that are based on the two documents: "Rules and Regulations for Research" of Hamad Medical Corporation (issued 2000), and "Research Policies, Procedures and Guidelines" of Shafallah Genetics Medical Center, (issued 2007), that, in turn, are based on the most famous international guidelines: the Nuremberg Code (1947), the Belmont Report(1979), Declaration of Helsinki (1964, amended 2000), the Canadian Tri-Council Policy Statement (1999), and the WHO recommendations presented in “ Proposed International Guidelines on Ethical Issues in Medical Genetics and Genetic Services”, (1998) and “Review of Ethical Issues in Medical Genetics and Genetic Services” (2003), the guidelines for using animal in research that regulate the use of animals in behavioral, physiological, pathological, toxicological, and therapeutic research. These guidelines are mainly adopted from the guidelines developed by the Council for International Organizations of Medical Sciences (CIOMS) 1985 , the guidelines regarding recombinant DNA research that regulate recombinant DNA research, which aims at specifying practices for constructing and handling: (i) recombinant deoxyribonucleic acid (DNA) molecules, and (ii) organisms and viruses containing recombinant DNA molecules that are based on the National Institutes of Health Guidelines for Research Involving Recombinant DNA Molecules

(1998), and, finally, the regulations regarding hazardous materials and radiation that comply with the commonly accepted international regulations of the toxic and hazardous substances.

For detailed information about regulations of any of the above parts that comprise this handbook, scientists are recommended to refer to the original text mentioned above.

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1. Principles of Science

1.1. Objectivity

The prima facie principle for the practice of science is objectivity. Objectivity is dealing with facts without interference of personal feelings, opinions or attitudes, to avoid all sorts of prejudices or biases. Scientists should refrain from fabricating data, changing data or results, and should be objective in all research steps, in collecting data, analysis and interpretation. As complete objectivity is impossible, scientists should be aware of, and strive to be committed to, the limitations their methods have for finding knowledge. Scientists should be also honest about their funding mechanisms and their commercial interests as these can influence the objectivity of science.

1.2. Cautiousness

Scientists should avoid erroneous results in research. They should strive to lessen the human, experimental and methodological errors to the minimum and avoid self-deception, bias and conflict of interests. This can be achieved by their continuous strive to be skeptic, critical and cautious.

1.3. Openness

Scientists should value, and be committed to, the principle of open research to maintain the advancement of knowledge, with some exceptions (e.g. military secrets). The principle of open research includes the scientists' exchanging data, results, methods, ideas and techniques. Scientists should also be open to criticism and peer review. Openness in science protects science from being dogmatic or uncritical, and helps create an atmosphere of truth and co-operation. Scientists have the ethical obligation to keep, as a sacred trust, the privileged communication of research findings given to them by colleagues prior to public distribution of this knowledge (e.g. for purpose of evaluation for publication or funding), otherwise it will encourage secrecy in science which, in turn, will impede the development of science, as well as, undermining the public trust in science.

1.4. Research Freedom and Social Responsibility

As a general rule, scientists are granted the freedom to pursue knowledge, to seek new ideas and examine the old ones. Placing too much restriction on new ideas may prevent advances in knowledge. However, the goal of science is to advance human health and welfare of all human beings. Therefore, scientists and the scientific community should bear and accept the responsibility for the consequences of their explorations by sticking only to those with social benefits and the minimum harm.

1.5. Promotion of Knowledge

Scientists are committed to a lifestyle of learning and teaching. They should make sure that they know how to practice good science as well as remaining current with developments in their field. Scientists should also transmit their knowledge, as well as teach future generations of scientists how to do good science. They should attract as many people as possible to the scientific profession to guarantee the development and promotion of science.

1.6. Compliance to the Law

All people, including scientists, have the ethical obligation of following laws. Science will suffer a great loss if scientists violate laws, as they may be arrested, grants withdrawn, scientific equipments seized and the public trust in science and scientists is undermined. In addition, there are specific laws that regulate scientific research that scientists have to comply to, like the laws that regulate the use of hazardous material, the use of animals and humans in research and methods of waste disposal as well as laws regulating printed materials and patents.

1.7. Equity

All scientists should be granted equal chances to do science, to pursue knowledge regardless of age, race, gender or nationality. All hypothesis, ideas or methods should be reviewed for originality, quality, efficiency or/ and benefit regardless of who they are produced by. Science produced by scientists from different social and cultural environments achieves the variety necessary for the advance of knowledge. All sorts of prejudice towards a certain race, age, gender or nationality will undermine the principle of fairness or equity that is necessary for the development of science.

1.8. Respect

The scientific community is based on the principles of co-operation and trust that may collapse if scientists don't mutually respect one another, and thus the social enterprise of science will dissociate, leading to an apparent delay in achieving the scientific goals. Therefore, scientists should mutually respect one another. Scientists' mutual respect includes abstention from harming one another, psychologically or physically, from the misuse of one another's experiments or results. Scientists should also treat associates and trainees with respect, encourage them and give credit for their contributions. In the fields of science where laboratory work is involved, scientists have responsibility for the health and welfare of their employees and trainees; therefore, they should seek to minimize any potential risk, informing their employees and trainees of these risks.

