



**THE RESEARCH ETHICS COMMITTEE (REC)
GUIDANCE IN THE CONDUCT OF RESEARCH AT KING FAISAL
SPECIALIST HOSPITAL & RESEARCH CENTRE**

Reviewed and Approved by:
THE RESEARCH ADVISORY COUNCIL
10 Shaban 1437 (17 May 2016)
Updated: 30 Jumada Al Awal 1438 (01 March 2017)

OVERVIEW

The King Faisal Specialist Hospital & Research Centre (KFSH&RC) guidelines, policies, and procedures related to all aspects of research particularly those involving human subjects are outlined in this document. This guidance and policy is in compliance with regulations of the Saudi National Committee of Medical and Bioethics (NCMB) and meets the international standards for the conduct of research including the Common Law and supports the principles outlined in the Belmont Report. KFSH&RC also holds a Federal Wide Assurance (FWA) Number from the United States Department of Health and Human Services which supports the conduct of federally funded clinical trials or internationally sponsored trials. The Research Ethics Committee (REC) is the approved Institutional Review Board (IRB) of record with the United States Department of Health and Human Services.

At KFSH&RC, all research activities including oversight of human subjects research, funded or non-funded, irrespective of risk, is under the purview of the Research Advisory Council (RAC) and its Committees. The RAC policies and guidelines apply to all KFSH&RC faculty, staff, affiliated faculty, students, and visitors conducting on site or off site nationally or internationally. The RAC has several committees under its purview; the Animal Care and Use Committee, Basic Research Committee, Clinical Research Committee, and Research Ethics Committee (REC). The REC serves as the IRB for the institution. (See Appendix 1)

The REC is charged with the responsibility of protecting the rights and welfare of human subjects involved in research. The number and composition of the REC members are in accordance with international guidelines. The members are appointed by the Chair of the Research Advisory Council (RAC) with recommendations from the members of the Council. Members are appointed for a renewable term. The Members include faculty with expertise in various disciplines engaged in human subjects' research from the Hospital, Research Centre, and community members. All members, whether regular or alternate, have full voting rights.

The REC may invite consultants with special expertise to assist from time to time with complex issues related to the conduct of research. Similarly, researchers may request or be invited to attend REC meetings to clarify issues that may arise regarding their proposals and or research activity. These consultants and researchers do not take part in committee deliberations or voting.

The REC reports to the Chief Executive Officer (CEO) of KFSH&RC. The Office of Research Affairs (ORA) and the Director of ORA serves as the liaison between the RAC Committees including the REC and the researchers/investigators. The ORA also functions to provide administrative support to RAC and its committees and facilitates the process of application and approval of research projects. The Director of ORA handles the regulatory compliance issues and provides assurance of human subjects' approval to sponsoring agencies. The Director of ORA and its staff are responsible for monitoring compliance, updating policies and procedures with relevant current regulations.

All correspondence to the REC should be directed to:

The Office of Research Affairs (ORA)

Research Centre, MBC-03

King Faisal Specialist Hospital & Research Centre

PO Box 3354, Riyadh 11211, Saudi Arabia

Phone: +966-11-442-4528

Fax: +966-11-442-7894

Email: ora@kfshrc.edu.sa

INTERNATIONAL GUIDELINES ON BIOMEDICAL RESEARCH & HUMAN SUBJECTS' PROTECTION IN RESEARCH

There are several international guiding documents that are used to establish the guidelines, policies, and procedures for the ethical conduct of research. The summaries of these international codes of ethical conduct are listed below:

A. The Nuremberg Code (1947): This is the first international document advocating voluntary participation and informed consent for individual participating in research. This document was a result of an American Military tribunal which began proceedings against 23 leading German Physicians and administrators for their willingness to participate in war crimes and crimes against humanity in 1946. These physicians were charged with conducting experiments on thousands of prisoners without their consent and as a result, most of these subjects died or were permanently crippled. Thus, the Nuremberg Code was established in 1948 and states that "The voluntary consent of the human participant is absolutely essential," making it clear that participants should give consent and that the benefits of research must outweigh the risks. The premises of this code are the backbone of current ethical considerations and guidelines on which the rights and protection of human subjects in research are established. These are listed as follows:

- The voluntary consent of the human subject is absolutely essential and the person being asked to participate:
 - Should have legal capacity to give consent
 - Should be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion;
 - Should have sufficient knowledge and comprehension of the elements of the study, treatment, or research to enable him/her to make an informed and enlightened decision. This means that before saying yes to participation, the subject should be informed of the nature, duration, and purpose of the study, research, or experimental treatment, the method and means for the conduct and the risks, benefits, side effects and inconveniences that he/she may endure by participating.
- The research/treatment/experiment should not be random or unnecessary in nature. It should result in benefits for the good of society.
- The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury to the participants.
- No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians or scientists also serve as subjects.
- The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.
- Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.
- The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.
- During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he/she has reached the physical or mental state where continuation of the experiment seems to him/her to be impossible.

- During the course of the experiment, the scientist in charge must be prepared to terminate the experiment at any stage, if he has cause to believe, in good faith and with his/her skills and judgment that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

B. The Belmont Report (1979): The National Research Act (Pub. L. 93-348) was signed into law On July 12, 1974 which created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The commission's charge was to identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects and to develop guidelines which should be followed to assure that such research is conducted in accordance with those principles. This report also known as The Belmont Report attempts to summarize the basic ethical principles identified by the Commission in the course of its deliberations. It is a statement of basic ethical principles and guidelines that assists in resolving the ethical problems surrounding the conduct of research with human subjects. The Commission recommended that the Belmont Report be adopted in its entirety, as a policy and therefore is referenced in its entirety in [Appendix 2 \(Hyperlink\)](#). The majority of the guiding principles from the report are integrated into the RAC Policies and procedures.

C. The Declaration of Helsinki (1964): The World Medical Association (WMA) developed the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data. The Declaration is intended primarily for physicians and is should be read as a whole and each of its constituent paragraphs should be applied with consideration of all other relevant paragraphs. The declaration is available in its entirety in [Appendix 3 \(Hyperlink\)](#).

D. Council of Europe Convention on Human Rights & Biomedicine (1997): This Convention is the first legally-binding international text designed to preserve human dignity, rights and freedoms, through a series of principles and prohibitions against the misuse of biological and medical advances. The Convention's starting point is that the interests of human beings must come before the interests of science or society. It lays down a series of principles and prohibitions concerning bioethics, medical research, consent, rights to private life and information, organ transplantation, public debate etc. The convention in its entirety is found in [Appendix 4 \(Hyperlink\)](#) of this document while some key areas addressed by the convention are highlighted below:

- All forms of discrimination based on the grounds of a person's genetic make-up are banned as well as carrying out of predictive genetic tests only for medical purposes.
- Genetic engineering is allowed only for preventive, diagnostic or therapeutic reasons and only where it does not aim to change the genetic make-up of a person's descendants.
- Techniques of medically assisted procreation to help choose the sex of a child, except where it would avoid a serious hereditary condition are prohibited.
- It prohibits the creation of human embryos for research purposes and requires an adequate protection of embryos where countries allow in-vitro research.
- The Convention states the principle according to which a person has to give the necessary consent for treatment expressly, in advance, except in emergencies, and that such consent may be freely withdrawn at any time.
- The treatment of persons unable to give their consent, such as children and people with mental illnesses, may be carried out only if it could produce real and direct benefit to his or her health.

- The Convention stipulates that all patients have a right to be informed about their health, including the results of predictive genetic tests.
- The Convention recognizes also the patient's right not to know.
- The Convention prohibits the removal of organs and other tissues which cannot be regenerated from people not able to give consent. The only exception is, under certain conditions, for regenerative tissue (especially bone marrow) between siblings.

E. The Canadian Tri-Council Policy Statement (1999): The Ethical Conduct of Research Involving Humans: This is a joint policy of Canada's three federal research agencies – the Canadian Institutes of Health Research, the Natural Sciences and Engineering Research Council of Canada and the Social Sciences and Humanities Research Council of Canada (the Agencies). This Policy expresses the Agencies' continuing commitment to the people of Canada to promote the ethical conduct of research involving human participants. The latest edition, adopted in 2010, represents the first substantive changes to the Policy since its adoption in 1998 and is a major revision. A comprehensive listing of all articles included in this Policy Statement is available as [Appendix 5 \(HYPERLINK\)](#).

INVESTIGATOR GUIDANCE

CONDUCT AND REVIEW OF RESEARCH AT KFSH&RC

This guidance represents the Research Advisory Council's (RAC) current position on the conduct of research and is the regulatory framework for all research activities at KFSH&RC. The use of the word, "must" or "shall" in the guidance means that something is required. The use of the word "should" in the guidance means that something is recommended or suggested, but not required.

1. Research is defined as any systematic investigation (i.e., the gathering and analysis of information designed, in whole or in part, to develop or contribute to generalizable knowledge.
2. The KFSH&RC Research Ethics Committee (REC), one of the four standing committees that support the RAC serves as the Institutional IRB and is charged with evaluating the religious and ethical aspects of all research undertaken by members of KFSH&RC within or without the Institute and its affiliated facilities in accordance with the Laws of Saudi Arabia and the international standards on the conduct of ethical research.
 - 2.1. This oversight includes monitoring, compliance, as well as interventions where appropriate to insure that the research conducted is ethical and of the highest quality.
 - 2.2. Additionally, while the research is ongoing, the REC reviews and considers proposed changes to the research as they are received, including protocol and consent form amendments.
3. General Procedure to be followed in the conduct of Human Subjects Research:
 - 3.1. Prior to beginning any research activities, investigators shall submit all research proposals involving human subject participation to the Office of Research Affairs (ORA) for review by the REC ([See Section on Submitting a Research Proposal to the Office of Research Affairs.....hyperlink](#)).
 - 3.2. After administrative review of all the necessary documents is complete, ORA will be responsible for submitting the proposals to other subcommittees if deemed necessary.
 - 3.3. Once the proposal is considered an approved study, the approval period for that study will be sent in a written communication from the REC to the Principal Investigator.
 - 3.4. No research involving human subjects shall be initiated without REC approval (unless specifically categorized as exempt from REC review, see below).
 - 3.5. All studies will be approved for 365 days; at the end of which a final report shall be submitted to REC by the Principal Investigator for review, approval, and closure of the study as complete.
 - 3.6. For studies being conducted that will exceed 365 days, a continued approval process in the form of an annual Progress Report to ORA is required until the study closure, at which time, a final report as above must be submitted.

INVESTIGATOR GUIDANCE

INVESTIGATOR QUALIFICATIONS/RESPONSIBILITIES

1. Principal Investigator (PI): The PI of the research study is ultimately responsible for assuring compliance with applicable policies and procedures, governmental rules and regulations, and international guidance.
2. The PI should be an Associate Consultant/Consultant for interventional clinical proposals and a permanent employee of KFSH&RC for all proposals.
3. The PI is also responsible for the informed consent process and all aspects of conducting the research. This is acknowledged when the PI fills and signs the Investigators Assurance Form.
4. Co-Investigators (Co-I) may be categorized as Internal Co-Investigators or External Collaborators.
 - 4.1 Internal Co-Investigators: These are employees of KFSH&RC.
 - These Co- Investigators are supervised by the Principal Investigator to perform critical trial-related procedures, and/or to make important trial-related decisions.
 - Co-Investigators should be able to answer questions about the study, among which include those concerning hypothesis, scope, methodology, anticipated outcome, and so forth.
 - 4.2 External Collaborators: These are individuals who are not employees of KFSH&RC but may be responsible for conducting research at KFSH&RC or at other institutions under the supervision of, or in collaboration with the PI (KFSH&RC Investigator).
5. KFSH&RC Investigator:
 - 5.1 A KFSH&RC Investigator is needed for External Collaborators (such as graduate or post graduate students, residents, and fellows who are interested in doing research at KFSH&RC.
 - 5.2 By acting as the KFSH&RC Investigator on a research study, the KFSH&RC Investigator agrees that the External Collaborator understands the regulations governing human subjects' research and is adequately trained and experienced to carry out the particular study for which they are applying.
 - 5.3 The KFSH&RC Investigator must agree to meet with the Co-investigators on a regular basis to monitor the research progress and be available to problem solve.
 - 5.4 The KFSH&RC Investigator agrees to inform the REC of their replacement if they cannot fulfill their role as a KFSH&RC Investigator. [Hyperlink : APP: 1435-05: Research Application Process](#)

INVESTIGATOR GUIDANCE

TYPES OF REC REVIEWS FOR RESEARCH PROPOSALS

There are primarily three (3) types of reviews conducted by the REC for research proposals/studies. The type of review that the research will be assigned to is based on the type of research that the investigator is planning to conduct.

1. **FULL Review process:** All research proposals/studies where human subject participation is taking place must be reviewed by a Full review. This is generally conducted by convening a meeting with all the members of the REC and after completion of the proposal review, a formal voting process is used to approve the study. When indicated, electronic platforms may be used to disseminate information and ensure timely communication for the review.
 - 1.1. Modifications to research studies or consent forms must be submitted for a Full Review in the following instances:
 - 1.1.1 There is an addition of a new drug or device
 - 1.1.2 There is an addition of an invasive procedure
 - 1.1.3 There is an increase in the medication dose or a decrease in dose that may change the risk of the research
 - 1.1.4 Prolongation of the subjects' participation in the study other than for observational purposes
 - 1.1.5 Change in the inclusion/exclusion criteria which may involve incorporation of populations at greater risk such as minors or pregnant women ([See Section on Vulnerable Populations in Research.pdf](#))
 - 1.1.6 Identification of new potentially significant risks
 - 1.1.7 Collection of additional blood samples that exceed the limits set in expedited category
2. **EXPEDITED Review process:** Research that may be reviewed by an expedited review process (review by the REC Chairman or assigned REC member) must NOT involve more than minimal risk and may NOT involve more than a minor change in a research project during an approved project period. The REC reserves the right to submit the research for full review rather than expedited review in the event that the reviewer feels it is necessary. Categories of research that may be considered for expedited review include:
 - 2.1. Clinical studies of drugs and medical devices only when condition (1) or (2) is met.
 - 2.2. Research using drugs/medications that are registered with the Saudi FDA.
 - 2.3. Research on medical devices that are cleared/approved for marketing by the Saudi FDA and the medical device is being used in accordance with its cleared/ approved labeling.
 - 2.4. Research that involves the collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
 - 2.4.1. From healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects:
 - 2.4.1.1 the amounts drawn may not exceed 550 ml in an 8-week period.
 - 2.4.1.2 the collection may not occur more frequently than 2 times per week.
 - 2.4.2. 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 with which it will be collected. For these subjects:
 - 2.4.2.1 The amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8-week period
 - 2.4.2.2 The collection may not occur more frequently than 2 times per week.

- 2.5. Research that involves prospective collection of biological specimens for non-genetic research purposes by noninvasive means and will not be placed in a tissue bank or repository for future research activities:
 - 2.5.1. Hair and nail clippings in a non-disfiguring manner.
 - 2.5.2. Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction.
 - 2.5.3. Permanent teeth if routine patient care indicates a need for extraction.
 - 2.5.4. Excreta and external secretions (including sweat).
 - 2.5.5. Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum base or wax or by applying a dilute citric solution to the tongue.
 - 2.5.6. Placenta removed at the time of delivery.
 - 2.5.7. Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor
 - 2.5.8. Supra- and subgingival 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.
 - 2.5.9. Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings.
 - 2.5.10. Sputum collected after saline mist nebulization.
- 2.6. Prospective collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Examples include:
 - 2.6.1. Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy
 - 2.6.2. Weighing or testing sensory acuity
 - 2.6.3. Magnetic resonance imaging
 - 2.6.4. Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography,
 - 2.6.5. Ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography
 - 2.6.6. Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual
- 2.7. 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).
 - 2.7.1. Collection of data from voice, video, digital, or image recordings made for research purposes.
 - 2.7.2. 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).
 - 2.7.3. Research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.
- 2.8. Continuing review of research may be submitted for expedited review if previously approved by the convened REC in the following instances:
 - 2.8.1. The research is permanently closed to the enrollment of new subjects and
 - 2.8.2. All subjects have completed all research-related interventions and
 - 2.8.3. The research remains active only for long-term follow-up of subject **OR**

- 2.8.4. Where no subjects have been enrolled and no additional risks have been identified **OR**
- 2.8.5. The remaining research activities are limited to data analysis

3. EXEMPT from REC Review:

- 3.1. It is important to note that the study of existing data (retrospective chart reviews) or the use of discards of tissue taken for clinical reasons can **ONLY** be exempted from REC review IF the information is recorded in such a manner that the subjects cannot be identified, either directly or through a code linked to the subject (i.e. the identity of the subject may NOT be readily ascertained or associated with the information).
- 3.2. It is also important to note that the types of research that can be exempted must pose **NO** risks to the subjects.
- 3.3. Research potentially eligible for exemption from REC review must be submitted to the ORA for registration and scientific approval and submission to other relevant committees such as the Clinical Research Committee (CRC) or Basic Research Committee (BRC), if indicated, and must contain a statement that justifies the request for exemption from REC Review.
- 3.4. Research involving the collection or study of EXISTING data, documents, records, pathological specimens, or diagnostic specimens if:
 - 3.4.1. These sources are publicly available **OR**
 - 3.4.2. 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.
- 3.5. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior **UNLESS**:
 - 3.5.1. The information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects.
 - 3.5.2. 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.
- 3.6. The research is conducted in established or commonly accepted educational settings, involving normal educational practices, such as:
 - 3.6.1. Research on regular and special education instructional strategies, OR
 - 3.6.2. Research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
- 3.7. Research and demonstration projects which are conducted by or subject to the approval of the Minister of Health, and which are designed to study, evaluate, or otherwise examine:
 - 3.7.1. Public benefit or service programs
 - 3.7.1.1. Procedures for obtaining benefits or services under those programs
 - 3.7.1.2. Possible changes in or alternatives to those programs or procedures **OR**
 - 3.7.1.3. Possible changes in methods or levels of payment for benefits or services under those programs.

3.8. Research involving the following may not be exempted from REC Review:

3.8.1. PRISONERS

3.8.2. FETUSES

3.8.3. PREGNANT WOMEN OR

3.8.4. HUMAN IN VITRO FERTILIZATION MINORS

3.8.5. SURVEYS INTERVIEW PROCEDURES OR OBSERVATION OF PUBLIC BEHAVIOR

INVESTIGATOR GUIDANCE

CONTINUING REVIEWS OF APPROVED RESEARCH

Continual annual review of all research being conducted by the REC is necessary as it provides the opportunity to reassess the totality of the project and helps to assure that the risks to subjects are being minimized and unanticipated problems are being monitored adequately.

1. It is the responsibility of the Principal Investigator to provide an annual progress report on time for uninterrupted REC approval of his/her research which must be submitted in a timely fashion ([Hyperlink Annual Progress Report form](#)).
2. Failure to do so shall result in:
 - 2.1. Automatic suspension of the study and suspension of all further enrollments of subjects until the study is re-approved by REC.
 - 2.2. Automatic expiration of all study consent forms.
 - 2.3. If subjects continue to be enrolled during this suspension period by the investigators, their information may not be used in the conducting, reporting, or analysis of the data or for any publications.
3. The Progress Report must be submitted at least 30-45 days prior to the date that the approval terminates to allow timely review and renewal.
4. The Annual Progress Report shall minimally contain, the following items ([see Annual Progress Report Template hyperlink](#)):
 - 4.1. RAC Number & Title
 - 4.2. Name of Investigators
 - 4.3. Indication of any modification in the research protocol and what
 - 4.4. Indications of any modifications in the consent form and what
 - 4.5. A summary of the progress up to the time of the report
 - 4.6. Future anticipated plans for the study during the next approval period
 - 4.7. A copy of the consent form used during last approval period
 - 4.8. Total number of subjects enrolled in the life time of the study
 - 4.9. Total number of subjects that withdrew or were removed from the study and the reason why
 - 4.10. Total number of subjects enrolled in the study during the previous approval period
 - 4.11. Any abstracts/presentations/publications that resulted as a result of the research
5. The REC must conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once per year.
 - 5.1. The REC uses the “effective date” when all the conditions of the approval have been satisfied rather than the meeting date at which the research study was approved.
 - 5.2. Subsequently, after the first approval date, for on-going continuing reviews of a research study, the date of the convened meeting at which the study was approved (with or without conditions) determines the latest permissible date of the next continuing review.
 - 5.3. It is important to note that when the research study has been approved by REC at the time of continuing review BEFORE THE EXPIRATION DATE of the preceding approval period, the REC approval does not lapse even if the investigators need additional time to satisfy the conditions.
 - 5.4. In order to keep the expiration date of the REC approval period constant throughout the life of the research project, when the REC performs the continuing review within 30 days before the REC

approval expires and re-approves the research (with or without conditions), the REC may keep the anniversary of the expiration date set from the previous year.