1.9. Respect for subjects

Though the goal of science is to advance human health and welfare of all human beings, scientists should uphold the highest ethical standards that respect all living beings, with profound respect granted to human life and dignity. In case of using animal subjects in research, it is the duty of scientists to show a peer-reviewed scientific rationale for the purpose and proposed use, justification of the species and number needed, and assurance that there are no other less-invasive or non-animal alternatives to answer the experimental question, minimizing as much as possible the suffering and harm to animals used in research. In case of using human subjects, the highest ethical standards, for which, are codified in the Nuremberg Code (1946-49), the Belmont Report (1979), and the Declaration of Helsinki (1964, amended in 2000).

2. Guidelines for Research Involving Human Subjects

2.1. Requirements of the Research Involving Human Subjects

2.1.1. General Requirements

a. All research that is to be conducted on human subjects must be submitted to the Office of Academic Research (OAR) for review of its scientific merit and to the Research Ethics Committee (REC) for ethical acceptability

b. The (REC), one of the standing committees that support the (OAR), is charged to evaluate the religious, social and ethical aspects of all research proposals involving human subjects, animal subject, and hazardous materials that are undertaken by members of, or within, Qatar University.

c. Human subject is defined as an individual about whom an investigator obtains (1) data through intervention or interaction with the individual or (2) identifiable private information (e.g. medical records).

d. In reviewing research protocols involving human subjects, the (REC) is to consider the expertise and experience of the investigators as a major indicator of the minimal risks the subjects might be exposed to and the maximum benefits resulting from the study.

e. Principal investigators and co-investigators are responsible for having knowledge of all study procedures as well as the risks, benefits and adverse effects. (This information is provided to subjects as part of the informed process).

2.1.2. Rules and Regulations

The Research Ethics Committee must determine that all of the following requirements are satisfied before it can approve the initiation of research on human subjects. These requirements comply with the National Health Authority in Qatar requirements.

a. Risks to subjects are minimized:
   - *by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and*
   - *by using, whenever appropriate, procedures already being performed on the subjects for diagnostic or treatment purposes.*

b. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may be reasonably expected to result. In evaluating risks and benefits, the REC 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 Research Ethics Committee 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.

c. Selection of subjects is equitable. In making this assessment, the Research Ethics Committee 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, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

d. Informed consent will be sought from each prospective subject or the subject's legally authorized representative and documented, in accordance with, and to the extent required by these rules and the Rules and Regulations of Research Committee. (See the requirements for informed consent, and waiver of signed consent).

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

f. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

g. When some, or all, of the subjects are likely to be vulnerable to coercion or undue influence, such as children, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have to be included in the study to protect the rights and welfare of these subjects.

2.2. Research Review

2.2.1. Research that may be Reviewed by the REC by an Expedited Review Process

All research in human subjects other than those which the Research Ethics Committee has the authority to review and approve by expedited review, or is exempt from Research Ethics Committee review, must be reviewed at a convened meeting of the full Research Ethics Committee. Categories of research that REC has the authority to approve by expedited review are itemized below.

A) Categories of New and Continuing Research that May be Reviewed by the REC through an Expedited Review Procedure:

1. <u>Clinical studies of drugs and medical devices only when condition (a) or (b) is met.</u>

a. Research on drugs that are registered at the National Health Authority of Qatar. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review).
b. Research on medical devices that are cleared /approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. <u>Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture, according to the research proposal, is as follows:</u>

a. From healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or

b. From other adults and children, considering the age, weight and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency in which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

3. <u>Prospective collection of biological specimens for research purpose by noninvasive means</u>

a. Hair and nail clippings in a non-disfiguring manner;

b. Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;

c. Permanent teeth if routine patient care indicates a need for extraction;

d. Excreta and external secretions (including sweat);

e. Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum base or wax or by applying dilute citric solution to the tongue;

f. Placenta removed at delivery;

g. Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;

h. Supra and sub gingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;

i. Mucosal and skin cells collected by buccal scrapping or swab, skin swab, or mouth washings;

j. Sputum collected after saline mist nebulization.

4. <u>Collection of data through non-invasive procedures (not involving general anesthesia or sedation)</u>

These are routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for

expedited review, including studies of cleared medical devices for new indications).

Examples:

a) Physical sensors that are applied either to the surface of the body or at a distance and that do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy

b) Weighing or testing sensory acuity

c) Magnetic resonance imaging

d) Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electro retinography, ultra sound, diagnostic infrared imaging, Doppler blood flow, and echo cardiography;

e) Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight and health of the individual.

5. Research involving materials (data, documents, records or specimens) that have been collected or will be collected solely for non - research purposes (such as medical treatment or diagnosis)

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.

8. Continuing review of research previously approved by the convened REC as follows:

a. where (1) the research is permanently closed to the enrollment of new subjects; (2) all subjects have completed all research related interventions; and (3) the research remains active only for long term follow up of subjects; or

b. where no subjects have been enrolled and no additional risks have been identified; or

c. where the remaining research activities are limited to data analysis

B Modifications in Research that May or May not be Reviewed by the REC through an Expedited Review Procedure during an Approved Project Period:

The RC Chairman is authorized to approve by expedited review of any change that falls into expedited categories 1 through 7, with the exception of interviews and surveys with children.

Modifications to the protocol or consent form that the REC Chairman is **NOT** authorized to approve by expedited review include:

a. Addition of a new drug

b. Addition of a new device

c. Addition of an invasive procedure

d. Increase in medication dose or a decrease in dose that may increase the risk

e. Addition of vulnerable subjects as a study population

f. Prolongation of a patient's participation in the study other than for observational purposes

g. Change in the inclusion/exclusion criteria which may involve incorporation of populations at greater risk

h. Identification of new potentially significant risks

i. Collection of additional blood samples that exceed the limits set in expedited category

2.2.2. Research that may be Exempted from REC Review

Research protocols that may be eligible for exemption from REC review must be submitted to the OAR for registration and approval by OAR and must contain a statement that justifies the request for exemption.

NOTE: **NONE OF THE EXEMPTIONS APPLIES TO RESEARCH ON PRISONERS, FETUSES, PREGNANT WOMEN OR HUMAN IN VITRO FERTILIZATION.**

NOTE: **EXEMPTION (2) CANNOT BE USED FOR RESEARCH ON MINORS IF IT INVOLVES SURVEYS OR INTERVIEW PROCEDURES OR OBSERVATION OF PUBLIC BEHAVIOR.**

Categories of research that may be exempted from REC review

a. Research involving the collection or the study of existing data, documents, records, pathological 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, DIRECTLY OR THROUGH IDENTIFIERS LINKED TO THE SUBJECTS.**

b. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior UNLESS:

   - Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and

   - Any disclosure of the human subject's 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.

c. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as:

   - Research on regular and special education instructional strategies, or
   - Research on the effectiveness or of the comparison among instructional techniques, curricula, or classroom management methods.

d. Research and demonstration projects which are conducted by, or subject to, the approval of the National Health Authority, and which are designed to study, evaluate or otherwise examine:

   - Public benefit or service programs;
   - Procedures for obtaining benefits or services under those programs;
   - Possible changes in or alternatives to those programs or procedures; or
   - Possible changes in methods or levels of payment for benefits or services under those programs.

2.2.3. Suspension / Termination of Research Projects by the REC

The OAR rules and regulations require that all research on human subjects be reviewed by the REC annually. Consequently, administrative extensions **cannot** be granted beyond the approved project period (maximally one year). Enrollment of new subjects and/or, performance of research beyond the REC approved project period are prohibited by OAR regulations. Accordingly, any project that has not received the OAR's final approval for continuation, prior to the project's expiration date, will automatically be suspended.

For the safety of subjects who are enrolled in research projects in which investigational therapy is being administered, the OAR do short-term continuation of the therapy beyond the RC approval date ONLY IF abrupt cessation of that therapy would be detrimental to the patient's health and upon the approval of Health Authorities. Although all Investigators are reminded of the upcoming expiration of REC approval of their projects, it is the investor's ultimate responsibility to ensure that the REC approval is continuous. If OAR approval has expired, and a research subject requires the investigational therapy, then, it is critically important that the Investigator rapidly reinstates the research project.

2.2.4. Reinstatement

Reinstatement and approval of a research project require that the REC review and approve the following at a convened meeting of the REC:

a. A complete progress report;
b. A memo to the Director of OAR that incorporates the following information:

- An explanation of circumstances that led to the failure to submit the application at the appropriate time;
- A statement indicating whether patients were enrolled during the period that the project was not OAR approved
- A statement indicating the number of patients maintained on a therapeutic intervention after the expiration date of RAC approval and why abrupt cessation of that therapy would have been detrimental to each patient's health.

NOTE: Funding agencies and sponsors in general require that the OAR notify them of any suspension or termination of a research project. Consequently, it is clearly in the best interest of the research subjects and all investigators that progress reports receive OAR approval prior to their date of expiration of OAR approval.

2.3. Informed Consent

2.3.1. Ethical Principles of Informed Consent

- **Respect of the rights, dignity and safety**

  Respect of the rights, dignity and safety of the subjects must be the primary determinant of the researcher's actions.

  As autonomous individuals, research subjects have **a right to be fully informed** about the nature of the research and extent of their participation. They must be free to agree, or to refuse, to participate in the research. Patients may feel obliged to agree because their physicians have asked them to participate. Co- workers in an Investigator's laboratory, office or clinic may agree in order to preserve the good will of the Investigator.

  Prospective research subjects must be re-assured, verbally, that refusal to participate will in no way affect their care. In addition, the RC strongly feels that workers directly supervised an investigator should not be recruited to serve as control subjects. Co-Investigators and colleagues (in the specific sense of having a comparable position in the institution) are appropriate potential control subjects.

  In addition, subjects must be free to withdraw their participation at any time.

  Circumstances, which could put subjects at risk if they withdraw and procedures of withdrawal, must be described in the consent document.

- **Who can give consent?**

  Subjects who are fully informed about the protocol and have had all of their questions answered.

- **Who can solicit an informed consent? What is the process?**

One who is completely familiar with all aspects of the study that relates to the subjects participation including the rationale for doing the study; eligibility requirements and exclusion criteria; the procedures to be used; costs, risks and benefits of participation; the time frame of participation; alternatives to participation; etc.

Informed consent must also be obtained at a time and in an environment which allows the potential subject to review, carefully and fully, the information provided (verbally and in writing), to have all questions answered fully and to consider the pros and cons of participation before making a decision.