6. There are some instances where the REC determines that the continuing review must occur more frequently than annually or when a research is reviewed by the expedited review process. In the above case, the same guidance will apply to the continuing review process as outlined in Section 5 of this guidance.
7. On completion of the research, a Final Report ([Hyperlink: Final Report Form](#)) must be submitted in place of the Annual Progress Report to close the research project.

INVESTIGATOR GUIDANCE

Patients Access to Clinical Research, Clinical Investigations or Clinical Trials

It is the policy of KFSH&RC, to inform patients and families about how to gain access to clinical research, clinical investigations or clinical trials. Health care providers have a vital role in raising awareness about the option of participation in clinical investigations by having focused conversation about treatment options, including relevant clinical investigations, the patient and family can be made aware of, and invited to enroll in.

Information about clinical investigations should be detailed, clear and easy to understand by the patients and their families. It would be very beneficial for improving patients' access to clinical research to enhance and systematize the information about ongoing studies and about the sites participating in them; therefore KFSH&RC recommends that Research Investigators/Sponsors to register their clinical research, clinical investigations or clinical trials in a public trials registry such as the World Health Organization (WHO) *International Clinical Trials Registry Platform* (ICTRP) or the Saudi Food and Drug Authority (SFDA) *Saudi Clinical Trials Registry*(SCTR) at or before the time of first patient enrollment. This is part of KFSH&RC responsibility towards patients' health and wellbeing. It is also a requirement for research results publication by most journals based on the recommendation from the International Committee of Medical Journal Editors (ICMJE).

Clinical trials registration may help to:

1. Fulfill ethical obligations to participants and the research community (i.e., that the results will be used to help others/inform science)
2. Boost public trust and confidence in clinical research.
3. Improve equity of access to clinical research.
4. Prevent duplication of trials of unsafe or ineffective interventions and unnecessary duplication of research efforts.
5. Provide Ethics Review Boards a view of similar work and data relevant to the new research studies under their review.
6. Promote more efficient allocation of research funds
7. Facilitate systematic reviews and other analyses of the research literature and help editors or researchers to understand the context of study results

INVESTIGATOR GUIDANCE

EMERGENCY USE OF AN INVESTIGATIONAL DRUG OR DEVICE

In cases of urgency, including life-threatening situations, the emergency use of an investigational agent such as a drug or device may be warranted. This situation may arise when:

1. When there is no known standard of treatment or the treatments have failed and the agent may be potentially life-saving, an emergency request for approval may be submitted to REC to use the investigational drug or device.
2. This approval is **temporary and for a one time use only**, however, the investigator may submit the proposal for a full review for future research at the same time.
3. The procedure for obtaining permission for emergency use of a DRUG is as follows:
 - 3.1. The physician/investigator may petition for "emergency use" of the agent (drug/device/procedure) in question when there is a life-threatening situation and the agent (drug/device/procedure):
 - 3.1.1. Is not on the formulary/not registered in Saudi Arabia.
 - 3.1.2. No RAC approved study exists.
 - 3.1.3. The patient in question is ineligible for participation in a RAC-approved study
 - 3.2. The physician/investigator must request permission for emergency use of the agent (drug/device/procedure) by:
 - 3.2.1. Submitting a formal request letter to REC for approval through the Enterprise Correspondence which must include:
 - 3.2.1.1 A description of the patient's condition and detailed explanation for why the agent is the only acceptable course of intervention that the patient may receive.
 - 3.2.1.2 The correspondence (labeled as URGENT/RUSH) is directed to the Director of ORA, from the physician/investigator, through his/her Section Head and Department Chair.
 - 3.2.1.3 The Recommendation is from the Head of the Pharmaceutical Care Services.
 - 3.2.1.4 The approval is from the Chair of the Formulary Therapeutics Committee (FTC).
 - 3.2.1.5 The request should also contain the associated Pharmacy forms such as Form A (non-formulary) and Form B (unapproved indication) as well as supporting literature or experience with the agent.
 - 3.2.2 It is strongly recommended that the physician/investigator call and speak to the Director of ORA and or Chair of REC to appraise them of the timeline and details to facilitate the process.
 - 3.2.3 The FTC must complete the request and decision and submit it to REC within five (5) working days of the request.
 - 3.3 When granted, "emergency use" of the agent, the physician/investigator may treat for one course of treatment.
 - 3.3.1 If continuation of therapy is required, the physician/investigator must submit a formal research proposal for REC approval.
 - 3.3.2 Information including results of tests, data, samples obtained during this emergent period **may not be used or submitted for research activities** including publications. This is based on the regulations that protect the human subjects participating in research.
 - 3.3.3 Once a formal REC approval of a research proposal is obtained, all data from that point may be submitted for research related activities.

- 4 The procedure for obtaining permission for **emergency use of a DEVICE** is the same as in section 3 except that in place of the Pharmacy, the physician/investigator must obtain an approval to use the device urgently from the Standardization Committee through an urgent request/review and communication with the Chairman of the Committee.
- 5 For ongoing use of the drug/device/procedure, a formal research proposal must be submitted to REC and also to the Saudi FDA for registration and approval as per the current guidelines (Hyperlink to [Saudi FDA Section](#)).

INVESTIGATOR GUIDANCE

INFORMED CONSENT: OBTAINING, MODIFICATION, AND WAIVERS

Ethical Principles of Informed Consent: The use of patients or healthy volunteers as subjects in research is a privilege which carries with it stringent obligations that must be met scrupulously by the investigators. Respect for the rights, dignity and safety of the subjects must be the primary determinant of the researcher's actions. Vigilance must be maintained in order not to jeopardize these rights at all stages of a research project involving human subjects. As autonomous individuals, research subjects have a right to be fully informed about the nature of the research and the extent of their participation.

General Considerations:

1. All consent forms must be translated into Arabic with the English and Arabic translations side by side.
2. 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.
 - 2.1. The subject must be free to agree, or to refuse to participate in the research.
 - 2.2. Subjects must be free to withdraw their participation at any time.
 - 2.3. Circumstances which could put subjects at risk if they withdraw and procedures for withdrawal must be described in the consent document.
 - 2.4. 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 its agents, from liability for negligence.
3. 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.
4. Research proposals must detail where and when informed consent generally will be obtained; e.g., Pre-admission screening, day-of-admission, waiting room, hospital room, emergency room, evening before surgery, etc.
5. Every effort must be made to avoid coercion in any form or to any degree at all stages of the consent process. Below are the areas where obtaining consent for research may be construed as coercive:
 - 5.1. For all, but emergency care protocols, it is inappropriate to solicit consent immediately before beginning a procedure or instituting a therapeutic regimen.
 - 5.2. Avoid crowded waiting rooms, public areas or operating room holding areas for obtaining informed consents.
 - 5.3. Do not obtain consent from patients who have received drugs (e.g., sedatives or pre-anesthetic medication) that may impair their ability to understand and weigh the information provided and are clearly not capable of giving informed consent.
 - 5.4. Avoid obtaining consents from families under undue stress due to a loved one's deteriorating medical condition.
6. Responsibility for obtaining informed consent rests with the Principal investigator who must ensure that the subject being asked to participate in the research is fully informed:
 - 6.1. All concerns of the subject have been addressed.

- 6.2. Rationale for the research has been fully explained.
 - 6.3. Eligibility requirements and reasons for exclusion or removal from study have been defined.
 - 6.4. Procedures to be used or medications have been outlined.
 - 6.5. That costs, risks and benefits of participation; the time frame of participation; alternatives to participation are clear.
 - 6.6. 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 to the subject.
 - 6.7. It is strongly recommended that for studies involving more than minimal risk, or procedures other than those performed for routine clinical care or examination, consent should be obtained by either the principal investigator or the co-investigator performing the procedure.
7. There are three types of Consent that an Investigator may obtain for his/her Research:
- 7.1. Written Informed Consent
 - 7.1.1 Informed Consent for Research Involving the Administration of Drugs, Use of Devices or Performance of Procedures ([ORA 5.1.5.1 Form hyperlink](#))
 - 7.1.2 Informed Consent for Research With No Direct Benefits to Participant ([ORA 5.1.5.2 Form hyperlink](#))
 - 7.1.3 Informed Consent for Genetic Research ([ORA 5.1.5.9 Form hyperlink](#))
 - 7.2 Waiver of Signed consent (Verbal Consent) with documentation of the verbal consent process in the research subjects/Investigators records ([ORA 5.1.5.4 Form hyperlink](#))
 - 7.3 Waiver of Informed Consent ([ORA 5.1.5.3 Form hyperlink](#))

INVESTIGATOR GUIDANCE

OBTAINING INFORMED CONSENT

General Considerations:

1. Under most circumstances patients must be enrolled in a study prior to any screening evaluations. This must be clearly reflected in the consent form. If it is found that the patient does not qualify, then he/she must be removed from the study.
2. The rationale for enrolling patients prior to evaluation is that it is inappropriate for patients to:
 - 2.1. Bear the responsibility for costs associated with such evaluations (e.g., examinations and tests).
 - 2.2. Be subjected to any risks associated with screening procedures.
 - 2.3. Be personally responsible for the costs associated with treatment for any adverse reactions.
3. At the time of the initial consent conference, the subjects are verbally given all the information regarding the research as well as a copy of the complete consent form.
 - 3.1. They are allowed time to think about the request, to ask questions and have them answered to their satisfaction.
 - 3.2. If they agree to participate, the subject signs in the appropriate place with date and time.
 - 3.3. The person obtaining consent (investigator or delegate) signs the attestation at the end of the form after the subject signs with the date and time.
 - 3.4. If translation takes place, it is recommended that the translator also sign the consent form or have his/her name and position documented in the documentation of consent note.
4. Upon completion of the consenting process, the following must take place:
 - 4.1. One copy of the signed complete consent form with the signature of the Principal Investigator (P.I.) must be given to the subject.
 - 4.2. A second copy must be placed in the patient's chart.
 - 4.3. The original, completed and signed consent form must be retained for inclusion in the Principal Investigator's research records.
5. Once a subject has signed a consent form, he/she is considered to have entered the study. The consent form must be retained by the P.I. even if the subject later withdraws for any reason or does not actually participate in the project. ([See RAC 7.5 Policy on Research Records Retention & Access hyperlink](#)).
6. Persons delegated to obtain consent by the P.I. must notify him/her of the completion of the recruitment of the subject before the subject begins participation in the research project.
7. It is the responsibility of the P.I. to ensure that a properly completed consent form, as required for the particular research, has been obtained by the delegate(s) and that copies have been distributed as required above.
8. Signatures and other elements required to complete the process of consenting include:
 - 8.1. Subject or guardian
 - 8.1.1. The subject must sign, date, and time the consent form.
 - 8.1.2. If the subject is incapacitated, his/her surrogate may sign, date, and time the consent form.
 - 8.1.2.1 The investigator is responsible for noting the name and the relationship of the

guardian or next of kin on the consent or in the documentation of consent note for medicolegal purposes.

8.1.3. For subjects age 18 years or less, the following apply:

8.1.3.1 The signature with date and time of at least one parent or guardian, or more depending on the risk is required to participate in the research study.

8.1.3.2 Children age 7 years and above must also provide an oral assent ([Assent of Minors Form](#)).

8.2. Signature of Investigator obtaining consent

8.2.1. Under most circumstances, the Principal Investigator or the co-investigator should obtain consent.

8.2.2. Circumstances where the research may become impractical to be carried out may require that the principal investigator delegate the consenting responsibility to other appropriate professionals.

8.2.2.1 Requests to delegate this responsibility will be considered by the REC on a case-by-case basis. The names and professional appointments of delegates (e.g., Fellow, Senior or Chief Resident, etc.) must be submitted for REC approval when the delegates are chosen and trained and before they obtain any consents.

8.2.2.2 Unlike investigators (principal or co-investigators), they are not responsible for the conduct of the research.

8.3. Signature of the Witness

8.3.1. A witness signature is only needed when a third party verbally transmits the consent form to a subject who is unable to read the consent or the consenting process needs translation.

8.3.2. The third party must sign as a witness to affirm that the consent was accurately translated and that the subject understood the information provided.

9. The Effective Period of Signed Consent

9.1. Once a consent is obtained from a subject, the consent does not need to be reobtained provided that the consent clearly states the duration of the study will be greater than one year.

9.2. The consent must be re-obtained under the following circumstances:

9.2.1. The consent document has been altered or amended since the subject signed the document or

9.2.2. The subject was a minor at the time of entry into the study and has since attained the age of maturity.

9.2.3. The original consent document did not specify the duration of the subject's participation in the study.

INVESTIGATOR GUIDANCE

REQUESTING A MODIFICATION OF THE SIGNED INFORMED CONSENT (WAIVER OF SIGNED CONSENT)

1. In general, research regulations involving human subjects require that the research subject sign an informed consent document. Under very specific circumstances, the REC may allow a modification of this and approve a waiver of signed consent for a particular type of research.
2. Request for Modification of Informed Consent may take place under certain circumstances where:
 - 2.1. Some elements of an informed consent may need to be altered or waived OR
 - 2.2. Requirements for the consent form to be signed may be waived.
3. A Waiver of Signed Consent is a type of informed consent in which the **subject's signature** component of the informed consent is modified or waived.
 - 3.1. This waiver of signed consent is considered by REC on a case-by-case basis and may apply in situations where:
 - 3.1.1. The research presents **no more than minimal risk of harm*** to the subject AND the research involves no procedure for which written consent is normally required outside the context of the research, OR
 - 3.1.2. The consent document would be the ONLY identifiable link between the subject and the research AND
 - 3.1.3. There would be potential harm to the subject if the confidentiality of the consent document were breached.
 - 3.2. Examples where a waiver of signed consent may be granted include:
 - 3.2.1. Drawing of additional blood samples while blood is already being obtained for clinical reasons or blood donation.
 - 3.2.2. Sampling of additional bodily secretions when such secretions are already being sampled for routine care and this sampling will not be an additional process.
 - 3.2.3. Questionnaires, surveys, or Interviews.
 - 3.3. When requesting a waiver of signed consent, the ORA form **“Request for Modification in Documentation of Informed Consent”** must be completed and submitted with the proposal application form and the appropriate Subject/Patient Information Sheet filled and submitted in place of a formal written consent form. ([Section](#) hyperlink).
 - 3.4. A waiver of signed consent does not exempt an investigator from informing the subject about the research prior to the start of the research.
 - 3.5. All of the elements of informed consent required in a signed consent must be included in the information sheet that is given to the subject is reviewed/translated and questions answered by the principal investigator.
 - 3.6. The investigator must do the following when obtaining a waived signed consent:
 - 3.6.1. The first part of the consent form (Research Participation Information sheet) is read to the patient and signed by the principal investigator or his/her designee to obtain informed consent.
 - 3.6.2. A copy of the signed Information Sheet must be given to the subject, a copy should be placed in the subject's chart, and the investigator must keep the original form in his/her research records.
 - 3.6.3. The documentation of the subject's verbal agreement to participate in the research is

completed by the principal investigator in the subject's health record (or Investigator records in case of unavailability of subjects' health records) and must minimally include the following elements:

- 3.6.3.1. The RAC number and title of research project
- 3.6.3.2. Statements that the nature, purpose and any associated risks of the study were explained fully to the participant, all questions were answered satisfactorily and that the participant gives a verbal consent to participate in the research study.
- 3.6.3.3. The date/time of obtaining the consent
- 3.6.3.4. The name of the person who gave the consent (i.e. subject or surrogate)
- 3.6.3.5. The signature /ID number /and contact information of the person who obtained the consent.

****Investigators must be aware that procedures which physicians/researchers consider to be minimal risk are not necessarily viewed as such by patients or subjects. They should be sensitive to the subject's perception of the procedure when classifying procedures as minimal risk. Thus, it is unlikely that the REC would approve a waiver for any invasive procedure, (e.g. venipuncture, catheterization, skin biopsy, etc.) that is performed solely for research purposes despite the fact that such procedures do not normally require written consent.***

REQUESTING A MODIFICATION OF INFORMED CONSENT (WAIVER OF INFORMED CONSENT)

In general, research regulations involving human subjects require that the research subject sign an informed consent document. Under very specific circumstances, the REC may completely waive this requirement for obtaining an informed consent.

1. A waiver of informed consent can only be granted when ALL four of the following are applicable:
 - 1.1. The Research bears no more than minimal risk to the subjects involved
AND
 - 1.2. The research could not practically be carried out without the waiver
AND
 - 1.3. The research will not adversely affect the rights and welfare of the subjects
AND
 - 1.4. The subjects will be provided with additional pertinent information after participation, whenever appropriate and feasible.

2. When requesting a waiver of informed consent, the ORA form **“REQUEST FOR MODIFICATION OF INFORMED CONSENT”** must be completed and submitted with the research proposal application form. A copy of this ([Request for Modification of Informed Consent Form](#)).

CONFIDENTIALITY & RECRUITMENT METHODS FOR RESEARCH

Confidentiality of Research Subjects

1. While planning a research study, investigators must consider how the subjects will be identified and recruited while maintaining confidentiality regarding their personal as well as health related information.
2. Investigators may only access medical information or contact information on those patients that they are directly caring for through a chart review process of a known research project (see Section XI, 10, Chart Review Protocols).
3. Investigators must not access the charts and medical information of patients where they are not directly involved in their care as patients would consider it a serious breach of confidentiality and of medical ethics that someone not involved in their care had access to their personal information and contacted them.

Recruitment Methods for Research

1. Permission to recruit a patient as a subject in a research study must be obtained from the patient's physician before the patient is contacted. This may be done in several ways:
 - 1.1. Where possible, the physician should first get permission from the potential subject to allow the investigator to contact him/her.
 - 1.2. If this is impractical, a letter can be sent out by the primary physician informing the patient that the investigator would like to contact him/her.
 - 1.3. The letter should include a mechanism that allows response back such as a card to be returned granting or refusing permission.
2. In some situations, a blanket consent may be obtained and documented by the physician which allows contact in the future by the physician or other investigators.
3. The investigator may then contact the patient(s) directly, without previous notification, indicating that their physician had given permission for the contact.
 - 3.1. If blanket permission is obtained and used, the investigator must inform the physician each time that a patient is contacted.
4. Recruitment of family members to participate in research:
 - 4.1. For confidentiality reasons, the index subject/patient should not be asked to provide the name of the family member(s) directly to the investigator but rather contact family members and inform them of the potential opportunity to participate.
 - 4.2. Investigator contact information may be given to the family member by the index subject to the family member(s) who can then directly contact the investigator if he/she is willing to participate.
 - 4.3. When planned research includes possible recruitment of family members, the protocol and the consent form must indicate how the family member(s) will be contacted.
5. Recruitment of Employee as research subjects:
 - 5.1 Whenever possible, researchers should avoid using their own employees, colleagues, or subordinates in research if another population of subjects is equally suited to the research question. Though the researcher may be careful to avoid potentially coercive behavior, the very nature of the relationship with the research subjects can create the appearance of coercion.

- 5.2 Information about how employees, colleagues, or subordinates will be recruited, how coercion will be avoided and confidentiality will be protected should be included in the information submitted to the REC; Recruitment through bulletin board advertisements (screened and approved by the REC), or recruitment through a third party unassociated in a power relationship with the employee are usually the best strategies.
 - 5.3 Co-investigators and colleagues (in the specific sense of having a comparable position in the institution) are appropriate potential control subjects.
6. Subjects recruited for a research study must be free of any outside influences while deciding whether to participate.
 - 6.1. Even in the absence of overt coercive or inducing statements, an element of coercion may be introduced because of the relationship between the potential subject and the investigator. For example:
 - 6.1.1. Patients may feel obliged to agree because their physicians have asked them to.
 - 6.1.2. Co-workers in an investigator's laboratory, office or clinic may agree in order to preserve the good will of the investigator.
 - 6.2. Prospective research subjects must be reassured verbally that, refusal to participate will in no way affect their care.
 7. Methods of Advertisement for Recruitment of 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, text messaging, email, or any form of social media which include recruitment information must be approved by the REC prior to distribution or publication of the material.