2.3.2. Recruitment of Subjects

Protocols submitted to the OAR for review and approval must specify how subjects will be identified and recruited.

Patients expect that **information on their medical condition will be kept confidential**, although an investigator may access this information in the conduct of a OAR approved research project. However, many patients would consider it a serious breach of confidentiality and of medical ethics that someone not involved in their care obtained this information and contacted them. For this reason,(permission to recruit a patient as a subject in a research study should be **obtained from the patient's physician** before the patient is contacted.

Where possible, the physician should first get permission from the potential subject, to allow the Investigator to contact him/her. If this is impractical, a letter, email or a message can be sent out by the physician informing the patient that the Investigator would like to contact him/her. The letter should include a reply card to be returned granting or refusing permission.)

Special circumstances:

If the nature of a study makes use of these procedures unrealistic, this must be fully justified to the REC by the Investigator.

Such studies may require very narrow time windows for collection of data or involve large numbers of physicians and potential subjects.

In addition, it must be clear that the patients would very likely not be distressed by being contacted by someone not involved in their care. For such studies, individual or *blanket permission may be obtained from the physician(s)

(preferably in writing) to contact a particular patient or all of the physician's eligible patients. The Investigator may, then, contact the patient(s) directly, without previous notification, indicating that their physician had given permission for the contact. If blanket permission is obtained and used, the Investigator must inform the physician each time that a patient is contacted.

Recruitment of Family Members:

If recruitment of family members is planned, for confidentiality reasons, the index patient should not be asked to provide the name of the family member(s) directly to the Investigator. Rather, the index patient should be asked to contact family members. If the family member is willing to speak with the Investigator, then the family member should be asked to contact the Investigator. Therefore, when research will include family members the protocol and consent form must indicate how family members will be contacted.

2.3.3. Advertisement for Research Subjects

All forms of advertising or dissemination of information for the purpose of recruitment of subjects into a research protocol, including newspaper advertisements, posters, and fliers, or newspaper articles which include recruitment information must be approved by the OAR prior to distribution or publication of the material.

In addition, letters to fellow physicians, both within and outside of the institution, must be approved. The following information must be contained in the advertisement:

- The purpose of the study
- The characteristics, which would qualify an individual for enrollment
- A straightforward description of any and all benefits to the subjects
- The OAR number of the protocol and the expiration date
- The name and number of whom to contact for further information

Nothing in the text should serve as an undue inducement to potential subjects to enter the study. Such inducements might include claims (explicit or implicit) about safety or efficacy of an investigational drug or device, equivalence or superiority to existing treatments, or closer monitoring of the patients condition.

The availability of compensation for time and effort related to participation can be included without mention of any specific amounts.

2.3.4. Guidelines for Consent Documents

NOTE:

Only consent documents officially dated with exclusive OAR approval dates and stamped may be used in the conduct of human subject studies. (for details of the effective period of a signed consent, see the original text: 7.3.9)

The forms used in soliciting consent must provide, in writing, all of the information that the subject would reasonably want about the study and the extent of his / her involvement in it.

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 informed consent, whether oral or written, may not 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 the agents, from liability for negligence.

By completing these documents, as suggested below, all of the international requirements for informed consent should be fulfilled.

2.3.5. Who may obtain consent

Obtaining informed consent from a subject is the responsibility of the Principal Investigator. The Principal Investigator may delegate this task to a named co-investigator on the project who is familiar with all aspects of the information to be provided the subject.

For studies involving more than minimal risk, or procedures other than those performed for routine clinical care examination, consent should be obtained by the PI or the Investigator performing the procedure.

(For details, see the original text, 7.3.5).

2.3.6. When and Where Consent should be solicited

The setting in which consent is requested and obtained must be one in which the potential subject can consider the request as an autonomous individual, free from time constraints or a sense of obligation or dependency.

(For details, see the original text, 7.3.6)

2.3.7. The Consent Process

- ***Consent form should be made in 3 copies***
- The consent form must be signed by the potential research subject(s) and the person obtaining consent (Investigator or delegate).

One copy of the full completed and signed consent form must be given to the subject, and a second copy must be placed in the patient's chart. The original completed and signed consent form must be retained for inclusion in the **Principal Investigator's research records**.

(For details, see the original text, 7.3.7 & 7.3.8)

2.4. Modification of the Informed Consent (Waiver of Informed Consent)

In general, OAR bylaws require that research subjects sign a consent document. Under very specific circumstances, the REC may totally waive the requirement for obtaining informed consents only when **ALL** of the following are applicable:

1- No more than minimal risk to the subject is involved
2- The research could not practically be carried out without the waiver
3- The research will not adversely affect the rights and welfare of the subject
4- The subjects will be provided with additional pertinent information after participation, whenever appropriate
5- Chart reviews & retrospective studies

(For details, see the original text, 7.4 & 7.5)

2.5. Pediatric Subjects in Research Studies

The enrollment of pediatric subjects requires that the research participant information sheet worded as “You/Your child”. This is required because permission must be obtained from the parent and, in instances as specified below, the assent of the child must be obtained. In addition, documentation must be kept that assent was obtained freely and without coercion.

2.5.1. Minors and vulnerable subjects

Vulnerable subjects encompass children, pregnant women, fetuses, prisoners, educationally or economically disadvantaged persons and individuals with diminished mental capacity.

If vulnerable subjects are to be recruited and subsequently enrolled in to a research project they must, of course, be provided with all of the protections that are required for every other research project.

Furthermore, additional, even more rigorous, protections must be provided for them:

- The investigator must ensure that:

    a. *the research might not equally well be carried out with normal non-vulnerable persons*
    b. *the purpose of the research is to obtain knowledge relevant to the particular health needs of these people and to the pregnant 's fetus(in case of pregnant women).*

As for children, there are additional protections for them.

(For details, see the original text, 7.6).

2.5.2. Pediatric Assent Guidelines

All Pediatric research subjects should be fully informed about a research study, in language appropriate for their age, maturity and previous experiences, whether assent is to be requested or not.

This information can be provided verbally and should include all tests and procedures to be performed, frequency of interventions, duration of participation in the study, risks, discomforts and potential benefits.

The child should be encouraged to ask questions, all of which should be answered.

Depending on the nature of the study and on the maturity, psychological state and previous experiences of the child, assent should be obtained, and documented, from children ages 14 and older.

For children ages 13 – 14, assent should be obtained and documented unless the child's pediatrician considers him/her to be too immature to provide a true assent. Children age 7 – 11 should be fully informed about the research, using language appropriate to their age

or maturity, and documented assent should be obtained from those deemed capable of making a meaningful decision.

Below age 7, information about study should be provided in a manner appropriate to child's age, but documented assent need not be obtained.

When enrolling minors into therapeutic research studies of potential therapies for their severely debilitating or life – threatening illness, the patients should be fully informed about the nature of the study and should be included in discussions of their participation, as is common pediatric practice. In such situations, however, documented assent need not be obtained since the wishes of parents or guardian would prevail. It would be inappropriate to ask for assent since a refusal by the child could be over – ruled by the parents or guardian.

2.5.3. Documentation of Assent

Assent given by the subject must be documented by a witness who is not a family member and not associated with the research study. The signed certification must be retained in the research study records.

If the documented assent is not obtained from minors, ages 12 and older, the reason for not obtaining assent must be noted in the research record for that subject.

3. Guidelines for using Animals in Research

An Experimental Animal includes any living non-human vertebrate, non-human vertebrate fetus, or any other animal species which has a functional nervous system that allows the animal to experience pain in much the same way that any vertebrate might experience it.

Most of these guidelines are adopted from guidelines developed by the Council for International Organizations of Medical Sciences (CIOMS) 1985 and have gained a considerable measure of acceptance internationally.

Preface:

Research involving animal models has made significant contributions to biological knowledge and to the welfare of man and animals, mainly in the treatment and prevention of diseases. Many basic biological researches as well as applied researches lead to important advances in medical science. There is still a vital need for basic and applied research to discover ways of control, prevention, and treatment of diseases.

The use of animals in behavioral, physiological, pathological, toxicological, and therapeutic research entails responsibility for their welfare. Same responsibility is applied in using animals for experimental surgery or surgical training and for testing drugs and biological preparations.

These guiding principles here provide a framework for more specific provisions applied by QU Animal Facility. They apply, not only to biomedical research but also to all uses of vertebrate animals for other biomedical purposes, including the production and testing of therapeutic, prophylactic, and diagnostic substances, the diagnosis of infections and intoxications in man and animals, and to any other procedures involving the use of intact live vertebrates.

3.1. Basic Principles

I. The advancement of biological knowledge and the development of improved means for the protection of the health and well-being both of man and of animals require recourse to experimentation on intact live animals of a wide variety of species.

II. Methods such as mathematical models, computer simulation and *in vitro* biological systems should be used wherever appropriate. (as will be explained in details in 4.2).

III. Animal experiments should be undertaken only after due consideration of their relevance for human or animal health and the advancement of biological knowledge.

IV. The animals selected for an experiment should be of an appropriate species and quality, and the minimum number required to obtain scientifically valid results.

V. Investigators and other personnel should never fail to treat animals as responsive, and should regard their proper care and use the prevention or minimization of discomfort, distress, or pain as ethical imperatives.

VI. Investigators should assume that procedures that would cause pain in human beings cause pain in other vertebrate species, although more needs to be known about the perception of pain in animals.

VII. Procedures with animals that may cause more than momentary or minimal pain or distress should be performed with appropriate sedation, analgesia, or anesthesia in accordance with accepted veterinary practice. Surgical or other painful procedures should not be performed on unanesthetized animals paralyzed by chemical agents.

VIII. Where waivers are required in relation to the provisions of article VII, the decisions should not rest solely with the investigators directly concerned but should be made, with due regard to the provisions of articles IV, V, and VI, by a suitably constituted review body (QU Animal Facility). Such waivers should not be made solely for the purposes of teaching or demonstration.

IX. At the end of, or, when appropriate, during an experiment, animals that would otherwise suffer severe or chronic pain, distress discomfort, or disablement that cannot be relieved should be painlessly killed.

X. The best possible living conditions should be maintained for animals kept for biomedical purposes. Normally the care of animals should be under the supervision of veterinarians having experience in laboratory animal science. In any case, veterinary care should be available as required.

XI. It is the responsibility of the director of QU Animal Facility and there after the department or the Principle Investigator using animals to ensure that investigators and personnel have appropriate qualifications or experience for conducting procedures on animals.