Letters to fellow physicians, both within and outside of the institution, must also be approved.

The following minimal information must be contained in the advertisement:

 1. The purpose of the study
 2. The characteristics which would qualify an individual for enrollment
 3. A straightforward description of any and all benefits to the subjects
 4. The RAC number of the protocol and the expiration date
 5. The name and number of the contact for further information

Recruitment material must not induce potential subjects into participating in the research. Such inducements might include claims (explicit or implicit) about:

1. safety or efficacy of an investigational drug or device
2. equivalence or superiority to existing treatments, or
3. closer monitoring of the subject's/ patient's condition

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

INVESTIGATOR GUIDANCE

COMPENSATION, EXERCISE TESTING, AND ENROLLMENT OF SUBJECTS ON MULTIPLE STUDIES

In order to ensure that research involving human subjects is standardized across the institution and to ensure that international and national regulations regarding research are followed, investigators must ensure that compensation of subjects, exercise testing facilities, and concurrent enrollment on more than one research study are taken into consideration. Guidance for including these in the research proposal and study design is outlined below:

1. Compensation for Participation in Research for Healthy Volunteers
 - 1.1. While an offer of payment may encourage a greater willingness and response from a volunteer to participate, the importance of recruiting volunteer subjects in non-therapeutic research justifies such payments.
 - 1.1.1. Since even a minimal amount of such payment could be considered a coercive inducement, it is strongly recommended that such payments must not be excessive.
 - 1.1.2. The REC rejects the idea that the amount of payment shall be based on an evaluation of risk and/or a fixed schedule of payment.
 - 1.1.3. The principal investigator must be able to justify the amount of any payment being offered to a consenting subject and take the following factors into account when determining compensation for research subjects:
 - 1.1.3.1. Out of pocket expenses borne by the subject for travel, meals, childcare, etc.
 - 1.1.3.2. Degree of anticipated discomfort or inconvenience
 - 1.1.3.3. Duration of the study and impact on work-related income and time lost from work.
 - 1.2. The REC will review the compensation offered in the consent form and ensure that the reasons for the compensation by the principal investigator are justified.
 - 1.2.1. Additionally, in order to minimize the possibly coercive nature of compensation, the investigator must indicate the following in the consent form,
"You will receive SR _____ for your time and the expenses that you incur as a result of your participation in this research."
2. Exercise Testing in Research Studies
 - 2.1. Exercise testing, while not without some risk, is an appropriate tool for subject evaluation in research protocols, when performed with proper equipment and when properly supervised.
 - 2.2. As testing will be administered for research purposes, and not for clinical indications, the inherent risk to the subject is higher and thus requires stringent guidelines for clinical testing in order to minimize the risk/benefit ratio.
 - 2.3. Additionally, investigators will be required to sign, on a yearly basis, an affidavit certifying a willingness to comply and indicating the name of the individual who will be performing the tests.
 - 2.4. Research involving exercise stress testing in research subjects, healthy or otherwise, must incorporate the criteria listed below:
 - 2.4.1. Inclusion and exclusion criteria
 - 2.4.2. Training and experience of supervisory personnel
 - 2.4.3. Site of testing
 - 2.4.4. A detailed description of the equipment to be used and emergency supplies available at the test site
 - 2.4.5. Exercise protocol to be followed
 - 2.4.6. Test end point and criteria for early termination

- 2.5. Pre-entry screening must be reviewed by a consultant physician, who will approve entry of the subject into the study and minimally include:
 - 2.5.1. A medical history
 - 2.5.2. A complete Physical Examination
 - 2.5.3. A Resting 12 - lead Electrocardiogram (EKG) and
 - 2.5.4. Relevant laboratory tests with particular emphasis on cardio-pulmonary, metabolic and relevant orthopedic problems.
- 2.6. The information provided to subjects in the consent document must:
 - 2.6.1. Fully describe the procedures to be followed and provide an estimate of the risks involved.
 - 2.6.2. Subjects must be informed that they are not undergoing a full, diagnostic stress test and that should they require such a test for medical reasons, it should be administered at an appropriate clinical facility.
 - 2.6.3. Subjects must be informed of the results of the research exercise test, and where relevant, appropriately counseled.
- 2.7. Equipment used for testing must be appropriately calibrated and tested and regularly cleaned.
 - 2.7.1. Parameters to be monitored during testing and for at least 10 minutes after termination of the exercise period must include:
 - 2.7.1.1. An EKG capable of providing recordings interpretable for rhythm and ischemic changes during the test must be used.
 - 2.7.1.2. A 12-lead record is required, except in low risk subjects or subjects in whom a recent diagnostic stress test was negative, where fewer leads may be accepted.
 - 2.7.1.3. Continuous, oscilloscopic monitoring and periodic strip recording must be available for all subjects.
 - 2.7.1.4. Appropriate blood pressure monitoring at frequent intervals during and after the testing must be performed.
 - 2.7.2. An emergency resuscitation cart, including a tested and maintained defibrillator, airways, ambu-bag, oxygen, I.V.'s, suction and appropriate drugs must be available at the test site.
 - 2.7.3. An emergency procedure flow chart with necessary telephone numbers, should be available at the test site.
 - 2.7.4. Evacuation procedures should be specified.
- 2.8. Supervisory Personnel for exercise tests must have taken part in emergency drills at the test site and:
 - 2.8.1. Be familiar with the test site
 - 2.8.2. The equipment being used and
 - 2.8.3. Emergency supplies available
- 2.9. Supervised testing by a physician must occur when the subjects are:
 - 2.9.1. Men 35 year or older
 - 2.9.2. Women 45 or older or postmenopausal
 - 2.9.3. Any subject with known risk factors including but not limited to:
 - diabetes
 - hypertension
 - smoking
 - significant hypercholesterolemia
 - significant cardiopulmonary
 - Significant renal
 - Significant metabolic
 - Significant orthopedic problems
 - 2.9.4. The supervising physician must be in the level of a Consultant who is fully licensed, and

with documented training and experience in stress testing, equivalent to that required by The American College of Cardiology for Cardiology certification with a current certification

- 2.9.5. This physician must be present in the test room.
- 2.10 Independently supervised testing by personnel with professional training and experience in supervision of clinical, diagnostic stress testing and in emergency procedures may take place for the following subjects:
 - 2.10.1 Men under the age of 35, with no known risk factors
 - 2.10.2 Premenopausal women under the age of 45, with no known risk factors
 - 2.10.3 Subjects whose screening exercise stress test was negative
 - 2.10.4 A physician, fully licensed to practice medicine at KFSH&RC, with training and experience in resuscitation must be available within one floor of the site, via stairs as a back-up for the individual(s) in 2.10.
3. Concurrent Participation of Research Subjects in Two Or More Research Projects
 - 3.1. While there may be some circumstances in which enrollment in two therapeutic research studies may be appropriate, however, due to the potential for interaction between two or more therapeutic interventions, concurrent enrollment of subjects in more than one research study is strongly discouraged.
 - 3.2. It is the principal investigator's or authorized designee's responsibility to determine if a potential subject is enrolled in another research study.
 - 3.3. In certain circumstances where one of the research studies is non-therapeutic and non-invasive, the research subject may be enrolled in more than one study provided that dual enrollment is with the knowledge and agreement of the Principal Investigators of both studies.
 - 3.4. When a subject will be enrolled on more than one therapeutic research study at a given time, the REC must be notified.
 - 3.5. REC approval for such situations will be on a case by case basis.

INVESTIGATOR GUIDANCE

WITHDRAWING DRUGS FROM SUBJECTS DURING AND/OR ON COMPLETION OF RESEARCH

Due to the inherent potential increase in risk with withdrawal of drugs from research subjects, special monitoring and considerations need to be incorporated into the research studies to ensure the safety of the research subjects.

1. The following procedure applies for any research study where the withdrawal of drugs from human subjects, particularly the withdrawal of neuroleptics from psychiatric subjects may occur.
2. Withdrawal of medication includes:
 - 2.1. A washout study
 - 2.2. A withdrawal study
 - 2.3. A study that entails a washout or drug withdrawal followed by administration of a drug or placebo.
3. Assessment of Subject:
 - 3.1. Assessment of Capacity:
 - 3.1.1. The subject's capacity to give informed consent must be assessed.
 - 3.1.2. Possibility of deterioration and loss of capacity during the study must be assessed. (See [Section on Vulnerable subjects-hyperlink](#))
 - 3.2. Assessment of Clinical Suitability:
 - 3.2.1. A qualified physician/investigator must assess the subject, and determine the subject's clinical suitability to participate in the study.
 - 3.3. Enrollment:
 - 3.3.1. At the time of a subject's enrollment, the informed consent process must take place and must be consistent with institutional guidelines for enrolling individuals in studies.
 - 3.3.2. Changes in the subject's therapeutic regime may only be made after the subject has signed the consent form agreeing to participate in the study.
 - 3.4. Monitoring:
 - 3.4.1. The mechanisms for monitoring the subject while on the study must be detailed in the research protocol (and the consent form) as described below.
 - 3.4.1.1 The subject must be seen and assessed by an independent physician with sufficient frequency to assure the subject's health will not deteriorate while on the study.
 - 3.4.1.2 This physician must be completely independent from the study and the physician's name should not appear as an author on any published paper reporting on the study as that might lead to the appearance of a conflict.
 - 3.4.1.3 Any study not requiring the periodic personal assessment by an independent physician must specifically state the reason for such omission.
 - 3.4.1.4 For some studies, particularly outpatient psychiatry protocols, an additional monitor, a "home monitor" should be identified who can evaluate the subject on a more frequent basis.
 - 3.4.1.5 The "home monitor" should be a reliable adult relative or friend who lives in close proximity to the subject and who is capable of reporting changes in the subject's status to the investigators.
 - 3.5. The Content of the Consent Form for Withdrawing Drugs from Subjects:

3.5.1. The consent form and the consent process must comply with all the requirements for consent forms in human subject research ([See Section on Development of an Informed Written Consent link](#))

INVESTIGATOR GUIDANCE

VULNERABLE POPULATIONS IN RESEARCH

Vulnerable subjects include 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 into a research project they must be provided all of the protections that is required for every other research subject. Furthermore, additional, even more rigorous protections must be provided for those who are vulnerable.

In order to ensure that the benefits of research are available to all individuals who have a particular disease or risk factor, research that involve human subjects must not discriminate on the basis of age, gender, tribal affiliation, or ethnicity. Every attempt must be made to include children, women, tribes, and minorities as research participants. The following points must be considered when developing a research proposal to address appropriate inclusion and care of vulnerable subjects:

1. Racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study.
2. Research studies involving human subjects must employ a study design with gender and ethnic/tribe representation (by age distribution, risk factors, incidence/prevalence, etc.) appropriate to the scientific objectives of the research.
3. If adequate inclusion of one gender and/or ethnic/tribe is impossible or inappropriate with respect to the purpose of the research because there is a disproportionate representation of one gender or tribe/general population, the rationale for the study population must be well explained and justified.

Special Considerations for Inclusion/Exclusion of Children in Research

1. In order to ensure that the maximum benefit from research are available to all populations, children (individuals under the age of 18 year) must be included in all human subject research, unless there are clear and compelling reasons to exclude them.
2. If children will be excluded from the research, the application or proposal must present an acceptable justification for the exclusion in the research plan as follows:
 - 2.1 Investigators should create a section titled "Participation of Children".
 - 2.2 This section should provide:
 - 2.2.1 A description of the plans to include children and a rationale for selecting or excluding a specific age range of child, or
 - 2.2.2 An explanation of the reason(s) for excluding children.
 - 2.3 When children are included, the plan must also include a description of the expertise of the investigative team for dealing with children at the ages included.
 - 2.4 Justifications for Exclusion of Children in research must be based on one of the following exclusionary criteria:
 - 2.4.1 The research topic to be studied is irrelevant to children.
 - 2.4.2 There are laws or regulations barring the inclusion of children in the particular research.
 - 2.4.3 The knowledge being sought in the research is already available for children or will be obtained from another ongoing study, and the addition of children to this research will be redundant.

- 2.4.4 A separate, age-specific study in children is warranted and preferable, for example, the relative rarity of the condition in children, as compared to adults.
 - 2.4.5 The number of children is limited because the majority are already accessed by a national or international pediatric disease research network.
 - 2.4.6 Issues of study design preclude direct applicability of hypotheses and/or interventions to both adults and children (including different cognitive, developmental, or disease stages or different age-related metabolic processes).
 - 2.4.7 Insufficient data are available in adults to judge potential risk in children.
 - 2.4.8 The study designs aimed at collecting additional data on pre-enrolled adult study participants (e.g., longitudinal follow-up studies) did not include data on children.
 - 2.4.9 Other special cases justified by the investigator.
3. Minors are Vulnerable Subjects and thus specific considerations with regards to their participation in research need to be addressed:
- 3.1 Permission must be obtained from the parent(s)/guardian for research participation.
 - 3.2 The assent of the child must be obtained in specific instances.
 - 3.3 Documentation that the assent was obtained freely and without coercion must be kept.
 - 3.4 The enrollment of pediatric subjects requires that the research participant information sheet be worded as "You/Your child" or a clearly stated explanation that "You or Your" throughout the document shall mean "You/Your child".
4. Additional protections for children based on the risk related to the research:
- 4.1 Research involving minimal risk:
 - 4.1.1. Defined as "probability and magnitude of harm or discomfort is not greater than that ordinarily encountered in daily life or during the performance of routine physical or psychological tests"
 - 4.1.2. Research may be performed only if:
 - 4.1.2.1. Adequate provision is made for obtaining the assent (an affirmative agreement to participate in the research) of the child AND
 - 4.1.2.2. The permission of the parent/guardian
 - 4.2 Research involving greater than minimal risk but with potential of direct benefit to the individual subjects:
 - 4.2.1 Research may only be performed if:
 - 4.2.1.1 The risk is justified by the anticipated benefit
 - 4.2.1.2 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
 - 4.2.1.3 Adequate provision is made for obtaining the assent of the child AND
 - 4.2.1.4 The permission of the parent/guardian
 - 4.3 Research involving greater than minimal risk and no potential direct benefit to the individual subject, but likely to yield generalizable knowledge about the subject's disorder or condition:
 - 4.3.1 Research may only be performed if:
 - 4.3.1.1 The risk is a minor increase over minimal risk
 - 4.3.1.2 The research presents subjects with experiences that are commensurate with those in their actual expected medical, dental, psychological, social or educational situations
 - 4.3.1.3 The research is likely to yield generalizable knowledge of vital importance to understanding or ameliorating the subject's condition
 - 4.3.1.4 Adequate provision is made for obtaining the assent of the child AND
 - 4.3.1.5 The permission of the parent/guardian

- 4.4 For research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children:
 - 4.4.1 Research in this category may require the approval of the Ministry of Health in addition to REC approval.
- 4.5 Requirements for parent/guardian consent for minor research subjects:
 - 4.5.1 Provision must be made for soliciting the permission of the child's parent/guardian and the permission must be documented in the consent form as well as the subject's medical chart (if applicable).
 - 4.5.1.1 The REC requires consent of only one parent if:
 - 4.5.1.1.1 The research involves no greater than minimal risk or
 - 4.5.1.1.2 Involves greater than minimal risk but presents the prospect of direct benefit to the individual subjects
 - 4.5.1.2 The REC requires consent of both parents/guardians if:
 - 4.5.1.2.1 The research involves greater than minimal risk and offers no prospect of direct benefit to individual subjects or
 - 4.5.1.2.2 The research is not otherwise approvable but presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children,
 - 4.5.1.3 Exception to the both parent/guardian consent is if:
 - 4.5.1.3.1 One parent is deceased
 - 4.5.1.3.2 Whereabouts unknown
 - 4.5.1.3.3 Declared incompetent
 - 4.5.1.3.4 Not reasonably available
 - 4.5.1.3.5 Only one parent has legal responsibility for the care and custody of the child
- 4.6 Waiver of Parent/guardian consent:
 - 4.6.1 Under very special circumstances the REC may waive the requirement for parental consent.
 - 4.6.2 Waivers can only be granted for conditions or for a subject population for which:
 - 4.6.2.1 Parental or guardian permission is not a reasonable requirement to protect the subjects (e.g. neglected or abused children)
 - 4.6.2.2 If an appropriate mechanism for protecting the child is provided, and
 - 4.6.2.3 If the waiver is not inconsistent with Regulations and the Laws of the Kingdom of Saudi Arabia
- 4.7 Requirements for assent by children ([ASSENT OF MINORS](#)).

INVESTIGATOR GUIDANCE

ASSENT OF MINORS

The Difference Between Assent and Consent

When conducting research with children, several aspects must be considered to ensure voluntary participation as well as parental/guardian consent. Generally, IRB's are charged with ensuring that "adequate provisions [be] made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent taking into account the ages, maturity, and psychological state of the children involved" [45 CFR 46.408].

Although children do not have the legal capacity to "consent" to participate in research, they should have the research explained to them in simple terms that are understandable, be given the right to ask questions, and give their verbal choice to participate or not in the study. For older children, in some cases, a written assent may be requested.

Obtaining and Documenting Assent from Minors

1. When protocols involving minors as subjects are submitted for REC approval, they should clearly indicate the P.I.'s assessment as to which of the four research categories ([sections 4-.1-4.4](#)): Additional protections for children based on the risk related to the research) the study belongs, and from which subjects' documented assent will be obtained.
2. If 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. A Certification of Assent Form ([see Appendix 8](#)), that indicates the Investigator met with the minor, discussed clearly and simply the study and answered all of his/her questions and obtained the verbal approval from the minor to participate in the research must be completed.
4. This Certification of Assent documents that assent was freely obtained and without any coercion.
5. This form must be signed by a witness who was present with the investigator during the assent process and is not a family member and not associated with the study.
6. Investigators must maintain each signed Certification of Assent form on file along with the consent document that was signed by the parent /guardian and other research records relevant to the individual research subject. ([See Documentation of assent, below](#)).
7. All children participating in research must have the research explained in simple terms in language appropriate for his/her age, maturity, and previous experiences, regardless of whether assent is to be requested or not.
 - 7.1 This information can be provided verbally and should minimally include:
 - 7.1.1 Significant tests and procedures to be performed
 - 7.1.2 Frequency of interventions
 - 7.1.3 Duration of participation in the study
 - 7.1.4 Risks and discomforts
 - 7.1.5 Potential benefits
8. The child should be encouraged to ask questions, all of which should be answered.

9. Guidance for Documentation of Assent from children is based on their age as follows:
 - 9.1. Age 14 -17 years, assent should be obtained and documented with a signature of the minor.
 - 9.2. Age 12-13 years, assent should be obtained and documented unless the child's pediatrician considers him/her to be too immature or too sick to provide true assent.
 - 9.3. Age 7-11 years should be fully informed about the research, using language appropriate to their age or maturity, and assent should be obtained from those deemed capable of making a meaningful decision.
 - 9.4. Less than 7 years, information about the study should be provided in a manner appropriate to the child's age, but documented assent need not be obtained.

10. Waiver of the Assent of Minor:

- 10.1. In some instances, even where the child is capable of giving assent, the REC may grant a waiver of assent.
 - 10.1.1. The capability of some or all of the children is so limited that they cannot reasonably be consulted; or
 - 10.1.2. 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.
 - 10.1.3. If either of the above is true then the assent of the children is not a necessary condition for proceeding with the research: In such circumstances as a child's dissent, which should normally be respected, the dissent may be overruled by the child's parents.
 - 10.1.4. When research involves the provision of experimental therapies for life-threatening diseases such as cancer. The investigator(s) should also keep in mind that when the likelihood of success is marginal and discomfort is high, and death may be imminent, the child's wishes should be respected as the parents may wish to pursue all avenues and options for therapy.
 - 10.1.5. Minors should be fully informed about the nature of the research at the age appropriate level and should be included in discussions of their participation. Documentation of this involvement should take place in the area for documentation of consent.

11. Waiver of Parental Consent:

- 11.1. In rare instances, the parental consent may be waived for research on children. The following cases apply:
 - 11.1.1. Children of abuse or neglect and/or where there is serious doubt as to whether the parents' interests reflect the child's interests. [45 CFR 46.408(c)].
 - 11.1.2. Research on people under 18 who are in circumstances where they are clearly outside of parental influence or control.
- 11.2. The REC would evaluate each study carefully to determine whether parental permission is not a reasonable requirement to protect the subjects.

INVESTIGATOR GUIDANCE

RESEARCH INVOLVING SUBJECTS WITH SUSPECTED DIMINISHED MENTAL CAPACITY

Assessment of a Subject's Mental Capacity to Participate in Research

1. In order for a subject to give his/her Informed Consent to enroll in research, that individual must fully understand all aspects of the study and his/her rights as a research participant.
2. This can only be done if subjects have the mental capacity to understand.
3. If there is a possibility that the subjects may have diminished capacity, their mental capacity must be assessed and monitored.
4. For research where subjects with altered or diminished mental capacity may be enrolled, or in cases where the condition of the subject may result in the development of impaired capacity while participating in the research, special measures must be instituted to assess capacity initially and to monitor it during the study.
5. Assessment of Capacity:
 - 5.1. The Principal Investigator should employ a standard methodology to assess and monitor mental capacity for subjects involved in the research which clearly outlines how the assessment of capacity will be undertaken.
 - 5.2. This assessment of the subject's capacity to consent must take place prior to enrolling subject in the study.
 - 5.3. For patients with psychiatric illnesses or diminished capacity, an assessment must be done by a physician who is not associated with the research and will not be a co-author.
 - 5.4. The physician performing the assessment must have professional training and credentials suitable given the nature of the subject's illness and the nature of the research.
 - 5.5. Factors to be considered in assessing capacity include:
 - 5.5.1. The prospective subject's medical condition
 - 5.5.2. The voluntariness of the subject's consent in light of the subject's hospitalization or relationship with the physicians conducting the study
 - 5.5.3. The subject's ability to assess the information provided to him/her and make informed and knowing decisions.
 - 5.5.4. In the event the subject lacks capacity to consent to participate, consent must be given by an individual legally authorized to consent on behalf of the subject.
6. Monitoring:
 - 1.6.1. If there is a likelihood that a subject's capacity may become impaired during the course of a study, then the specific mechanisms for monitoring the subjects to determine if there is a decrease in capacity must be detailed in the protocol and/or the consent form.

INVESTIGATOR GUIDANCE

GENETIC TESTING AND RESEARCH

Genetic testing on biological samples is an exciting and important area that is expanding both as a clinical and research tool. Genetic testing using established, validated methods in clinical laboratories and for clinical application does not represent research and will not be discussed further. Genetic testing that is done for the acquisition of generalizable new knowledge or uses a new technique not previously validated for that particular area is considered research. This guidance is for the conduct of genetic research where the participants are human subjects.

1. A full REC review is required if a biological sample can be linked back to a subject, directly or indirectly and genetic testing is being performed which involves constitutional genes.
2. On occasion, there is overlap between the genetic testing for research and the results obtained that investigators/physicians may want to use to alter clinical care. To be used for clinical decision making, the testing must be performed under the auspices of a clinical laboratory that has been certified in accordance with the local regulations of Saudi Arabia, is a CLIA Certified (Clinical Laboratory Improvement Amendment-1988, USA), or College of American Pathologists (CAP) accredited to perform the testing and reporting of patient-specific results for Constitutional (host) genes.
3. Common types of Genetic Research include:
 - 3.1. Research on constitutional genes: This will likely involve sensitive information about research participants.
 - 3.2. Research involving pathologic human tissue (e.g. malignancies): This rarely poses a risk (and no direct benefit) to participants because genetic abnormalities in this setting are usually focused on non-constitutional mutations, and are not representative of the participant's individual genetic makeup.
 - 3.3. Whole Exome Sequencing (WES): This is the identification of exome DNA sequence; an exome contains sequence data for all of the known genes that are used by the body to make proteins.
 - 3.4. Whole Genome Sequencing (WGS): This is the identification of both coding (exome) and non-coding DNA sequence data for an individual.
4. Risk & Confidentiality related to Genetic Research:
 - 4.1. The research subjects must feel that they have control over the extent, timing, and circumstances of sharing their genetic information results with others and that the data associated with the research will be protected.
 - 4.2. Investigators must use appropriate methods to secure and disclose information related to genetic testing in order to protect privacy and confidentiality.
 - 4.3. Information about Family Members: Because genetic information can have implications for a participant's relatives, it is important to consider the privacy and confidentiality of family members as well.
 - 4.4. Recruitment of a participant's family members must be designed so that the privacy of family members is not violated.
 - 4.5. Recruitment from such a narrow pool of participants may place undue influence on individuals to participate. Research proposals should be designed to minimize this risk so that family members who are not interested in participating are not compelled to do so.

- 4.6. The investigator should not directly contact the research subject's family members. 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.
 - 4.7. Personal, private information about an individual should be protected against disclosure to other family members in the study.
 - 4.8. Investigators must consider appropriate methods when disclosure of individual results to a participant will infer genetic and health status of others in the family.
5. Linking of biological samples with the Research Subject: Although genetic testing of biological samples (tissue, blood, and other body fluids) appears to have no major direct harm to subjects, these studies cannot be categorized as presenting no risk or minimal risk.
 - 5.1. This type of research carries with it the very real possibility of psychosocial and informational risks to the subject including:
 - 5.1.1. The risk of harm from learning genetic information about oneself.
 - 5.1.2. Social stigmatization, discrimination, and labeling.
 - 5.1.3. Potential loss of, or difficulty in, obtaining employment or insurance.
6. Disclosure of Incidental Findings:
 - 6.1. Investigators must be prepared for the possibility of identifying incidental findings during genetic analysis and have a plan for determining which incidental findings should be returned to the participants.
 - 6.1.1. Investigators are not expected or required to complete exhaustive genetic testing to identify all possible, known genetic variants as part of the research however, because of the potentially sensitive and private nature of the results of genetic testing, the REC must have a clear understanding of the consent form which must include:
 - 6.1.1.1 A statement that indicates whether or not the information that derives from genetic studies will be given to that subject, who will have access to study information, and under what circumstances access will be granted.
 - 6.1.1.2 A description of the information and expert consultation that will be used to make this determination.
 - 6.1.1.3 The results of incidental findings and sensitive genetic information must be withheld until such time as the genetic test is validated as a reliable predictor of disease and appropriate counseling can be provided to the subjects.
 - 6.2. The following is a recommended process for disclosure of sensitive genetic information that must be considered when planning genetic research and incorporated into the consent form:
 - 6.2.1. Ensure that the protocol and consent document(s) have a clause for disclosure of results and incidental findings to participants and/or affected family members.
 - 6.2.2. Determine the appropriateness of disclosing genetic information to participants and/or affected family members. This includes the following considerations:
 - 6.2.2.1 Whether the information to be disclosed has evidence of clinical application, i.e., the claimed association between marker/gene and disease is generally accepted by the medical genetics community.
 - 6.2.2.2 If age is a consideration in determining who will receive results, the investigator should indicate at what age subjects will receive their results directly. In minor subjects, special attention should be given on whether it is appropriate to disclose genetic information to subjects less than 18 years of age.
 - 6.2.2.3 Initial contact to discuss the results may be made by phone or in person by the investigator, his/her primary physician to whom the results have been conveyed, or by a genetics counselor who is specifically assigned to discuss such results. The

participant must be told that receipt of results is not required and he/she may choose to decline.

INVESTIGATOR GUIDANCE

USE OF BIOLOGICAL SPECIMENS FOR RESEARCH

1. Use of Tissue and Surgical Specimens in Research
 - 1.1. Before any part of the specimen is sampled for research, all tissue specimens removed during a procedure or surgery must be examined and the diagnosis confirmed by a pathologist at KFSH&RC as per the clinical standards and hospital policies.
 - 1.1.1. Tissue may be released for RAC-approved research only through the supervision of the pathologist once a verification of the consent form indicating that the subject/patient agrees for the specimen to be submitted for research has been made by the pathologist.
 - 1.1.2. Investigators must submit the consent form to the Pathology Department for verification for each MRN for which they are requesting tissue or a waiver of the signed consent if the research has been granted a waiver.
 - 1.1.3. It is the responsibility of the pathologist to ensure that adequate tissue is retained for purposes of clinical diagnosis and care as per the guidelines of the College of American Pathologists (CAP).
 - 1.1.4. Prosthetic devices and hardware removed during surgery are also to be examined by a pathologist and will be released for research purposes at the discretion of the pathologist to ensure that there are no medico-legal issues related to the device.
 - 1.1.5. For surgical specimens obtained only for research purposes, it is the responsibility of the treating physicians to ensure that item 1.1 has occurred before the specimen is taken to the research laboratory.
 - 1.1.6. Specimens that are archived or already collected prior to the initiation of a research proposal may be used in subsequent research projects provided that:
 - 1.1.6.1 The research proposal is approved by the REC and
 - 1.1.6.2 Prior consent exists from research subjects to use their sample in future research proposals. **or**
 - 1.1.6.3 A waiver of Informed consent has been granted by the REC.
 - 1.1.6.4 The REC will decide on a case by case basis whether the new research is covered by the previous consent **or**
 - A consent can be waived **or**
 - Subjects should be contacted to obtain a new consent
 - 1.1.7. Specimens that are collected through routine clinical care or analysis and are planned to be discarded may also be used in research **providing:**
 - 1.1.7.1 The research proposal is approved by the REC.
 - 1.1.7.2 The specimens provided to the investigator are accompanied by only minimal clinical information such as age, sex, and existing laboratory results.
 - 1.1.7.3 The specimens are not individually identifiable.
 - 1.1.7.4 The specimens are provided to the investigator(s) without identifiers and the supplier of the specimens has established policies and procedures to prevent the release of personal information.
 - 1.1.7.5 The individuals caring for the patients are different from, and do not share information with those conducting the investigation.

INVESTIGATOR GUIDANCE

TISSUE BANKING AND DATA REPOSITORIES

A tissue bank or biobank collects, stores and distributes human tissue for research purposes. Using a tissue bank, a large amount and variety of samples may be stored for analysis and future research. Human tissue is a broad description for any “human biological specimen or byproduct obtained from a living or deceased individual that is sufficient in type and quantity to permit an analysis of its physical or biochemical properties. This definition includes solid tissues, cells, cell cultures, molecules derived from tissues (DNA, RNA, proteins, etc.) and body fluids, as well as associated data and information.

Creating and managing a tissue bank and or data repository requires REC approval as it is considered part of Human Subjects’ Research. Research proposals submitted for approval need to also have a detailed Tissue Banking Management Plan as part of the application and consents and authorization forms must clearly describe the tissue bank’s plan for storage, use, and sharing of the tissue, information, and data.

1. Once specimens have been collected for research through the use of an informed consent process, they are considered the property of the KFSH&RC.
 - 1.1. Individuals who make a voluntary and informed decision to contribute their biological tissues to a particular institution for medical research do not retain an ownership interest that would allow them to direct or authorize that the specimens be transferred to a third party.
2. De-identification of data:
 - 2.1. The REC recommends using the standard of de-identifying recommended by the U.S. Department of Health & Human Services (HHS) for Protected Health Information wherein the 18 identifiers are removed.
 - 2.2. It also means that a code number assigned to each individual in the dataset cannot be used to re-identify the individuals.
 - 2.3. The REC uses the standards of de-identification as described in this definition, even when a study does not involve the use of protected health information (PHI).
3. Tissue Banking Model Management Plan: The investigators operating and managing the tissue bank must maintain a detailed written plan for the operation and management of the bank/repository in addition to the usual information requested for research proposals by the REC. The details must include:
 - 3.1. The purpose of the bank/repository
 - 3.2. How samples and data will be collected.
 - 3.3. Types of samples to be collected.
 - 3.4. Type(s) of samples collected.
 - 3.5. Data points to be collected and linked to the samples.
 - 3.6. Process for obtaining consent and authorization.
 - 3.7. Storage of samples and data.
 - 3.8. Who manages the tissue bank.
 - 3.9. Where will the samples and data be stored.
 - 3.10. Procedures for protecting privacy and confidentiality while samples and data are stored in the tissue bank.
 - 3.11. Procedures for a participant to withdraw samples and data from the tissue bank.
 - 3.12. Process for transfer or destruction of samples and data if the tissue bank closes or the principal investigator leaves the managing institution.
 - 3.13. Release of Samples and Data for Future Research.

- 3.14. Description of the governance and oversight for determining if and when samples may be released to investigators for future research.
- 3.15. Procedures for an investigator to request access to samples and data for use in future research.
- 3.16. Procedures to ensure approval from the governance/oversight body of the tissue bank prior to sample release.
- 3.17. Procedure to ensure accompanying data are appropriately prepared (identifiable or de-identified) prior to sample release.
- 3.18. Process for returning future research results to participants, if applicable.
- 3.19. Informed Consent and Authorization.
- 3.20. Informed consent must be obtained from participants prior to including individual human samples in a tissue bank for future research, unless a waiver of informed consent is justified.

INVESTIGATOR GUIDANCE

REVIEWING PATIENT HEALTH INFORMATION (CHART REVIEWS)

The Patient Health Information Record (PHIR) contains sensitive and specific demographic, health related, and medical information regarding the patient's medical condition and care. This includes but is not limited to an Electronic Medical Record (EMR), a paper chart, healthcare portal(s), clinical application software programs, databases, or information kept in the departments or areas designated for clinical research/trials.

This information is privileged and access is limited only to healthcare providers directly participating in the care of the individual. The PHIR must not be accessed for research purposes unless there is a consent given by the patient or a waiver of the consent which is documented through the process of having a RAC approved study. Only individuals who are approved as part of the research may have access to the PHIR based on their role in the conduct of research.

This guidance applies to the review of all patient information found in the PHIR in order to protect the Patient Confidentiality and the rights of the individual participating in human subjects research.

1. Research, which includes reviewing patient demographic and health information, must specify what procedures will be followed to ensure confidentiality of the information abstracted from the record.
2. While the REC allows access to medical records for approved research purposes, approval of such protocols does not convey permission to contact or recruit identified patients.
3. Guidance for procedures used to recruit subjects into research studies are detailed above ([hyperlink Recruitment of Subjects](#)) and must be specified in the submitted research protocol.
4. Research involving prospective chart review requires an informed consent from the subjects in the form of a:
 - 4.1. Written informed consent or
 - 4.2. Verbal informed consent
 - 4.3. If this is not feasible, investigators must obtain a waiver of informed consent following the procedures detailed in this manual ([Hyperlink section of informed consent types](#)).
5. The Medical Records Department may be able to perform searches of the EMR and provide reports of grouped or individual data. This form of chart review should be used whenever possible.
6. Linking of medical record numbers and names to the data being reviewed is sometimes necessary in studies where clinical correlation, outcomes, and contact back with the subject is required.
 - 6.1 If medical record numbers are retained in such reports, they should be linked to a code number and the medical record numbers removed from the reports.
 - 6.2 The list linking the medical record number and code number should be secured separately and access to it limited to the principal investigator and essential personnel.
 - 6.3 If physical review of the actual patient charts is required, the following procedures should be utilized to maximize confidentiality for the research subjects:
 - 6.3.1 Medical record numbers, which allow referral back to an individual patient, should be linked to a code number and removed from the research record.

- 6.3.2 The list linking the code number to the patient name should be secured separately and access limited to the principal investigator only or essential personnel.
 - 6.3.3 The REC must be informed if patient names are to be recorded.
7. Presentation/publication of individually identifying pictures and family pedigree:
- 7.1. All individually identifying pictures, family pedigrees, or individually identifying data of research subjects may not be presented or published unless the subject/family has given an explicit written informed consent.
 - 7.2. Such a presentation/publication is allowed only if approved as necessary and cleared by the REC.

INVESTIGATOR GUIDANCE

REPORTING OF ADVERSE EVENTS TO REC

An adverse event for the purposes of this document is defined as an event, occurrence, or unanticipated problem that occurs during the course of a research study. This event may or may not be a related consequence of the intervention being used as part of the research.

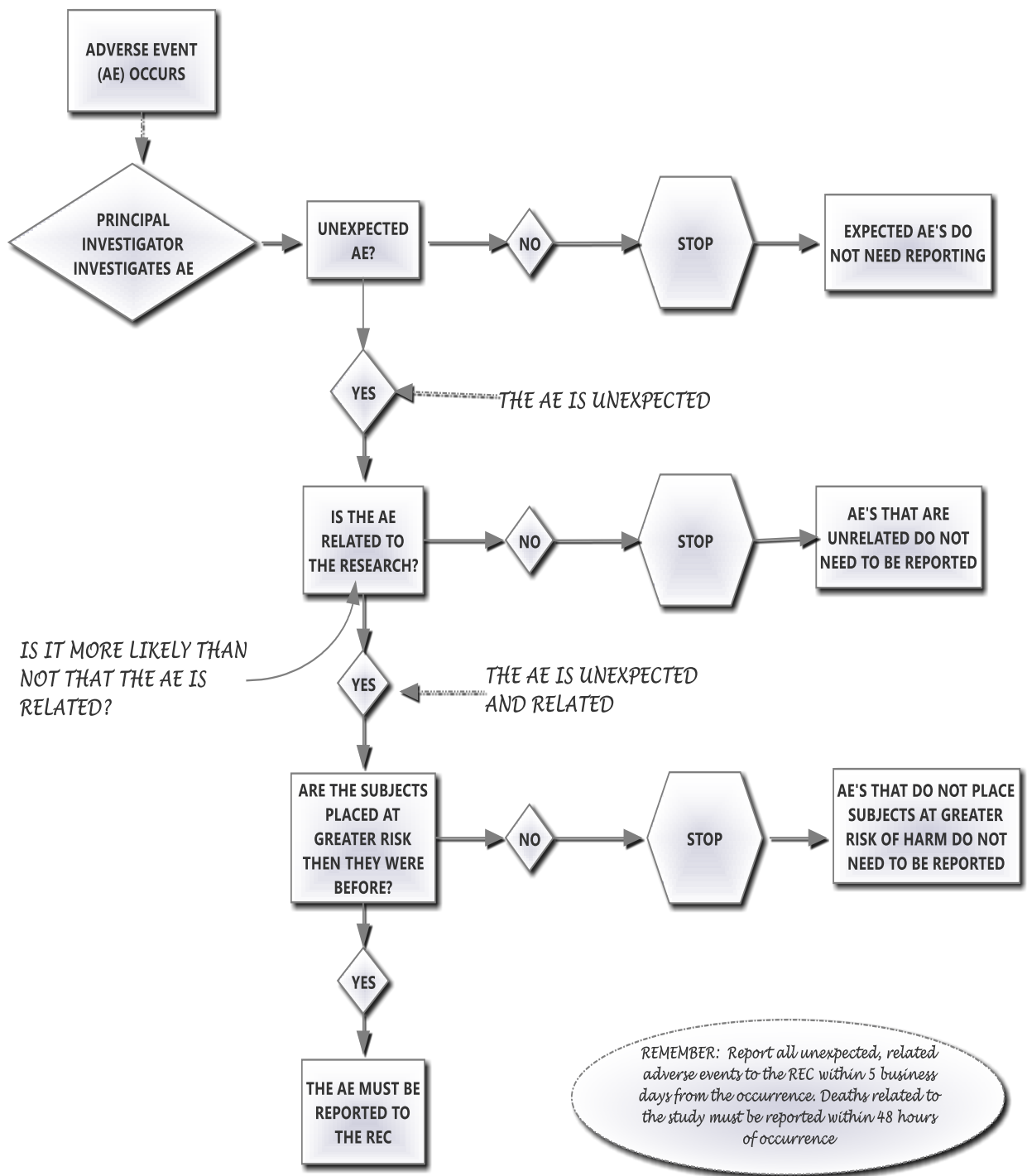
1. Serious Adverse Events/Reactions include, but are not necessarily limited to, events which are:
 - 1.1. Fatal
 - 1.2. Life-threatening or potentially life-threatening
 - 1.3. Result in permanent disability
 - 1.4. Require inpatient hospitalization or prolongation of hospitalization stay
 - 1.5. Considered significant by the investigator

2. Reporting of Serious Unexpected Adverse Events including Death:
 - 2.1. All deaths and serious adverse events which occur during the study, or in a post-study period of reasonable duration, regardless of treatment group or relationship to the research, must be reported to the ORA by:
 - 2.1.1. Filing a Serious Unexpected Adverse Event (SUAE) Form with ORA to be submitted to REC Adverse Event Report Form ([ORA 5.4 SUA Form hyperlink](#)).
 - 2.1.2. This must be done immediately or within 5 business days, upon the knowledge that the event has occurred
 - 2.1.3. Deaths related to the research must be reported immediately or within 48 hours from the occurrence of the event.