XII. In case of lacking appropriate qualifications or experience for handling or conducting procedures on animal; adequate training will be provided by QU animal facility including the proper and humane concern for the animals under their care.

3.2. Special Provisions

Where they are quantifiable, rules for the following provisions should be established by the director of QU Animal Facility.

3.2.1. Acquisition

Specialized breeding establishments are the best source of the most commonly used experimental animals. Nonspecifically bred animals may be used only if they meet the research requirements, particularly for health and quality, and their acquisition is not in contradiction with national legislation and conservation policies.

3.2.2. Transportation

Where there are no regulations or statutory requirements governing the transport of animals, it is the duty of the director of the animal Facility or department using animals to emphasize to the supplier and the carrier that the animals should be transported under humane and hygienic conditions.

3.2.3. Housing

Animal housing should be such as to ensure that the general health of the animals is safeguarded and that undue stress is avoided. Special attention should be given to the space allocation for each animal, according to species, and adequate standards of hygiene should be maintained as well as protection against predators, vermin, and other pests. Facilities for quarantine and isolation should be provided. Entry should normally be restricted to authorized persons.

3.2.4. Environmental Conditions

Environmental needs such as temperature, humidity, ventilation, lighting, and social interaction should be consistent with the needs of the species concerned. Noise and odour levels should be minimal. Proper facilities should be provided for the disposal of animals and animal waste.

3.2.5. Nutrition

Animals should receive a supply of foodstuffs appropriate to their requirements and of a quality and quantity adequate to preserve their health and they should have free access to potable water, unless the object of the experiment is to study the effects of variations of these nutritional requirements.

3.2.6. Veterinary Care

Veterinary care, including a programmed of health surveillance and disease prevention, should be available to QU Animal Facility or departments using animals for biomedical purposes. Sick or injured animals should, according to circumstances, either receive appropriate veterinary care or be painlessly killed.

3.2.7. Records

Records should be kept of all experiments with animals and should be available for inspection. Information should be included regarding the various procedures which were carried out and the results of post mortem examinations if conducted.

3.3. Monitoring of the Care and use of Animals for Experimentation

- Wherever animals are used for biomedical purposes, their care and use should be subject to the general principles and criteria set out above as well as to existing national policies or QU Animal Facility. The observance of such principles and criteria should be encouraged by procedures for independent monitoring.

- Monitoring procedures should have as their objectives the encouragement of appropriate care and use before, during, or after experimentation. They should be established by: specific legislation (Director of QU Animal Facility) laying down standards and providing for enforcement by an official inspectorate; by more general legislation requiring biomedical research institutions to provide for peer review in accordance with defined principles and criteria, sometimes with informed lay participation; or by voluntary self-regulation by the biomedical community. There are many possible variants of monitoring systems, according to the stress laid upon legislation on the one hand, and voluntary self-regulation on the other.

3.4. Methods not involving animals “Alternatives”

- There remain many areas in biomedical research which, at least for the foreseeable future, will require animal experimentation. An intact live animal is more than the sum of the responses of isolated cells, tissues or organs; there are complex interactions in the whole animal that cannot be reproduced by biological or nonbiological "alternative" methods. The term "alternative" has come to be used by some to refer to a replacement of the use of living animals by other procedures, as well as methods which lead to a reduction in the numbers of animals required or to the refinement of experimental procedures.

- The experimental procedures that are considered to be "alternatives" include non-biological and biological methods. The non-biological methods include mathematical modeling of structure-activity relationships based on the physico-chemical properties of drugs and other chemicals, and computer modeling of other biological processes. The biological methods include the use of micro-organisms, *in vitro* preparations (subcellular fractions, short-term cellular systems, whole organ perfusion, and cell and organ culture) and under some circumstances, invertebrates and vertebrate embryos. In addition to experimental procedures, retrospective and prospective epidemiological investigations on human and animal populations represent other approaches of major importance.

- The adoption of "alternative" approaches is viewed as being complementary to the use of intact animals and their development and use should be actively encouraged for both scientific and humane reasons.

4. Guidelines Regarding Recombinant DNA Research

4.1. Recombinant DNA Molecule

Recombinant DNA molecules are defined as either: (i) molecules that are constructed outside living cells by joining natural or synthetic DNA segments to DNA molecules that can replicate in a living cell, or (ii) molecules that result from the replication of those described in (i) above.

Synthetic DNA segments which are likely to yield a potentially harmful polynucleotide or polypeptide (e.g., a toxin or a pharmacologically active agent) are considered as equivalent to their natural DNA counterpart. If the synthetic DNA segment is not expressed *in vivo* as a biologically active polynucleotide or polypeptide product, it is exempt from these Guidelines.

Genomic DNA of plants and bacteria that have acquired a transposable element, even if the latter was donated from a recombinant vector no longer present, are not subject to these *Guidelines* unless the transposon itself contains recombinant DNA among others.

4.2. Scope of the Guidelines

- ***Purpose***

  The purpose of the Qatar University Guidelines regarding Biotechnology/ genetic Engineering research is to specify practices for constructing and handling: (i) recombinant deoxyribonucleic acid (DNA) molecules, and (ii) organisms and viruses containing recombinant DNA molecules.