3. Reporting of Adverse Events:
 - 3.1. All adverse events related or not related to the research must be reported annually to REC.
 - 3.2. This reporting must be included in the annual progress report.
 - 3.3. The investigator must include the following items when recording an adverse event:
 - 3.3.1. The Medical Records number of the subject
 - 3.3.2. A descriptive narrative of the event
 - 3.3.3. A descriptive narrative of any further action taken as a result of the event
 - 3.3.4. Indicate the outcome of the event
 - 3.3.5. A statement as to whether the investigator feels the event was:
 - definitely related to the subject's participation in the research or
 - probably related, possibly related or
 - definitely not related

4. A statement as to whether the consent form has to be modified to incorporate the adverse event (if not already enumerated).
 - 4.1. if the sponsoring agency (i.e. - industry or governmental agency) requires that a special form be completed and submitted, the investigator should forward a copy of that form to the ORA

ADVERSE EVENT REPORTING FLOWCHART



INVESTIGATOR GUIDANCE

REPORTING OF RESEARCH RELATED MATTERS TO GOVERNMENTAL AGENCIES

National Committee of Medical & Bioethics (NCMB)

The National Committee of Medical & Bioethics was approved by the Royal Decree on 18/5/1422H, to be headquartered at KACST in Riyadh. It consists of the following sub-committees:

- The legal sub-committee.
- The human research sub-committee.
- The flora & animal sub-committee.
- The education & media sub-committee.

Human Subjects Research is under the purview of the NCMB. Investigators are required to submit a notification for all biological specimens sent for research outside the country. This committee also oversees all Institutional Review Boards and Ethics Committees throughout the country.

Saudi Food & Drug Authority (SFDA)

The Saudi Food and Drug Authority was established under the Council of Ministers resolution no. (1) Issued on 10/3/2003, as an independent Authority reporting to the Council of Ministers.

Based on the Council of Ministers resolution no. (181) issued on 18/6/2007, that gave SFDA the right to issue regulations for medical devices registration rules and procedures, the SFDA issued a medical devices interim regulation, which was adopted by SFDA board of director's decision no. (1-8-1429) issued on 27/12/2008. This regulation will apply until the medical devices comprehensive law is approved.

As part of this interim regulation, the SFDA has launched the Medical Devices National Registry (MDNR) for the purpose of obtaining a profile of the KSA medical device industry and establishing a database of all establishments, manufacturers, agents, and suppliers working in the field of medical devices. All sponsors and investigators are required to register all trials with drugs and medical devices with the Saudi FDA before embarking on the research study.

The applicant (sponsor) has to be registered in the Medical Devices National Registry (MDNR) and shall ensure that it is able to manage appropriately the imported and/or distributed devices in relation to storage, transport, traceability, installation and the like.

SFDA has established the National Center for Medical Devices Reporting (NCMDR) to record, analyze and manage medical device recalls and adverse events occurring with devices during their use.

The main objective is to reduce the likelihood of occurrence of incidents and/or to prevent repetition of adverse events. Authorized representatives, manufacturers, importers, distributors and users are expected to inform the SFDA about any device recalls or adverse events of which they are aware. The reports will be analyzed and appropriate action shall be taken. This process applies to all medical devices placed on the market and/or in use within the KSA.

SUBMITTING A RESEARCH PROPOSAL TO THE OFFICE OF RESEARCH AFFAIRS (ORA)

1. Investigators should refer to the ORA website ([hyperlink](#)) from where the appropriate forms for their planned research proposal may be downloaded as well as instructions for completing the forms.
2. In addition to completing the research related forms, all Principal Investigators and Co-Investigators must sign the Investigator's Assurance Form/Investigators Declaration of Conflict of Interest Form ([ORA 5.1.2, Investigator Assurance Form](#)) which ensures that:
 - 2.1. Investigators participating in the research are knowledgeable in their areas and have an active role in developing the research proposal.
 - 2.2. Investigators are experienced in the performance and evaluation of procedures to be used in the research.
 - 2.3. Investigators will assume the responsibility for the accuracy, integrity, and appropriateness of the parts of the proposal related to their particular expertise ([Hyperlink : RAC 8.3, Guidelines for Proposal Authorship](#))
 - 2.4. Investigators understand completely the risks, benefits, and adverse events that may result from the research.
3. All consents must be formatted as recommended per ORA Policies and REC Guidance.
4. The REC must determine that the following requirements and considerations are satisfied before approval of a study takes place and the investigator initiates the research ([hyperlink REC checklist for expedited and full review](#)):
 - 4.1 Ensure that the purpose of the research as well as the procedures and methods which the investigators are using are consistent with sound research design.
 - 4.2 Ensure that investigators do not expose human subjects to unnecessary risk.
 - 4.3 Ensure that, whenever appropriate, procedures that are already being performed on the subjects for diagnostic or treatment purposes as part of their treatment plan are incorporated into the research to avoid undue discomfort or distress.
 - 4.4 Ensure that the risk to subjects are reasonable in relation to the anticipated benefits, if any, from the study i.e. assessment of the risk/benefit ratio of the study.
 - 4.5 Ensure that the location and setting of the research is appropriate.
 - 4.6 Ensure that the selection of subjects is equitable.
 - 4.7 Ensure that the rights and special needs of the vulnerable populations are protected if they are involved in research ([See section-----Hyperlink---definition of vulnerable populations](#)).
 - 4.8 Ensure that informed consent is appropriately obtained and documented from subjects participating in the research ([See section on informed consent---hyperlink](#))
 - 4.9 Ensure that there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
 - 4.10 Ensure the safety of the subjects through adequate provisions for timely monitoring of the data being collected.
 - 4.11 Ensure that appropriate safeguards have been included in the study to protect the rights and welfare of vulnerable subjects and that subjects are not coerced or unduly influenced to participate in the research.

FORMS FOR RESEARCH PROPOSAL SUBMISSION

**RESEARCH ADVISORY COUNCIL
COVER PAGE**

I Title of Proposal:			
II Duration of Study:		III Is there External Sponsor(s)/Collaborator(s)? <input type="checkbox"/> No <input type="checkbox"/> Yes (specify)	
IV Does the Study involve sending Biological Samples (blood, urine, tissue, saliva) outside Saudi Arabia? <input type="checkbox"/> No <input type="checkbox"/> Yes (where) _____			
V Does the Study involve the use of Investigational Drug/Device or investigational use of approved Drug/Device? <input type="checkbox"/> No <input type="checkbox"/> Yes (where) _____			
VI Principal Investigator(s) (or KFSH&RC Primary Investigator(s):			
Name/ Primary Contact:	Title & Position	ID # (Affiliation & contact # if not KFSH&RC Staff)	Department (Affiliation & contact # if not KFSH&RC Staff)
VI I Co-Investigator(s) (or KFSH&RC Co-investigator(s):			
Name	Title & Position	ID # (Affiliation & contact # if not KFSH&RC Staff)	Department (Affiliation & contact # if not KFSH&RC Staff)

***All Fields should be completed**

**RESEARCH ADVISORY COUNCIL
INVESTIGATORS ASSURANCE FORM**

Proposal Title:

The Investigators named below affirm that they:

- 1 Have had a substantial contribution to this proposal as outlined in “Guidelines for Proposal Authorship.”
- 2 Will abide by the rules and regulations of the RAC including the Intellectual Property Policy, Research Ethics Committee Guidelines & Policy Manual, Animal Care & Use Committee Guidelines & Policy Manual, Policy on Research Conflict of Interest and Commitment and the Good Clinical Practice and Good Laboratory Guidelines.
- 3 Will submit progress and final reports and correspond with the RAC in a timely manner (Principal Investigator).
- 4 Will accept responsibility to maintain original data and consent forms and submit them for review if requested, as outlined in Policy on Research Records Retention and Access.
- 5 Will use scientific rigor and integrity in obtaining, recording, and analyzing data; and in reporting and publishing results as outlined in the Policy on Integrity in the Performance of Research and Policy on Responsibility for Research.
- 6 Will ensure that authorship of any resulting published work includes all, and only those, who have materially contributed to, and shared responsibility for, the contents of the publication as outlined in the “Guidelines for Manuscript Authorship.”
- 7 Will reveal material conflicts of interest, financial or other, that might influence their research objectivity in reality, or in the reasonable perception of others (all investigators should complete the attached Investigators Declaration of Conflicts of Interest Form).
- 8 Have personally completed the on-line NIH Course "Protecting Human Research Participants" <http://phrp.nihtraining.com/users/register.php> for research involving human subjects and the on-line course Working with the IACUC: non-VA version (<https://www.aalaslearninglibrary.org/demo/lessons.asp?strKeyID=9BE7F07D-7CF3-4413-82FB-659BF8846B14-0&Library=10&Track=12&Series=20&Course=38>) for research involving vertebrate animals (attach copy of certificate for each investigator if not previously submitted to ORA).
- 9 Will adhere to the approved proposal.

Name	ID	Signature	Date
Principal Investigator(s)			
Co-investigator(s)			

**RESEARCH ADVISORY COUNCIL
INVESTIGATORS DECLARATION OF CONFLICTS OF INTEREST FORM**

Proposal Title:

The KFSH&RC requires all investigators to make written declarations of their relevant interests including those of their immediate family, spouses, and children. Declarations should include all financial

interests and any other relationships with any company that owns or has licensed or has rights to license the product, device or novel treatment being evaluated. This should include but not be limited to:

- a. Employment, directorship or leadership position - any full or part time employment or service as an officer or board member.
- b. Advisory role – Consultant or advisory arrangements (paid or unpaid).
- c. Stock ownership or options – any ownership interest or options in a start –up company, the stock of which is not publicly traded, or in a publicly traded company (unless in a diversified fund not controlled by the individual).
- d. Any other direct or indirect financial interest.
- e. Honoraria – payments for specific speeches, seminar presentations or appearances.
- f. Research funding.
- g. Expert testimony.
- h. Other remuneration (trips, gifts, in-kind payments ... etc.).

Investigators must declare to the RAC of any change in circumstances during the development of, or in the course of a project that would mean that they or their spouse, or children would receive or hold any of the declarable items described here.

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

Name	ID	Signature	Date

I have read the above statement on conflicts of interest. I have conflicts of interest to declare now (attach a separate sheet for each investigator) and I will immediately declare in writing to the RAC of any future conflicts of interest:

Name	ID	Signature	Date

I, the undersigned, have the following conflicts of interest to declare:

Investigator name

Signature

date

**RESEARCH ADVISORY COUNCIL
PROPOSAL CLEARANCE FORM**

Proposal Title:

Principal Investigator: (Name, Degree, Title, Department)

Title of Proposal:

Are Departments other than the Department of the Principal Investigator involved? ©

- Yes, please list the Departments involved below
- No

Department Name	Chairman's Signature	Cleared		If no, please justify
		Yes	No	

Principal Investigator: _____ Date: _____

© Involvement may include personnel, space, facilities, or equipment

RESEARCH ADVISORY COUNCIL

PHARMACY INFORMATION LETTER (page 1 of 2)

Proposal Title:

RAC #: (if available) _____ **Principal Investigator:** _____

A This part is to be completed by the Principal Investigator

1 Please itemise all the drugs the study subjects will receive including drugs used for routine medical care and placebo
(*Rou = routine medical care: Exp: = Experimental*) (if more space is needed, use copies of this form)

Drug Name										
	<i>Rou</i>	<i>Exp</i>	<i>Rou</i>	<i>Exp</i>	<i>Rou</i>	<i>Exp</i>	<i>Rou</i>	<i>Exp</i>	<i>Rou</i>	<i>Exp</i>
Dose										
Administration Route										
Administration Frequency										
Length of treatment										
Drug Status *										
Number of patients										
Provider: Hospital or Sponsor (Identify Sponsor)										
Total Drugs Required (Pharmacy will calculate)										
(For Pharmacy Use)	<i>Rou:</i>	<i>Exp:</i>	<i>Rou:</i>	<i>Exp:</i>	<i>Rou:</i>	<i>Exp:</i>	<i>Rou:</i>	<i>Exp:</i>	<i>Rou:</i>	<i>Exp:</i>
Medication Cost										
Research Pharmacist time					_____ (hrs) X		_____ SR/hr		= SR _____	

2 If this a randomised study, who is responsible for Randomisation? _____

3 Over what period of time do you intend to accrue the patients? _____

* The Pharmacy must seek approval through the MOH in order to import drugs. Approval of the proposal by the RAC does not guarantee that the drugs will be approved and/or released by the MOH. Being a registered or investigational drug in any of the five reference countries (USA, Canada, UK, Sweden, Saudi Arabia) would help in obtaining MOH approval.

Please use the following abbreviations: **HF** – on Hospital Formulary; **MOH** – registered by the Saudi Ministry of Health; **USA** – registered in USA; **CA** – registered in Canada; **UK** – registered in UK; **SW** – registered in Sweden; **USAI** – being investigated in USA; **CAI** – being investigated in Canada; **UKI** – being investigated in UK; **SWI** – being investigated in Sweden.

Principal Investigator:

Name (print) _____ **Signature:** _____ **Date:** _____

THE DEVELOPMENT OF AN INFORMED WRITTEN CONSENT DOCUMENT

The process of obtaining informed consent is a key element in the process of conducting research where participation of human subjects is involved. The following is a guidance for determining the type of consent form and the content based on the type of research to be conducted and must be strictly adhered to.

CONSENT DOCUMENTS OFFICIALLY DATED WITH THE INCLUSIVE REC APPROVAL DATES MUST BE USED IN THE CONDUCT OF HUMAN SUBJECT STUDIES

1. When a research proposal is approved by REC, the consent documents will be stamped with an approval period.
2. For sponsored research studies where funding is needed before the start of the project, (i.e. NIH, KACST), consent documents will not be released to the investigators until official notification of funding is received by ORA or the investigator requests the start of the project without the funding (in this case the project should be submitted for scientific review by the Research Advisory Council, as well).
3. Consent forms may not be used beyond their expiration date under any circumstances.
4. The following templates must be used to prepare the written consent:
 - 4.1. Consent for Research with No Direct Benefits to Participants ([Appendix 2](#)).
 - 4.2. Consent for Research Involving the Administration of Drugs, Use of Devices, or Performance of Procedures ([Appendix 1](#)).
 - 4.3. Consent for Genetic Research ([Genetic Consent Form](#)).
5. Components of the Written Informed Consent must minimally include the following elements:
 - 5.1. A research Participant Information Sheet which must be written by the Principal Investigator and explains the details of the research unique to the particular proposal.
 - 5.2. The Research Participant Information Sheet must incorporate the following components with an appropriate subject heading for each component:
 - 5.2.1. TITLE OF PROJECT:
 - Place at the top of the first page of the consent document.
 - 5.2.2. PURPOSE OF THE RESEARCH:
 - Begin by writing “You are being asked to participate in a research study. The purpose of this study is ...”.
 - Then state “You qualify for participation in this study because...”.
 - 5.2.3. DESCRIPTION OF THE RESEARCH:
 - Must be written in language that is fully understandable to an individual with a sixth-grade education.
 - Scientific terms must be defined in language easily to understand (see [Glossary of Lay Terms for Use in Preparing Informed Consent Documents](#) [Appendix 3](#) hyperlink).
 - Describe the study design
 - Describe specifically what will be required of the subject.
 - Specify which procedures or tests are being performed solely for research, and which are being done for clinically indicated reasons.
 - Describe in detail those procedures or tests or components that are being done for research purposes.

- Indicate if the drug, device or procedure is approved or not by the Food and Drug Administration or similar agencies for the proposed use in the research proposal.
 - Indicate the approximate number of subjects to be enrolled.
 - Indicate the duration of the subject's participation.
- 5.2.4. POTENTIAL RISKS AND DISCOMFORTS:
- Describe all potential risks and discomforts of participating in the research whether major or minor.
 - Estimate the likelihood and severity of such risks and describe the reversibility of adverse reactions.
 - If blood drawing is included in the study, be sure to indicate the risks involved (eg, fainting, pain, hematoma, etc).
 - A statement should be included, if applicable, that participation may result in currently unforeseeable risks to the subject (and possibly the fetus or embryo, in the event of pregnancy).
- 5.2.5. POTENTIAL BENEFITS:
- Describe the potential benefits of participation for the subject, the general benefits for science, the population at large, or other patients with similar diseases.
 - Estimate the likelihood of such benefits.
 - Do not include information regarding compensation or procedures or medications provided at no cost in this section.
- 5.2.6. ALTERNATIVES TO PARTICIPATION (where applicable):
- The Principal Investigator should state: "The following are possible alternatives to participation..." and/or
 - "Treatment comparable to that being proposed in the context of this study is/is not available to you outside of such a study."
 - If the study does not involve treatment and there are no alternatives, simply state "The alternative is not to participate."
- 5.2.7. COSTS/REIMBURSEMENTS:
- Indicate whether the subject will incur any costs by participating and
 - Whether the subject will receive any reimbursement for time and expenses.
- 5.2.8. TERMINATION OF PARTICIPATION:
- Include the following: "You may discontinue participation in the study at any time without penalty or loss of benefits to which you are otherwise entitled."
 - When applicable, describe potential consequences of a subject's decision to withdraw and procedures for early termination.
 - Explain circumstances under which participation may be terminated by the investigator without the subject's consent.
- 5.2.9. COMPENSATION/TREATMENT:
- You may include ONE of the following standard statements, as appropriate:
 - For minimal risk protocols: "If you believe that you have suffered an injury related to this study, you should contact Dr. _____, ID number _____ at telephone _____, pager _____.
 - For more than minimal risk protocols: If the subject might receive direct benefit from participation: "In the event of injury resulting from your participation in this research study, short-term hospitalization and professional attention will be made available to you at no expense to you. Financial compensation from KFSH&RC will not be provided. If have questions or an injury related to this research as a participant in the

study, you should contact Dr. _____, ID number _____
at telephone _____, pager _____.

5.2.10. VOLUNTARY PARTICIPATION:

The entire section of voluntary participation should be in bold

- Include the following: **“Participation in the study is voluntary. If you decide not to participate this will not affect your ability to receive medical care at KFSH&RC, or to receive any benefits to which you are otherwise entitled.”**
- **“Any new information that develops during this study, which might affect your decision to participate, will be given to you immediately.”**
- **“A signed copy of this consent form will be given to you.”**

5.2.11. CONFIDENTIALITY:

- Include the following statement: “Your identity as a participant in this research study will be kept confidential in any presentation/publication of the results of this study. Your medical record in connection with this study will be kept confidential to the extent permitted by the law. However, your medical record may be reviewed by government agencies including the National Committee on Medical and Bioethics , the Ministry of Health, the Saudi FDA, or the agency sponsoring this research as per the regulations of the government of Saudi Arabia. The Office of Research Affairs (ORA), Research Ethics Committee (REC), and the Research Advisory Council (RAC) and/or their designees will also have access to your information.”

5.2.12. CONTACT PERSON(s):

- Include the following: “If you have any questions, at any time, about this research, please contact Dr. _____, ID number _____
at telephone _____, pager _____. If you have general questions about the conduct of research at KFSH&RC or your questions have not been answered fully by your doctor or his team, you may contact the Office of Research Affairs, telephone _____, email: _____.

6. Considerations for Consents for Withdrawing Drugs from Subjects:

6.1. The consent form and the consent process must comply with all the requirements for consent forms in human subject research with the inclusion of the following **ADDITIONAL** critical elements:

6.1.1. Specific Monitoring details to be included in the Study and consent form:

- Identify who will do the monitoring.
- The frequency of monitoring, including a justification for the intervals between monitoring that is dependent on the disease process.
- Site at which monitoring will be done (clinic, hospital, doctor's office, home)
- Itemization of the tests, lab data, examinations, etc. that will be used to monitor the subject.

6.1.2. Identification of Risk:

- The risks associated with the withdrawal from the subject's current medication.
- The risks of being maintained on a placebo (if applicable).
- The risks of the experimental drug(s).
- Include Self-Monitoring procedures clearly for subjects that are self-monitored.

6.1.3. Subjects should be notified clearly of:

- Any additional monitoring and the purpose of the monitoring.
- Details of the potential symptoms outlined in the consent and explained to the subject.

6.1.4. The reversibility of any recurrence of symptoms as the result of medication withdrawal or

placebo administration must be specifically described as well as the clinical steps that will be necessary to return the subject to the subject's former baseline.

6.1.5. The threshold for initiating treatment and removal from the research should be described as well as how the decision to return the subject to the subject's medication will be made and by whom.

6.1.6. The subject's right to withdraw from the research must be clearly outlined as below:

- A clear statement should be written regarding the right to withdraw from the study.
- A clear statement that the subject has the right to be returned to an appropriate clinical regimen at any time during the study period.
- In the event the subject's participation ends because the study ends, the subject and family must be advised whether the subject will be returned to the subject's old medication or in the case of experimental drugs, should they be useful, be available to the subject.
- The consent document for biological specimens (see hyperlink) must describe how the biological sample will be labeled and must indicate whether or not it will be possible to link the data obtained from the sample back to the subject. Retrospective (banked) or prospectively obtained biological samples may be categorized (labeled) in one of 4 ways:
 - Identified: The sample is labeled with the subject's name or a code, which can be directly linked to the subject and the subject's records.
 - Identifiable: The sample is labeled with a code number, which may be directly or indirectly linked back to the subject and the subject's records.
 - Anonymized or de-identified: A sample that was previously identified or identifiable, that has had all identifiers removed and can no longer be linked back to the subject or the subject's medical records by any means; or
 - Anonymous: a sample that is coded at the time it is obtained, but that code is completely unrelated to any information through which the subject or the subject's medical records can ever be directly or indirectly linked back to the subject.

7. Consideration for Consents for Biological Specimens for Research:

8. If subjects are not told how the samples will be categorized, but rather they are to be given a choice of whether they are willing to have their samples identified/ identifiable (and possibly contacted again in the future for other research studies) or whether they want to have their samples anonymous/ anonymized, then the options should be written as questions.

8.1.1. The following are examples of such questions (which should be included in the body of the document that is requesting consent for the original biological sample).

8.1.2. Subjects should be asked to initialize their answer, not just check off the choice they make.

- Do you consent to have your sample labeled in a way that will make it impossible to directly or indirectly link the sample back to you?
Yes No
- Do you consent to have your sample labeled in a way that it will be possible to directly or indirectly link the sample back to you?
Yes No
- If you consent to have your sample labeled in a way that it will be possible to directly or indirectly link the sample back to you, do you consent to be

contacted again in the future for possible participation in another research project?

Yes No

9. Future use of samples by investigators:

9.1. When the specimens are to be banked, investigators should indicate that the specimens might be banked for an indefinite period of time.

9.2. Based on the goals of the study the investigator may want to:

9.2.1. Ask consent for the investigator to use the sample in the current study only [If this is the case then it is appropriate to indicate what will be done with the sample at the end of the study (i.e. discarded)].

9.2.2. Ask consent for the investigator to store the sample and use it in future studies that are directly related to the current study.

9.2.3. Ask consent for the investigator to store the sample and use it in future studies that are unrelated to the purpose(s) of the current study (this option may not be acceptable because the consent given will not be “informed”) or

9.2.4. Ask consent for the investigator to distribute portions of the sample to other investigators, at KFSH&RC or other institutions, for use in related or unrelated research (this option may not be acceptable because the consent given will not be “informed”).

9.3. If the investigator wants to use the specimens obtained in the current study for future studies that are related or unrelated to the current study, and to distribute portions of the sample to other investigators at KFSH&RC or other institutions (as indicated in 9.2.3 & 9.2.4, then a blanket statement incorporating these points) must be included in the consent document.

9.4. If the investigator will allow the subject to choose between options then the investigator should specifically request consent for each option (in the body of the document that is requesting consent for the original biological sample).

9.5. The options may be written as questions and as follows:

9.5.1. Subjects should be asked to initial their answer, not just check off the choice they make.

- Do you consent to have portions of the biological sample that will be obtained from you in the present study used by the investigator(s) in future research studies that are directly related to the current research?

Yes No

- Do you consent to have portions of the biological sample that will be obtained from you in the present study used by the investigator(s) in future research studies that are unrelated to the purpose(s) of the current research?

Yes No

- Do you consent to have portions of the biological sample that will be obtained from you in the present study distributed to other investigators at KFSH&RC or other institutions for use in research that is either related or unrelated to the purpose of this study?

Yes No

The Nuremberg Code (1947)

1- The voluntary consent of the human subject is absolutely essential.

- This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other

ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.

- The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.
- 2- The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.
 - 3- The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.
 - 4- The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.
 - 5- No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.
 - 6- The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.
 - 7- Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.
 - 8- The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.
 - 9- During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seemed to him to be impossible.
 - 10- During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probably [sic] cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

The Belmont Report (1979)

National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

Ethical Principles & Guidelines for Research Involving Human Subjects

Scientific research has produced substantial social benefits. It has also posed some troubling ethical questions. Public attention was drawn to these questions by reported abuses of human subjects in biomedical experiments, especially during the Second World War. During the Nuremberg War Crime Trials, the Nuremberg code was drafted as a set of standards for judging physicians and scientists who had conducted biomedical experiments on concentration camp prisoners. This code became the prototype of many later codes⁽¹⁾ intended to assure that research involving human subjects would be carried out in an ethical manner.

The codes consist of rules, some general, others specific, that guide the investigators or the reviewers of research in their work. Such rules often are inadequate to cover complex situations; at times they come into conflict, and they are frequently difficult to interpret or apply. Broader ethical principles will provide a basis on which specific rules may be formulated, criticized and interpreted.

Three principles, or general prescriptive judgments, that are relevant to research involving human subjects are identified in this statement. Other principles may also be relevant. These three are comprehensive however, and are stated at a level of generalization that should assist scientists, subjects, reviewers and interested citizens to understand the ethical issues inherent in research involving human subjects. These principles cannot always be applied so as to resolve beyond dispute particular ethical problems. The objective is to provide an analytical framework that will guide the resolution of ethical problems arising from research involving human subjects.

This statement consists of a distinction between research and practice, a discussion of the three basic ethical principles, and remarks about the application of these principles.

A. Boundaries Between Practice and Research

It is important to distinguish between biomedical and behavioral research, on the one hand, and the practice of accepted therapy on the other, in order to know what activities ought to undergo review for the protection of human subjects of research. The distinction between research and practice is blurred partly because both often occur together (as in research designed to evaluate a therapy) and partly because notable departures from standard practice are often called "experimental" when the terms "experimental" and "research" are not carefully defined.

For the most part, the term "practice" refers to interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success. The purpose of medical or behavioral practice is to provide diagnosis, preventive treatment or therapy to particular individuals.⁽²⁾ By contrast, the term "research" designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships). Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective.

When a clinician departs in a significant way from standard or accepted practice, the innovation does not, in and of itself, constitute research. The fact that a procedure is "experimental," in the sense of new, untested or different, does not automatically place it in the category of research. Radically new procedures of this description should, however, be made the object of formal research at an early stage in order to determine whether they are safe and effective. Thus, it is the responsibility of medical practice committees, for example, to insist that a major innovation be incorporated into a formal research project.⁽³⁾

Research and practice may be carried on together when research is designed to evaluate the safety and efficacy of a therapy. This need not cause any confusion regarding whether or not the activity requires review; the general rule is that if there is any element of research in an activity, that activity should undergo review for the protection of human subjects.

B. Basic Ethical Principles

The expression "basic ethical principles" refers to those general judgments that serve as a basic justification for the many particular ethical prescriptions and evaluations of human actions. Three basic principles, among those generally accepted in our cultural tradition, are particularly relevant to the ethics of research involving human subjects: the principles of respect of persons, beneficence and justice.

1. Respect for Persons. -- Respect for persons incorporates at least two ethical convictions: first, that individuals should be treated as autonomous agents, and second, that persons with diminished autonomy are entitled to protection. The principle of respect for persons thus divides into two separate moral requirements: the requirement to acknowledge autonomy and the requirement to protect those with diminished autonomy.

An autonomous person is an individual capable of deliberation about personal goals and of acting under the direction of such deliberation. To respect autonomy is to give weight to autonomous persons' considered opinions and choices while refraining from obstructing their actions unless they are clearly detrimental to others. To show lack of respect for an autonomous agent is to repudiate that person's considered judgments, to deny an individual the freedom to act on those considered judgments, or to withhold information necessary to make a considered judgment, when there are no compelling reasons to do so.

However, not every human being is capable of self-determination. The capacity for self-determination matures during an individual's life, and some individuals lose this capacity wholly or in part because of illness, mental disability, or circumstances that severely restrict liberty. Respect for the immature and the incapacitated may require protecting them as they mature or while they are incapacitated.

Some persons are in need of extensive protection, even to the point of excluding them from activities which may harm them; other persons require little protection beyond making sure they undertake activities freely and with awareness of possible adverse consequence. The extent of protection afforded should depend upon the risk of harm and the likelihood of benefit. The judgment that any individual lacks autonomy should be periodically reevaluated and will vary in different situations.

In most cases of research involving human subjects, respect for persons demands that subjects enter into the research voluntarily and with adequate information. In some situations, however, application of the principle is not obvious. The involvement of prisoners as subjects of research provides an instructive example. On the one hand, it would seem that the principle of respect for persons requires that prisoners not be deprived of the opportunity to volunteer for research. On the other hand, under prison conditions they may be subtly coerced or unduly influenced to engage in research activities for which they would not otherwise volunteer. Respect for persons would then dictate that prisoners be protected. Whether to allow prisoners to "volunteer" or to "protect" them presents a dilemma. Respecting persons, in most hard cases, is often a matter of balancing competing claims urged by the principle of respect itself.

2. Beneficence. -- Persons are treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well-being. Such treatment falls under the principle of beneficence. The term "beneficence" is often understood to cover acts of kindness or charity that go beyond strict obligation. In this document, beneficence is understood in a stronger sense, as an obligation.

Two general rules have been formulated as complementary expressions of beneficent actions in this sense: **(1)** do not harm and **(2)** maximize possible benefits and minimize possible harms.

The Hippocratic maxim, "do no harm" has long been a fundamental principle of medical ethics. Claude Bernard extended it to the realm of research, saying that one should not injure one person regardless of the benefits that might come to others. However, even avoiding harm requires learning what is harmful; and, in the process of obtaining this information, persons may be exposed to risk of harm. Further, the Hippocratic Oath requires physicians to benefit their patients "according to their best judgment."

Learning what will in fact benefit may require exposing persons to risk. The problem posed by these imperatives is to decide when it is justifiable to seek certain benefits despite the risks involved, and when the benefits should be foregone because of the risks.

The obligations of beneficence affect both individual investigators and society at large, because they extend both to particular research projects and to the entire enterprise of research. In the case of particular projects, investigators and members of their institutions are obliged to give forethought to the maximization of benefits and the reduction of risk that might occur from the research investigation. In the case of scientific research in general, members of the larger society are obliged to recognize the longer term benefits and risks that may result from the improvement of knowledge and from the development of novel medical, psychotherapeutic, and social procedures.

The principle of beneficence often occupies a well-defined justifying role in many areas of research involving human subjects. An example is found in research involving children. Effective ways of treating childhood diseases and fostering healthy development are benefits that serve to justify research involving children -- even when individual research subjects are not direct beneficiaries. Research also makes it possible to avoid the harm that may result from the application of previously accepted routine practices that on closer investigation turn out to be dangerous. But the role of the principle of beneficence is not always so unambiguous. A difficult ethical problem remains, for example, about research that presents more than minimal risk without immediate prospect of direct benefit to the children involved. Some have argued that such research is inadmissible, while others have pointed out that this limit would rule out much research promising great benefit to children in the future. Here again, as with all hard cases, the different claims covered by the principle of beneficence may come into conflict and force difficult choices.

3. Justice. -- Who ought to receive the benefits of research and bear its burdens? This is a question of justice, in the sense of "fairness in distribution" or "what is deserved." An injustice occurs when some benefit to which a person is entitled is denied without good reason or when some burden is imposed unduly. Another way of conceiving the principle of justice is that equals ought to be treated equally. However, this statement requires explication. Who is equal and who is unequal? What considerations justify departure from equal distribution? Almost all commentators allow that distinctions based on experience, age, deprivation, competence, merit and position do sometimes constitute criteria justifying differential treatment for certain purposes. It is necessary, then, to explain in what respects people should be treated equally. There are several widely accepted formulations of just ways to distribute burdens and benefits. Each formulation mentions some relevant property on the basis of which burdens and benefits

should be distributed. These formulations are **(1)** to each person an equal share, **(2)** to each person according to individual need, **(3)** to each person according to individual effort, **(4)** to each person according to societal contribution, and **(5)** to each person according to merit.

Questions of justice have long been associated with social practices such as punishment, taxation and political representation. Until recently these questions have not generally been associated with scientific research. However, they are foreshadowed even in the earliest reflections on the ethics of research involving human subjects. For example, during the 19th and early 20th centuries the burdens of serving as research subjects fell largely upon poor ward patients, while the benefits of improved medical care flowed primarily to private patients. Subsequently, the exploitation of unwilling prisoners as research subjects in Nazi concentration camps was condemned as a particularly flagrant injustice. In this country, in the 1940's, the Tuskegee syphilis study used disadvantaged, rural black men to study the untreated course of a disease that is by no means confined to that population. These subjects were deprived of demonstrably effective treatment in order not to interrupt the project, long after such treatment became generally available.

Against this historical background, it can be seen how conceptions of justice are relevant to research involving human subjects. For example, the selection of research subjects needs to be scrutinized in order to determine whether some classes (e.g., welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are being systematically selected simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied. Finally, whenever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands both that these not provide advantages only to those who can afford them and that such research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.

C. Applications

Applications of the general principles to the conduct of research leads to consideration of the following requirements: informed consent, risk/benefit assessment, and the selection of subjects of research.

1. Informed Consent. -- Respect for persons requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them. This opportunity is provided when adequate standards for informed consent are satisfied.

While the importance of informed consent is unquestioned, controversy prevails over the nature and possibility of an informed consent. Nonetheless, there is widespread agreement that the consent process can be analyzed as containing three elements: information, comprehension and voluntariness.

Information. Most codes of research establish specific items for disclosure intended to assure that subjects are given sufficient information. These items generally include: the research procedure, their purposes, risks and anticipated benefits, alternative procedures (where therapy is involved), and a statement offering the subject the opportunity to ask questions and to withdraw at any time from the research. Additional items have been proposed, including how subjects are selected, the person responsible for the research, etc.

However, a simple listing of items does not answer the question of what the standard should be for judging how much and what sort of information should be provided. One standard frequently invoked in medical practice, namely the information commonly provided by practitioners in the field or in the locale, is inadequate since research takes place precisely when a common understanding does not exist. Another standard, currently popular in malpractice law, requires the practitioner to reveal the information that

reasonable persons would wish to know in order to make a decision regarding their care. This, too, seems insufficient since the research subject, being in essence a volunteer, may wish to know considerably more about risks gratuitously undertaken than do patients who deliver themselves into the hand of a clinician for needed care. It may be that a standard of "the reasonable volunteer" should be proposed: the extent and nature of information should be such that persons, knowing that the procedure is neither necessary for their care nor perhaps fully understood, can decide whether they wish to participate in the furthering of knowledge. Even when some direct benefit to them is anticipated, the subjects should understand clearly the range of risk and the voluntary nature of participation.

A special problem of consent arises where informing subjects of some pertinent aspect of the research is likely to impair the validity of the research. In many cases, it is sufficient to indicate to subjects that they are being invited to participate in research of which some features will not be revealed until the research is concluded. In all cases of research involving incomplete disclosure, such research is justified only if it is clear that **(1)** incomplete disclosure is truly necessary to accomplish the goals of the research, **(2)** there are no undisclosed risks to subjects that are more than minimal, and **(3)** there is an adequate plan for debriefing subjects, when appropriate, and for dissemination of research results to them.

Information about risks should never be withheld for the purpose of eliciting the cooperation of subjects, and truthful answers should always be given to direct questions about the research. Care should be taken to distinguish cases in which disclosure would destroy or invalidate the research from cases in which disclosure would simply inconvenience the investigator.

Comprehension. The manner and context in which information is conveyed is as important as the information itself. For example, presenting information in a disorganized and rapid fashion, allowing too little time for consideration or curtailing opportunities for questioning, all may adversely affect a subject's ability to make an informed choice.

Because the subject's ability to understand is a function of intelligence, rationality, maturity and language, it is necessary to adapt the presentation of the information to the subject's capacities. Investigators are responsible for ascertaining that the subject has comprehended the information. While there is always an obligation to ascertain that the information about risk to subjects is complete and adequately comprehended, when the risks are more serious, that obligation increases. Occasionally, it may be suitable to give some oral or written tests of comprehension.

Special provision may be made when comprehension is severely limited -- for example, by conditions of immaturity or mental disability. Each class of subjects that one might consider as incompetent (e.g., infants and young children, mentally disabled patients, the terminally ill and the comatose) should be considered on its own terms. Even for these persons, however, respect requires giving them the opportunity to choose to the extent they are able, whether or not to participate in research. The objections of these subjects to involvement should be honored, unless the research entails providing them a therapy unavailable elsewhere. Respect for persons also requires seeking the permission of other parties in order to protect the subjects from harm. Such persons are thus respected both by acknowledging their own wishes and by the use of third parties to protect them from harm.

The third parties chosen should be those who are most likely to understand the incompetent subject's situation and to act in that person's best interest. The person authorized to act on behalf of the subject should be given an opportunity to observe the research as it proceeds in order to be able to withdraw the subject from the research, if such action appears in the subject's best interest.

Voluntariness. An agreement to participate in research constitutes a valid consent only if voluntarily given. This element of informed consent requires conditions free of coercion and undue influence. Coercion occurs when an overt threat of harm is intentionally presented by one person to another in order to obtain compliance. Undue influence, by contrast, occurs through an offer of an excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance. Also, inducements that would ordinarily be acceptable may become undue influences if the subject is especially vulnerable.

Unjustifiable pressures usually occur when persons in positions of authority or commanding influence -- especially where possible sanctions are involved -- urge a course of action for a subject. A continuum of such influencing factors exists, however, and it is impossible to state precisely where justifiable persuasion ends and undue influence begins. But undue influence would include actions such as manipulating a person's choice through the controlling influence of a close relative and threatening to withdraw health services to which an individual would otherwise be entitled.

2. Assessment of Risks and Benefits. -- The assessment of risks and benefits requires a careful array of relevant data, including, in some cases, alternative ways of obtaining the benefits sought in the research. Thus, the assessment presents both an opportunity and a responsibility to gather systematic and comprehensive information about proposed research. For the investigator, it is a means to examine whether the proposed research is properly designed. For a review committee, it is a method for determining whether the risks that will be presented to subjects are justified. For prospective subjects, the assessment will assist the determination whether or not to participate.

The Nature and Scope of Risks and Benefits. The requirement that research is to be justified on the basis of a favorable risk/benefit assessment bears a close relation to the principle of beneficence, just as the moral requirement that informed consent to be obtained is derived primarily from the principle of respect for persons. The term "risk" refers to a possibility that harm may occur. However, when expressions such as "small risk" or "high risk" are used, they usually refer (often ambiguously) both to the chance (probability) of experiencing a harm and the severity (magnitude) of the envisioned harm.

The term "benefit" is used in the research context to refer to something of positive value related to health or welfare. Unlike "risk," "benefit" is not a term that expresses probabilities. Risk is properly contrasted to probability of benefits, and benefits are properly contrasted with harms rather than risks of harm. Accordingly, so-called risk/benefit assessments are concerned with the probabilities and magnitudes of possible harm and anticipated benefits. Many kinds of possible harms and benefits need to be taken into account. There are, for example, risks of psychological harm, physical harm, legal harm, social harm and economic harm and the corresponding benefits. While the most likely types of harms to research subjects are those of psychological or physical pain or injury, other possible kinds should not be overlooked.

Risks and benefits of research may affect the individual subjects, the families of the individual subjects, and society at large (or special groups of subjects in society). Previous codes and federal regulations have required that risks to subjects be outweighed by the sum of both the anticipated benefit to the subject, if any, and the anticipated benefit to society in the form of knowledge to be gained from the research. In balancing these different elements, the risks and benefits affecting the immediate research subject will normally carry special weight. On the other hand, interests other than those of the subject may on some occasions be sufficient by themselves to justify the risks involved in the research, so long as the subjects' rights have been protected. Beneficence thus requires that we protect against risk of harm to subjects and also that we be concerned about the loss of the substantial benefits that might be gained from research.