  Any recombinant DNA experiment, which according to the Qatar University Guidelines requires approval by the Research Ethics Committee, must be submitted to OAR of the Qatar University for review and approval. Once

approvals, or other applicable clearances have been obtained, the experiment may proceed.

- ***Compliance with the Qatar University Research compliance Guidelines***

  As a condition for Qatar University Research Ethics Committee approval of recombinant DNA research, colleges and departments shall ensure that such research conducted, irrespective of the source of funding, shall comply with the University guidelines.

  Information concerning noncompliance may be brought forward by any person. It should be delivered to both the department concerned and Qatar University**.** The University, generally through the Research Ethics Committee, shall take appropriate action.

  The essential elements of the four biosafety levels for activities involving infectious microorganisms and laboratory animals are summarized in Tables 1 of this section and Section IV. The levels are designated in ascending order, by degree of protection provided to personnel, the environment, and the community.

4.3. Table 1: Summary of Recommended Biosafety Levels for Infectious Agents

BSL	Agents	Practices	Safety Equipment (Primary Barriers)	Facilities (Secondary Barriers)
1	Not known to consistently cause disease in healthy adults	Standard Microbiological Practices	None required	Open bench top sink required
2	Associated with human disease, hazard = percutaneous injury, ingestion, mucous membrane exposure	BSL-1 practice plus: Limited access Biohazard warning signs "Sharps"	Primary barriers = Class I or II BSCs or other physical containment devices used for all manipulations of agents that cause splashes or aerosols of infectious materials; PPEs:	BSL-1 plus: Autoclave available

		precautions Biosafety manual defining any needed waste decontamination or medical surveillance policies	laboratory coats; gloves; face protection as needed	
3	Indigenous or exotic agents with potential for aerosol transmission; disease may have serious or lethal consequences	BSL-2 practice plus: Controlled access Decontamination of all waste Decontamination of lab clothing before laundering Baseline serum	Primary barriers = Class I or II BCSs or other physical containment devices used for all open manipulations of agents; PPEs: protective lab clothing; gloves; respiratory protection as needed	BSL-2 plus: Physical separation from access corridors Self-closing, double-door access Exhausted air not recirculated Negative airflow into laboratory
4	Dangerous/exotic agents which pose high risk of life-threatening disease, aerosol-transmitted lab infections; or related agents with unknown risk of transmission	BSL-3 practices plus: Clothing change before entering Shower on exit All material decontaminated on exit from facility	Primary barriers = All procedures conducted in Class III BSCs or Class I or II BSCs in combination with full-body, air-supplied, positive pressure personnel suit	BSL-3 plus: • Separate building or isolated zone Dedicated supply and exhaust, vacuum, and decon systems Other requirements outlined in the text

(For detailed biosafety levels, their practices, safety equipment and laboratories facilities see the original text 9.3)

4.4. Risks Assessment

"Risk" implies the probability that harm, injury, or disease will occur. In the context of the microbiological and biomedical laboratories, the assessment of risk focuses primarily on the prevention of laboratory-associated infections. When addressing laboratory activities involving infectious or potentially infectious material, risk assessment is a critical and productive exercise. It helps to assign the biosafety levels (facilities, equipment, and practices) that reduce the worker's and the environment's risk of exposure to an agent to an absolute minimum. The intent of this section is to provide guidance and to establish a framework for selecting the appropriate biosafety level.

The laboratory director or principal investigator is responsible for assessing risks in order to set the biosafety level for the work. This should be done in close collaboration with the Institutional Biosafety Committee (and/or other biosafety professionals as needed) to ensure compliance with established guidelines and regulations.

In performing risk assessment, all the risk factors are first identified and explored. There may be related information available, such as this manual, the NIH Recombinant DNA Guidelines, the Canadian Laboratory Biosafety Guidelines, or the WHO Biosafety Guidelines. In some cases, one must rely on other sources of information such as field data from subject matter experts. This information is interpreted for its tendency to raise or lower the risk of laboratory-acquired infection.

The infectious agents whose risk is evaluated often will fall into the following discrete categories.

Materials containing known infectious agents
Materials containing unknown infectious agents
Materials containing recombinant DNA molecules
Materials that may or may not contain unknown infectious agents
In the absence of information that suggests an infectious agent, universal precautions are indicated.
(For details, see the original text, 9.4)

5. Regulations Regarding Hazardous Materials and Radiation

5.1. Definitions

(a) "**Banned chemical**" means a chemical which has, for health or environmental reasons, been prohibited for all uses by final governmental regulatory action.

(b) "**Severely restricted chemical**" means a chemical for which, for health or environmental reasons, virtually all uses have been prohibited nationally by final government regulatory action, but for which certain specific uses remain authorized.

(c) "**Hazardous material**" means a **material** which represents a threat to human or animal health or to the environment.

(d) **"Hazardous waste"** means a controlled product that is intended for disposal or is sold for recycling or recovery.

5.2. General Requirements

It is not possible to make any generalizations about the safety of all materials: one must consider each type of material separately, the risks of materials may be different according to the way of exposure, and the risks of exposure to manufactured materials may be different from the risks of exposure to the naturally occurring materials.