The Systematic Assessment of Risks and Benefits. It is commonly said that benefits and risks must be "balanced" and shown to be "in a favorable ratio." The metaphorical character of these terms draws attention to the difficulty of making precise judgments. Only on rare occasions will quantitative techniques be available for the scrutiny of research protocols. However, the idea of systematic, nonarbitrary analysis of risks and benefits should be emulated insofar as possible. This ideal requires those making decisions about the justifiability of research to be thorough in the accumulation and assessment of information about all aspects of the research, and to consider alternatives systematically.

This procedure renders the assessment of research more rigorous and precise, while making communication between review board members and investigators less subject to misinterpretation, misinformation and conflicting judgments. Thus, there should first be a determination of the validity of the presuppositions of the research; then the nature, probability and magnitude of risk should be distinguished with as much clarity as possible. The method of ascertaining risks should be explicit, especially where there is no alternative to the use of such vague categories as small or slight risk. It should also be determined whether an investigator's estimates of the probability of harm or benefits are reasonable, as judged by known facts or other available studies.

Finally, assessment of the justifiability of research should reflect at least the following considerations: **(i)** Brutal or inhumane treatment of human subjects is never morally justified. **(ii)** Risks should be reduced to those necessary to achieve the research objective. It should be determined whether it is in fact necessary to use human subjects at all. Risk can perhaps never be entirely eliminated, but it can often be reduced by careful attention to alternative procedures. **(iii)** When research involves significant risk of serious impairment, review committees should be extraordinarily insistent on the justification of the risk (looking usually to the likelihood of benefit to the subject -- or, in some rare cases, to the manifest voluntariness of the participation). **(iv)** When vulnerable populations are involved in research, the appropriateness of involving them should itself be demonstrated. A number of variables go into such judgments, including the nature and degree of risk, the condition of the particular population involved, and the nature and level of the anticipated benefits. **(v)** Relevant risks and benefits must be thoroughly arrayed in documents and procedures used in the informed consent process.

3. Selection of Subjects. -- Just as the principle of respect for persons finds expression in the requirements for consent, and the principle of beneficence in risk/benefit assessment, the principle of justice gives rise to moral requirements that there be fair procedures and outcomes in the selection of research subjects. Justice is relevant to the selection of subjects of research at two levels: the social and the individual. Individual justice in the selection of subjects would require that researchers exhibit fairness: thus, they should not offer potentially beneficial research only to some patients who are in their favor or select only "undesirable" persons for risky research. Social justice requires that distinction be drawn between classes of subjects that ought, and ought not, to participate in any particular kind of research, based on the ability of members of that class to bear burdens and on the appropriateness of placing further burdens on already burdened persons. Thus, it can be considered a matter of social justice that there is an order of preference in the selection of classes of subjects (e.g., adults before children) and that some classes of potential subjects (e.g., the institutionalized mentally infirm or prisoners) may be involved as research subjects, if at all, only on certain conditions.

Injustice may appear in the selection of subjects, even if individual subjects are selected fairly by investigators and treated fairly in the course of research. Thus injustice arises from social, racial, sexual and cultural biases institutionalized in society. Thus, even if individual researchers are treating their research subjects fairly, and even if IRBs are taking care to assure that subjects are selected fairly within a particular institution, unjust social patterns may nevertheless appear in the overall distribution of the burdens and

benefits of research. Although individual institutions or investigators may not be able to resolve a problem that is pervasive in their social setting, they can consider distributive justice in selecting research subjects.

Some populations, especially institutionalized ones, are already burdened in many ways by their infirmities and environments. When research is proposed that involves risks and does not include a therapeutic component, other less burdened classes of persons should be called upon first to accept these risks of research, except where the research is directly related to the specific conditions of the class involved. Also, even though public funds for research may often flow in the same directions as public funds for health care, it seems unfair that populations dependent on public health care constitute a pool of preferred research subjects if more advantaged populations are likely to be the recipients of the benefits.

One special instance of injustice results from the involvement of vulnerable subjects. Certain groups, such as racial minorities, the economically disadvantaged, the very sick, and the institutionalized may continually be sought as research subjects, owing to their ready availability in settings where research is conducted. Given their dependent status and their frequently compromised capacity for free consent, they should be protected against the danger of being involved in research solely for administrative convenience, or because they are easy to manipulate as a result of their illness or socioeconomic condition.

The Declaration of Helsinki
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
and the 52nd WMA General Assembly, Edinburgh, Scotland, October 2000

A. INTRODUCTION

1. The World Medical Association has developed the Declaration of Helsinki as a statement of ethical principles to provide guidance to physicians and other participants in medical research involving human subjects. Medical research involving human subjects includes research on identifiable human material or identifiable data.
2. It is the duty of the physician to promote and safeguard the health of the people. The physician's knowledge and conscience are dedicated to the fulfillment of this duty.
3. The Declaration of Geneva of the World Medical Association binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient."
4. Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects.
5. In medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and society.
6. The primary purpose of medical research involving human subjects is to improve prophylactic, diagnostic and therapeutic procedures and the understanding of the aetiology and pathogenesis of disease. Even the best proven prophylactic, diagnostic, and therapeutic methods must continuously be challenged through research for their effectiveness, efficiency, accessibility and quality.
7. In current medical practice and in medical research, most prophylactic, diagnostic and therapeutic procedures involve risks and burdens.
8. Medical research is subject to ethical standards that promote respect for all human beings and protect their health and rights. Some research populations are vulnerable and need special protection. The particular needs of the economically and medically disadvantaged must be recognized. Special attention is also required for those who cannot give or refuse consent for themselves, for those who may be subject to giving consent under duress, for those who will not benefit personally from the research and for those for whom the research is combined with care.

9. Research Investigators should be aware of the ethical, legal and regulatory requirements for research on human subjects in their own countries as well as applicable international requirements. No national ethical, legal or regulatory requirement should be allowed to reduce or eliminate any of the protections for human subjects set forth in this Declaration.

B. BASIC PRINCIPLES FOR ALL MEDICAL RESEARCH

- 1) It is the duty of the physician in medical research to protect the life, health, privacy, and dignity of the human subject.

- 2) Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and on adequate laboratory and, where appropriate, animal experimentation.

Appropriate caution must be exercised in the conduct of research which may affect the environment, and the welfare of animals used for research must be respected.

- 3) The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol. This protocol should be submitted for consideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review committee, which must be independent of the investigator, the sponsor or any other kind of undue influence. This independent committee should be in conformity with the laws and regulations of the country in which the research experiment is performed. The committee has the right to monitor ongoing trials. The researcher has the obligation to provide monitoring information to the committee, especially any serious adverse events. The researcher should also submit to the committee, for review, information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest and incentives for subjects.

- 4) The research protocol should always contain a statement of the ethical considerations involved and should indicate that there is compliance with the principles enunciated in this Declaration. Medical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given consent.

- 5) Every medical research project involving human subjects should be preceded by careful assessment of predictable risks and burdens in comparison with foreseeable benefits to the subject or to others. This does not preclude the participation of healthy volunteers in medical research. The design of all studies should be publicly available.

- 6) Physicians should abstain from engaging in research projects involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Physicians should cease any investigation if the risks are found to outweigh the potential benefits or if there is conclusive proof of positive and beneficial results.

- 7) Medical research involving human subjects should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the subject. This is especially important when the human subjects are healthy volunteers.

- 8) Medical research is only justified if there is a reasonable likelihood that the populations in which the research is carried out stand to benefit from the results of the research.
- 9) The subjects must be volunteers and informed participants in the research project.
- 10) The right of research subjects to safeguard their integrity must always be respected. Every precaution should be taken to respect the privacy of the subject, the confidentiality of the patient's information and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.
- 11) In any research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail. The subject should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. After ensuring that the subject has understood the information, the physician should then obtain the subject's freely-given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed.
- 12) When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship with the physician or may consent under duress. In that case the informed consent should be obtained by a well-informed physician who is not engaged in the investigation and who is completely independent of this relationship.
- 13) For a research subject who is legally incompetent, physically or mentally incapable of giving consent or is a legally incompetent minor, the investigator must obtain informed consent from the legally authorized representative in accordance with applicable law. These groups should not be included in research unless the research is necessary to promote the health of the population represented and this research cannot instead be performed on legally competent persons.
- 14) When a subject deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the investigator must obtain that assent in addition to the consent of the legally authorized representative.
- 15) Research on individuals from whom it is not possible to obtain consent, including proxy or advance consent, should be done only if the physical/mental condition that prevents obtaining informed consent is a necessary characteristic of the research population. The specific reasons for involving research subjects with a condition that renders them unable to give informed consent should be stated in the experimental protocol for consideration and approval of the review committee. The protocol should state that consent to remain in the research should be obtained as soon as possible from the individual or a legally authorized surrogate.
- 16) Both authors and publishers have ethical obligations. In publication of the results of research, the investigators are obliged to preserve the accuracy of the results. Negative as well as positive results should be published or otherwise publicly available. Sources of funding, institutional affiliations and any possible conflicts of interest should be declared in the publication. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.

ADDITIONAL PRINCIPLES FOR MEDICAL RESEARCH COMBINED WITH MEDICAL CARE

- 1) The physician may combine medical research with medical care, only to the extent that the research is justified by its potential prophylactic, diagnostic or therapeutic value. When medical research is combined with medical care, additional standards apply to protect the patients who are research subjects.
- 2) The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists.
- 3) At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study.
- 4) The physician should fully inform the patient which aspects of the care are related to the research. The refusal of a patient to participate in a study must never interfere with the patient-physician relationship.
- 5) In the treatment of a patient, where proven prophylactic, diagnostic and therapeutic methods do not exist or have been ineffective, the physician, with informed consent from the patient, must be free to use unproven or new prophylactic, diagnostic and therapeutic measures, if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, these measures should be made the object of research, designed to evaluate their safety and efficacy. In all cases, new information should be recorded and, where appropriate, published. The other relevant guidelines of this Declaration should be followed.

Council of Europe. Convention on Human Rights and Biomedicine (1997)

CONVENTION FOR THE PROTECTION OF HUMAN RIGHTS AND DIGNITY OF THE HUMAN BEING WITH REGARD TO THE APPLICATION OF BIOLOGY AND MEDICINE:

Chapter I - General provisions

Article 1 - Purpose and object

Parties to this Convention shall protect the dignity and identity of all human beings and guarantee everyone, without discrimination, respect for their integrity and other rights and fundamental freedoms with regard to the application of biology and medicine.

Each Party shall take in its internal law the necessary measures to give effect to the provisions of this Convention.

Article 2 - Primacy of the human being

The interests and welfare of the human being shall prevail over the sole interest of society or science.

Article 3 - Equitable access to health care

Parties, taking into account health needs and available resources, shall take appropriate measures with a view to providing, within their jurisdiction, equitable access to health care of appropriate quality.

Article 4 - Professional standards

Any intervention in the health field, including research, must be carried out in accordance with relevant professional obligations and standards.

Chapter II - Consent

Article 5 - General rule

An intervention in the health field may only be carried out after the person concerned has given free and informed consent to it.

This person shall beforehand be given appropriate information as to the purpose and nature of the intervention as well as on its consequences and risks.

The person concerned may freely withdraw consent at any time.

Article 6 - Protection of persons not able to consent

1. Subject to Articles 17 and 20 below, an intervention may only be carried out on a person who does not have the capacity to consent, for his or her direct benefit.

2. Where, according to law, a minor does not have the capacity to consent to an intervention, the intervention may only be carried out with the authorization of his or her representative or an authority or a person or body provided for by law.

The opinion of the minor shall be taken into consideration as an increasingly determining factor in proportion to his or her age and degree of maturity.

3. Where, according to law, an adult does not have the capacity to consent to an intervention because of a mental disability, a disease or for similar reasons, the intervention may only be carried out with the authorization of his or her representative or an authority or a person or body provided

for by law. The individual concerned shall as far as possible take part in the authorization procedure.

4. The representative, the authority, the person or the body mentioned in paragraphs 2 and 3 above shall be given, under the same conditions, the information referred to in Article 5.
5. The authorization referred to in paragraphs 2 and 3 above may be withdrawn at any time in the best interests of the person concerned.

Article 7 - Protection of persons who have mental disorder

Subject to protective conditions prescribed by law, including supervisory, control and appeal procedures, a person who has a mental disorder of a serious nature may be subjected, without his or her consent, to an intervention aimed at treating his or her mental disorder only where, without such treatment, serious harm is likely to result to his or her health.

Article 8 - Emergency situation

When because of an emergency situation the appropriate consent cannot be obtained, any medically necessary intervention may be carried out immediately for the benefit of the health of the individual concerned.

Article 9 - Previously expressed wishes

The previously expressed wishes relating to a medical intervention by a patient who is not, at the time of the intervention, in a state to express his or her wishes shall be taken into account.

Chapter III - Private life and right to information

Article 10 - Private life and right to information

1. Everyone has the right to respect for private life in relation to information about his or her health.
2. Everyone is entitled to know any information collected about his or her health. However, the wishes of individuals not to be so informed shall be observed.
3. In exceptional cases, restrictions may be placed by law on the exercise of the rights contained in paragraph 2 in the interests of the patient.

Chapter IV - Human genome

Article 11 - Non-discrimination

Any form of discrimination against a person on grounds of his or her genetic heritage is prohibited.

Article 12 - Predictive genetic tests

Tests which are predictive of genetic diseases or which serve either to identify the subject as a carrier of a gene responsible for a disease or to detect a genetic predisposition or susceptibility to a disease may be performed only for health purposes or for scientific research linked to health purposes, and subject to appropriate genetic counselling.

Article 13 - Interventions on the human genome

An intervention seeking to modify the human genome may only be undertaken for preventive, diagnostic or therapeutic purposes and only if its aim is not to introduce any modification in the genome of any descendants.

Article 14 - Non-selection of sex

The use of techniques of medically assisted procreation shall not be allowed for the purpose of choosing a future child's sex, except where serious hereditary sex-related disease is to be avoided.

Chapter V - Scientific research

Article 15 - General rule

Scientific research in the field of biology and medicine shall be carried out freely, subject to the provisions of this Convention and the other legal provisions ensuring the protection of the human being.

Article 16 - Protection of persons undergoing research

Research on a person may only be undertaken if all the following conditions are met:

- i there is no alternative of comparable effectiveness to research on humans,
- ii the risks which may be incurred by that person are not disproportionate to the potential benefits of the research,
- iii the research project has been approved by the competent body after independent examination of its scientific merit, including assessment of the importance of the aim of the research, and multidisciplinary review of its ethical acceptability,
- iv the persons undergoing research have been informed of their rights and the safeguards prescribed by law for their protection,
- v the necessary consent as provided for under Article 5 has been given expressly, specifically and is documented. Such consent may be freely withdrawn at any time.

Article 17 - Protection of persons not able to consent to research

1. Research on a person without the capacity to consent as stipulated in Article 5 may be undertaken only if all the following conditions are met:
 - i the conditions laid down in Article 16, sub-paragraphs i to iv, are fulfilled;
 - ii the results of the research have the potential to produce real and direct benefit to his or her health;
 - iii research of comparable effectiveness cannot be carried out on individuals capable of giving consent;
 - iv the necessary authorisation provided for under Article 6 has been given specifically and in writing, and
 - v the person concerned does not object.
2. Exceptionally and under the protective conditions prescribed by law, where the research has not the potential to produce results of direct benefit to the health of the person concerned, such research may be authorized subject to the conditions laid down in paragraph 1, sub-paragraphs i, iii, iv and v above, and to the following additional conditions:
 - i the research has the aim of contributing, through significant improvement in the scientific understanding of the individual's condition, disease or disorder, to the ultimate attainment of results capable of conferring benefit to the person concerned or to other persons in the same age category or afflicted with the same disease or disorder or having the same condition.
 - ii the research entails only minimal risk and minimal burden for the individual concerned.

Article 18 - Research on embryos in vitro

1. Where the law allows research on embryos in vitro, it shall ensure adequate protection of the embryo.
2. The creation of human embryos for research purposes is prohibited.

Chapter VI - Organ and tissue removal from living donors for transplantation purposes

Article 19 - General rule

1. Removal of organs or tissue from a living person for transplantation purposes may be carried out solely for the therapeutic benefit of the recipient and where there is no suitable organ or tissue

available from a deceased person and no other alternative therapeutic method of comparable effectiveness.

2. The necessary consent as provided for under Article 5 must have been given expressly and specifically either in written form or before an official body.

Article 20 - Protection of persons not able to consent to organ removal

1. No organ or tissue removal may be carried out on a person who does not have the capacity to consent under Article 5.
2. Exceptionally and under the protective conditions prescribed by law, the removal of regenerative tissue from a person who does not have the capacity to consent may be authorised provided the following conditions are met:
 - i there is no compatible donor available who has the capacity to consent,
 - ii the recipient is a brother or sister of the donor,
 - iii the donation must have the potential to be life-saving for the recipient,
 - iv the authorisation provided for under paragraphs 2 and 3 of Article 6 has been given specifically and in writing, in accordance with the law and with the approval of the competent body,
 - v the potential donor concerned does not object.

Chapter VII - Prohibition of financial gain and disposal of a part of the human body

Article 21 - Prohibition of financial gain

The human body and its parts shall not, as such, give rise to financial gain.

Article 22 - Disposal of a removed part of the human body

When in the course of an intervention any part of a human body is removed, it may be stored and used for a purpose other than that for which it was removed, only if this is done in conformity with appropriate information and consent procedures.

Chapter VIII - Infringements of the provisions of the Convention

Article 23 - Infringement of the rights or principles

The Parties shall provide appropriate judicial protection to prevent or to put a stop to an unlawful infringement of the rights and principles set forth in this Convention at short notice.

Article 24 - Compensation for undue damage

The person who has suffered undue damage resulting from an intervention is entitled to fair compensation according to the conditions and procedures prescribed by law.

Article 25 - Sanctions

Parties shall provide for appropriate sanctions to be applied in the event of infringement of the provisions contained in this Convention.

Chapter IX - Relation between this Convention and other provisions

Article 26 - Restrictions on the exercise of the rights

1. No restrictions shall be placed on the exercise of the rights and protective provisions contained in this Convention other than such as are prescribed by law and are necessary in a democratic society in the interest of public safety, for the prevention of crime, for the protection of public health or for the protection of the rights and freedoms of others.
2. The restrictions contemplated in the preceding paragraph may not be placed on Articles 11, 13, 14, 16, 17, 19, 20 and 21.

Article 27 - Wider protection

None of the provisions of this Convention shall be interpreted as limiting or otherwise affecting the possibility for a Party to grant a wider measure of protection with regard to the application of biology and medicine than is stipulated in this Convention.

Chapter X - Public debate

Article 28 - Public debate

Parties to this Convention shall see to it that the fundamental questions raised by the developments of biology and medicine are the subject of appropriate public discussion in the light, in particular, of relevant medical, social, economic, ethical and legal implications, and that their possible application is made the subject of appropriate consultation.

Chapter XI - Interpretation and follow-up of the Convention

Article 29 - Interpretation of the Convention

Article 30 - Reports on the application of the Convention

Chapter XII - Protocols

Article 31 - Protocols

Chapter XIII - Amendments to the Convention

Article 32 - Amendments to the Convention

Chapter XIV - Final clauses

Article 33 - Signature, ratification and entry into force

Article 34 - Non-member States

Article 35 - Territories

Article 36 - Reservations

Article 37 - Denunciation

Article 38 - Notifications

**The Canadian Tri-Council Policy Statement:
Ethical Conduct of Research Involving Humans (1999)**

The following is a comprehensive listing of all articles included in the statement.

Article 1.1

- a. All research that involves living human subjects requires review and approval by an REB in accordance with this Policy Statement, before the research is started, except as stipulated below.
- b. Research involving human remains, cadavers, tissues, biological fluids, embryos or fetuses should also be reviewed by the REB.
- c. Research about a living individual involved in the public arena, or about an artist, based exclusively on publicly available information, documents, records, works, performances, archival materials or third-party interviews, is not required to undergo ethics review. Such research only requires ethics review if the subject is approached directly for interviews or for access to private papers, and then only to ensure that such approaches are conducted according to professional protocols and to Article 2.3 of this Policy.
- d. Quality assurance studies, performance reviews or testing within normal educational requirements should also not be subject to REB review.

Article 1.2

The institution in which research involving human subjects is carried out shall mandate the REB to approve, reject, propose modifications to, or terminate any proposed or ongoing research involving human subjects which is conducted within, or by members of, the institution, using the considerations set forth in this Policy as the minimum standard.