Each researcher must develop, document and routinely evaluate appropriate hazard control procedures and practices for all activity relating to the handling, use and storage of hazardous materials. Principal Investigator must ensure that routine workplace health and safety inspections, which would include monitoring the maintenance and use of personal protective devices, engineering controls and safety equipment, are conducted.

Materials	Recommendation
“Banned chemical"	Not acceptable to use
“Severely restricted chemical"	Certain specific uses remain authorized;
"Hazardous chemical"	All purchases of hazardous materials are appropriately reviewed for approval. This review must consider the quantity purchased, toxicity, and availability of appropriate storage and use facilities and equipment (i.e. fume hood). The section of the purchase requisition form labeled "Mark For" must state the name of the supervisor and the intended use location.

5.3. Identifications

Where possible, all hazardous materials must be identified on an inventory system to allow emergency response teams to have access to information about the location of hazardous materials and on the hazards they represent.

All researchers shall maintain a current chemical inventory of all chemical materials and biological agents indicating their exact location, means of storage, quantity, supplier or manufacturer’s name and hazard classification.

5.4. Storage

Hazardous materials must be stored in secure places in the laboratory (e.g. separate shelves, cabinets or cupboards) and segregated by chemical compatibility. Material Safety Data Sheets should be consulted for storage safety information.

5.5. Safety Data Sheet

Safety data sheets should be accessible to all users of all types of materials. This sheet must be obtained, reviewed by and available to employees prior to handing or using a hazardous material.

5.6. Experiments

Experiments and processes utilizing hazardous materials must not be left unattended unless appropriate safety provisions are made. The following precautions may be appropriate for common laboratory operations:

- Use closed systems with double-walled containment;
- Apparatus requiring coolant shall have automatic shutdown devices in the event of loss of coolant;
- heating mantles shall be restarted manually;
- heating apparatus shall be equipped with a thermostat;
- Experiments shall be identified with a contact name, 24 hour telephone number, and the nature of the hazards. A responsible party shall be available in the event of an emergency to attend to the experiment.

5.7. Labeling

When hazardous materials are received they must ensure that the products are labeled as prescribed:

a. **Product Identifier:** brand name, code name or number, chemical name, common name or trade name.

b. **Supplier Identifier:** the name of the supplier. A distributor can choose to use the original supplier identifier on his/her own.

c. **Hazard Symbol**: symbols corresponding to all the classes and divisions applicable to the product.

d. **Risk Phrases:** statements appropriate to the hazards of the classes and divisions which apply.

e. **Precautionary Measures**: precautions to be used during handling, storage and use.

f. **First Aid Measures**: action to minimize injury from accidental exposure to the product.

5.8. Hazardous Waste

Waste Disposal: Semi-annual chemical waste pick-up by a licensed carrier must be coordinated.

It is the responsibility of each researcher individual to know the possible dangers associated with any material being used or generated, and know how the material should be handled and disposed of before a research is begun.

Chemical waste to include:

- Highly Toxic Material.
- Used oil (handle the same as chemical waste).
- Biological/Infectious Waste.
- Fluorescent Bulbs and Ballast.
- Batteries.
- Lead-Based Paint.
- Radioactive waste, to include mixed (chemical and radiological), is the responsibility of the Radiation Safety Officer.
- Broken glass, whose only danger comes from its ability to inflict wounds, is not considered hazardous waste.

5.9. Reduce Risks

Each researcher must make every reasonable effort, to the extent practicable, to reduce risks by:

- Introducing appropriate procedures to minimize adverse health and environmental effects from materials being manufactured and managed, taking into account their entire life cycle, under both normal operating conditions as well as emergency situations.

- Developing safer packaging, and using clear and concise labeling, taking into account existing international scheme with respect to packaging and labeling.

- Take initiatives, to the extent possible, in following materials to the ultimate consumer, keeping track of any problems arising in actual using.

- When safe manufacture and management of a chemical, taking into account its entire life cycle, does not seem possible, voluntarily, take corrective action and help find solutions to difficulties.

5.10. Radiation

- All staff and visitors who use radioactive substances or ionizing radiation apparatus must have an appropriate radiation licence issued by the Supreme Council for the Environment and Natural Reserves to ensure that personnel who are involved in the use of radioactive substances receive adequate supervision and information, instruction and training.

- Prior to using ionizing radiation (e.g. gamma rays, x-rays, etc.) a written approval must be conducted by the University Radiation Protection Officer (URPO) to ensure that all radioactive substances are adequately controlled and accounted for.

- A definition of the harm, genetic changes and the level of changing in the environment must be determined.

- The use of ionizing radiation is justifiable such that the benefits it produces outweigh any detrimental effects.

- Doses are kept as low as reasonably achievable. In relation to a particular radiation source, the magnitude of the individual exposure and the number of people exposed should be kept as low as practicable.

- Doses are at all times maintained, at the, or below acceptable limits and under no circumstances should radiation doses exceed the recommended dose limits as set in NSW Radiation Control Regulation.

- Using human subject requires a full review by a qualified expert committee.

- Radioactive waste can only be disposed of when it has decayed to below a specific activity of 100 Becquerels per gram. The waste can then be given to the URPO.

- It is a requirement that radiation accidents are reported to the URPO.

Office of Academic Research

Qatar University

P. O. Box: 2713, Doha, Qatar

Telephone: +974 485 6346

Email: acdresearch@qu.edu.qa