Article 1.3

The REB shall consist of at least five members, including both men and women, of whom:

- a. at least two members have broad expertise in the methods or in the areas of research that are covered by the REB;
- b. at least one member is knowledgeable in ethics;
- c. for biomedical research, at least one member is knowledgeable in the relevant law; this is advisable but not mandatory for other areas of research; and
- d. at least one member has no affiliation with the institution, but is recruited from the community served by the institution.

Article 1.4

- a. REBs shall be established by the highest levels of the institution, and cover as broad a range of research as is consistent with manageable workloads. Departmental REBs normally are not acceptable (except as discussed below for review of undergraduate research within course requirements). A multiplicity of REBs with small workloads within the same institution should be avoided.

- b. Large institutions may find it necessary to create more than one REB, usually to cover different areas of research. The jurisdiction of each REB should be clearly defined by the normal processes of governance within the Institution, and a mechanism should be established to coordinate the practices of all REBs within the Institution.
- c. Small institutions may wish to explore regional cooperation or alliances, including the sharing of REBs.

Article 1.5

- a. The REB shall satisfy itself that the design of a research project that poses more than minimal risk is capable of addressing the questions being asked in the research.
- b. The extent of the review for scholarly standards that is required for biomedical research that does not involve more than minimal risk will vary according to the research being carried out.
- c. Research in the humanities and the social sciences which poses, at most, minimal risk shall not normally be required by the REB to be peer reviewed.
- d. Certain types of research, particularly in the social sciences and the humanities, may legitimately have a negative effect on public figures in politics, business, labor, the arts or other walks of life, or on organizations. Such research should not be blocked through the use of harms/benefits analysis or because of the potentially negative nature of the findings. The safeguard for those in the public arena is through public debate and discourse and, *in extremis*, through action in the courts for libel.

Article 1.6

The REB should adopt a proportionate approach based on the general principle that the more invasive the research, the greater should be the care in assessing the research.

Article 1.7

REBs shall meet regularly to discharge their responsibilities.

Article 1.8

Minutes of all REB meetings shall be prepared and maintained by the REB. The minutes shall clearly document the REB's decisions and any dissents, and the reasons for them. In order to assist internal and external audits or research monitoring, and to facilitate reconsideration or appeals, the minutes must be accessible to authorized representatives of the institution, researchers and funding agencies.

Article 1.9

REBs shall meet face-to-face to review proposed research that is not delegated to expedited review. REB review shall be based upon fully detailed research proposals or, where applicable, progress reports. The REB shall function impartially, provide a fair hearing to those involved and provide reasoned and appropriately documented opinions and decisions. The REB shall accommodate reasonable requests from researchers to participate in discussions about their proposals, but not be present when the REB is making its decision. When an REB is considering a negative decision, it shall provide the researcher with all the reasons for doing so and give the researcher an opportunity to reply before making a final decision.

Article 1.10

Researchers have the right to request, and REBs have an obligation to provide, reconsideration of decisions affecting a research project.

Article 1.11

In cases when researchers and REBs cannot reach agreement through discussion and reconsideration, an institution should permit review of an REB decision by an appeal board, provided that the board is within the same institution and its membership and procedures meet the requirements of this Policy. No *ad hoc* appeal boards are permitted.

The Councils will not entertain any appeals of REB decisions.

Article 1.12

If an REB is reviewing research in which a member of the REB has a personal interest in the research under review (e.g., as a researcher or as an entrepreneur), conflict of interest principles require that the member not be present when the REB is discussing or making its decision. The REB member may disclose and explain the conflict of interest and offer evidence to the REB provided the conflict is fully explained to the REB, and the proposer of the research has the right to hear the evidence and to offer a rebuttal.

Article 1.13

- a. Ongoing research shall be subject to continuing ethics review. The rigor of the review should be in accordance with a proportionate approach to ethics assessment.
- b. As part of each research proposal submitted for REB review, the researcher shall propose to the REB the continuing review process deemed appropriate for that project.
- c. Normally, continuing review shall consist of at least the submission of a succinct annual status report to the REB. The REB shall be promptly notified when the project concludes.

Article 1.14

Research to be performed outside the jurisdiction or country of the institution which employs the researcher shall undergo prospective ethics review both (a) by the REB within the researcher's institution; and (b) by the appropriate REB, where such exists, which has authority in the country or jurisdiction where the research is to be done.

Article 2.1

- a. Research governed by this Policy (see Article 1.1) may begin only if (1) prospective subjects, or authorized third parties, have been given the opportunity to give free and informed consent about participation, and (2) their free and informed consent has been given and is maintained throughout their participation in the research. Articles 2.1(c), 2.3 and 2.8 provide exceptions to Article 2.1(a).
- b. Evidence of free and informed consent by the subject or authorized third party should ordinarily be obtained in writing. Where written consent is culturally unacceptable, or where there are good reasons for not recording consent in writing, the procedures used to seek free and informed consent shall be documented.
- c. The REB may approve a consent procedure¹ 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 that the REB finds and documents that:
 - i. The research involves no more than minimal risk to the subjects;

- ii. The waiver or alteration is unlikely to adversely affect the rights and welfare of the subjects;
 - iii. The research could not practicably be carried out without the waiver or alteration;
 - iv. Whenever possible and appropriate, the subjects will be provided with additional pertinent information after participation; and
 - v. The waived or altered consent does not involve a therapeutic intervention.
- d. In studies including randomization and blinding in clinical trials, neither the research subjects nor those responsible for their care know which treatment the subjects are receiving before the project commences. Such research is not regarded as a waiver or alteration of the requirements for consent if subjects are informed of the probability of being randomly assigned to one arm of the study or another.

Article 2.2

Free and informed consent must be voluntarily given, without manipulation, undue influence or coercion.

Article 2.3

REB review is normally required for research involving naturalistic observation. However, research involving observation of participants in, for example, political rallies, demonstrations or public meetings, should not require REB review since it can be expected that the participants are seeking public visibility.

Article 2.4

Researchers shall provide, to prospective subjects or authorized third parties, full and frank disclosure of all information relevant to free and informed consent. Throughout the free and informed consent process, the researcher must ensure that prospective subjects are given adequate opportunities to discuss and contemplate their participation. Subject to the exception in Article 2.1(c), at the commencement of the free and informed consent process, researchers or their qualified designated representatives shall provide prospective subjects with the following:

- a. Information that the individual is being invited to participate in a research project;
- b. A comprehensible statement of the research purpose, the identity of the researcher, the expected duration and nature of participation, and a description of research procedures;
- c. A comprehensible description of reasonably foreseeable harms and benefits that may arise from research participation, as well as the likely consequences of non-action, particularly in research related to treatment, or where invasive methodologies are involved, or where there is a potential for physical or psychological harm;
- d. An assurance that prospective subjects are free not to participate, have the right to withdraw at any time without prejudice to pre-existing entitlements, and will be given continuing and meaningful opportunities for deciding whether or not to continue to participate; and
- e. The possibility of commercialization of research findings, and the presence of any apparent or actual or potential conflict of interest on the part of researchers, their institutions or sponsors.

In light of (b) and (c), REBs may require researchers to provide below:

Additional information that may be required for some projects:

- 1. An assurance that new information will be provided to the subjects in a timely manner whenever such information is relevant to a subject's decision to continue or withdraw from participation;

2. The identity of the qualified designated representative who can explain scientific or scholarly aspects of the research;
3. Information on the appropriate resources outside the research team to contact regarding possible ethical issues in the research;
4. An indication as to who will have access to information collected on the identity of subjects, and descriptions of how confidentiality will be protected, and anticipated uses of data;
5. An explanation of the responsibilities of the subject;
6. Information on the circumstances under which the researcher may terminate the subject's participation in the research;
7. Information on any costs, payments, reimbursement for expenses or compensation for injury;
8. In the case of randomized trials, the probability of assignment to each option;
9. For research on biomedical procedures, including health care interventions; information about (a) foregoing alternative procedures that might be advantageous to the subject, (b) which aspects of the research involve the use of procedures that are not generally recognized or accepted; and, (c) particularly in trials of therapeutic interventions, the care provided if the potential subject decides not to consent to participation in the study;
10. The ways in which the research results will be published, and how the subjects will be informed of the results of the research.

Article 2.5

Subject to applicable legal requirements, individuals who are not legally competent shall only be asked to become research subjects when:

- a. the research question can only be addressed using the identified group(s); and
- b. free and informed consent will be sought from their authorized representative(s); and
- c. the research does not expose them to more than minimal risks without the potential for direct benefits for them.

Article 2.6

For research involving incompetent individuals, the REB shall ensure that, as a minimum, the following conditions are met:

- a. The researcher shall show how the free and informed consent will be sought from the authorized third party, and how the subjects' best interests will be protected.
- b. The authorized third party may not be the researcher or any other member of the research team.
- c. The continued free and informed consent of an appropriately authorized third party will be required to continue the participation of a legally incompetent subject in research, so long as the subject remains incompetent.
- d. When a subject who was entered into a research project through third-party authorization becomes competent during the project, his or her informed consent shall be sought as a condition of continuing participation.

Article 2.7

Where free and informed consent has been obtained from an authorized third party, and in those circumstances where the legally incompetent individual understands the nature and consequences of the

research, the researcher shall seek to ascertain the wishes of the individual concerning participation. The potential subject's dissent will preclude his or her participation.

Article 2.8

Subject to all applicable legislative and regulatory requirements, research involving emergency health situations shall be conducted only if it addresses the emergency needs of individuals involved, and then only in accordance with criteria established in advance of such research by the REB. The REB may allow research that involves health emergencies to be carried out without the free and informed consent of the subject or of his or her authorized third party if ALL of the following apply:

- a. A serious threat to the prospective subject requires immediate intervention; and
- b. Either no standard efficacious care exists or the research offers a real possibility of direct benefit to the subject in comparison with standard care; and
- c. Either the risk of harm is not greater than that involved in standard efficacious care, or it is clearly justified by the direct benefits to the subject; and
- d. The prospective subject is unconscious or lacks capacity to understand risks, methods and purposes of the research; and
- e. Third-party authorization cannot be secured in sufficient time, despite diligent and documented efforts to do so; and
- f. No relevant prior directive by the subject is known to exist. s dissent will preclude his or her participation.

When a previously incapacitated subject regains capacity, or when an authorized third party is found, free and informed consent shall be sought promptly for continuation in the project and for subsequent examinations or tests related to the study.

Article 3.1

Subject to the exceptions in Article 1.1(c), researchers who intend to interview a human subject to secure identifiable personal information shall secure REB approval for the interview procedure used and shall ensure the free and informed consent of the interviewee as required in Article 2.4. As indicated in Article 1.1c, REB approval is not required for access to publicly available information or materials, including archival documents and records of public interviews or performances.

Article 3.2

Subject to Article 3.1 above, researchers shall secure REB approval for obtaining identifiable personal information about subjects. Approval for such research shall include such considerations as:

- a. The type of data to be collected;
- b. The purpose for the which the data will be used;
- c. Limits on the use, disclosure, and retention of the data;
- d. Appropriate safeguards for security and confidentiality;

- e. Any modes of observation (e.g., photographs or videos) or access to information (e.g., sound recordings) in the research that allow identification of particular subjects;
- f. Any anticipated secondary uses of identifiable data from the research;
- g. Any anticipated linkage of data gathered in the research with other data about subjects, whether those data are contained in public or personal records; and
- h. Provisions for confidentiality of data resulting from the research.

Article 3.3

If identifying information is involved, REB approval shall be sought for secondary uses of data. Researchers may gain access to identifying information if they have demonstrated to the satisfaction of the REB that:

- a. Identifying information is essential to the research; and
- b. They will take appropriate measures to protect the privacy of the individuals, to ensure the confidentiality of the data, and to minimize harms to subjects;
- c. Individuals to whom the data refer have not objected to secondary use.

Article 3.4

The REB may also require that a researcher's access to secondary use of data involving identifying information be dependent on:

- a. The informed consent of those who contributed data or of authorized third parties; or
- b. An appropriate strategy for informing the subjects; or
- c. Consultation with representatives of those who contributed data.

Article 3.5

Researchers who wish to contact individuals to whom data refer shall seek the authorization of the REB prior to contact.

Article 3.6

The implications of approved data linkage in which research subjects may be identifiable shall be approved by the REB.

Article 4.1

Researchers and REB members shall disclose actual, perceived or potential conflicts of interest to the REB. REBs should develop mechanisms to address and resolve conflicts of interest.

Article 5.1

- a. Where research is designed to survey a number of living research subjects because of their involvement in generic activities (e.g., in many areas of health research or in some social science research such as studies of child poverty or of access to legal clinics) that are not specific to particular identifiable groups, researchers shall not exclude prospective or actual research subjects on the basis of such attributes as culture, religion, race, mental or physical disability, sexual

orientation, ethnicity, sex or age, unless there is a valid reason for doing so.

- b. This article is not intended to preclude research focused on a single living individual (such as in a biography) or on a group of individuals who share a specific characteristic (as in a study of an identifiable group of painters who happen to be all of one sex, colour or religion, or of a religious order which is restricted to one sex).

Article 5.2

Women shall not automatically be excluded from research solely on the basis of sex or reproductive capacity.

Article 5.3

Subject to the provisions in Articles 2.6 to 2.8, those who are not competent to consent for themselves shall not be automatically excluded from research which is potentially beneficial to them as individuals, or to the group that they represent.

Article 6

(None)

Article 7.1

Phase I non-therapeutic clinical trials shall undergo both stringent review and continuous monitoring by an REB independent of the clinical trials sponsor.

Article 7.2

In combined Phase I/II clinical trials, researchers and REBs shall carefully examine the integrity of the free and informed consent process. Where appropriate, the REB may require an independent monitoring process.

Article 7.3

REBs shall examine the budgets of clinical trials to assure that ethical duties concerning conflict of interest are respected.

Article 7.4

The use of placebo controls in clinical trials is generally unacceptable when standard therapies or interventions are available for a particular patient population.

Article 8.1

The genetics researcher shall seek free and informed consent from the individual and report results to that individual if the individual so desires.

Article 8.2

The researcher and the REB shall ensure that the results of genetic testing and genetic counselling records are protected from access by third parties, unless free and informed consent is given by the subject. Family information in databanks shall be coded so as to remove the possibility of identification of subjects within the bank itself.

Article 8.3

Researchers and genetic counsellors involving families and groups in genetic research studies shall reveal potential harms to the REB and outline how such harms will be dealt with as part of the research project.

Article 8.4

Genetics researchers and the REB shall ensure that the research protocol makes provision for access to genetic counselling for the subjects, where appropriate.

Article 8.5

Gene alteration (including "gene therapy") that involves human germ-line cells or human embryos is not ethically acceptable. Gene alteration for therapeutic purposes and involving human somatic cells may be considered for approval.

Article 8.6

Though the banking of genetic material is expected to yield benefits, it may also pose potential harms to individuals, their families and the groups to which they may belong. Accordingly, researchers who propose research involving the banking of genetic material have a duty to satisfy the REB and prospective research subjects that they have addressed the associated ethical issues, including confidentiality, privacy, storage, use of the data and results, withdrawal by the subject, and future contact of subjects, families and groups.

Article 8.7

At the outset of a research project, the researcher shall discuss with the REB and the research subject the possibility and/or probability that the genetic material and the information derived from its use may have potential commercial uses.

Article 9.1

Researchers shall obtain free and informed consent from the individual whose gametes are to be used in research.

Article 9.2

In research, it is not ethical to use in research ova or sperm that have been obtained through commercial transactions, including exchange for service.

Article 9.3

It is not ethically acceptable to create, or intend to create, hybrid individuals by such means as mixing human and animal gametes, or transferring somatic or germ cell nuclei between cells of humans and other species.

Article 9.4

It is not ethically acceptable to create human embryos specifically for research purposes. However, in those cases where human embryos are created for reproductive purposes, and subsequently are no longer required for such purposes, research involving human embryos may be considered to be ethically acceptable, but only if all of the following apply:

- a. The ova and sperm from which they were formed are obtained in accordance with Articles 9.1 and 9.2;
- b. The research does not involve the genetic alteration of human gametes or embryos;
- c. Embryos exposed to manipulations not directed specifically to their ongoing normal development will not be transferred for continuing pregnancy; and

- d. Research involving human embryos takes place only during the first 14 days after their formation by combination of the gametes.

Article 9.5

It is not ethically acceptable to undertake research that involves ectogenesis, cloning human beings by any means including somatic cell nuclear transfer, formation of animal/human hybrids, or the transfer of embryos between humans and other species.

Article 10.1

Research proposing the collection and use of human tissues requires ethics review by an REB. Amongst other things, the researcher shall demonstrate the following to the REB:

- a. That the collection and use of human tissues for research purposes shall be undertaken with the free and informed consent of competent donors;
- b. In the case of incompetent donors, free and informed consent shall be by an authorized third party;
- c. In the case of deceased donors, free and informed consent shall be expressed in a prior directive or through the exercise of free and informed consent by an authorized third party.

Article 10.2

For the purpose of obtaining free and informed consent, researchers who seek to collect human tissue for research shall, as a minimum, provide potential donors or authorized third parties information about:

- a. The purpose of the research;
- b. The type and amount of tissue to be taken, as well as the location where the tissue is to be taken;
- c. The manner in which tissue will be taken, the safety and invasiveness of acquisition, and the duration and conditions of preservation;
- d. The potential uses for the tissue including any commercial uses;
- e. *The safeguards to protect the individual's privacy and confidentiality;*
- f. Identifying information attached to specific tissue, and its potential traceability; and
- g. How the use of the tissue could affect privacy.

Article 10.3

- a. When identification is possible, researchers shall seek to obtain free and informed consent from individuals, or from their authorized third parties, for the use of their previously collected tissue. The provisions of Article 10.2 also apply here.
- b. When collected tissue has been provided by persons who are not individually identifiable (anonymous and anonymized tissue), and when there are no potential harms to them, there is no need to seek donors' permission to use their tissue for research purposes, unless applicable law so requires.

Endnotes

¹ Article 2.1(c) was adapted from *Protection of Human Subjects*, U.S. Dept. Of Health & Human Services, Title 45; *Code of Federal Regulations, Part 46.116(d)*.

SECTION XII. MODEL CONSENTS

Please see Appendix 1: Consent for Research Involving the Administration of Drug, Use of Devices or Performance Procedures, and Appendix 2: Consent for Research with NO Direct Benefits to the Subjects.

The following are model consents/statements that can be incorporated in (or added to or used instead of) the consent templates, as applicable.

1 HIV Testing in Research Protocols

The RAC has adopted a standard consent for HIV testing which is to be used in all instances in which HIV testing is performed as part of a research study. It is intended for use as a supplement to the primary consent. Additionally, the primary consent must contain the statement, ***"Part of your participation in this study involves being tested for the presence of antibodies to the Human Immunodeficiency Virus (HIV), the virus which causes AIDS. You will be asked to sign a separate consent for this procedure."***

RAC Proposal

KING FAISAL SPECIALIST HOSPITAL & RESEARCH CENTRE

Consent for HIV Antibody Test

Research Participant Information Sheet

You have been asked to participate in a research study, for which you have signed a separate consent. As indicated on that consent, part of your participation in that study will involve undergoing an HIV antibody test. This consent is specifically for the HIV antibody test. The HIV antibody test is a blood test used to ascertain whether you have antibodies to the Human Immunodeficiency Virus (HIV), the virus which causes Acquired Immunodeficiency Syndrome (AIDS). Less than one teaspoon of blood will be drawn from a vein in your arm using a needle. This may cause some discomfort and you may develop a black and blue mark. It takes approximately one to two weeks between the time your blood is drawn and the time you are notified of the results.

Both before and after your blood is tested, you will receive counseling from trained HIV counselors involved in this research project about the implications of negative and positive results, how to prevent future transmission, and the options available to you. Your wife/husband may be notified of the results of this test and urged to undergo testing as well. You will not incur any costs nor receive any payment for participating in this part of the study.

A positive HIV antibody test means that your body is making antibodies to HIV but it does not mean that you will necessarily develop AIDS in the future. A negative test means that you are probably not infected; however, it is possible that you may be infected but that your body has not produced antibodies to HIV. If your results are negative and you have been exposed to HIV recently, you should be retested in a few months to make sure you are not infected.

There are several possible benefits to taking the HIV antibody test. If your test results are negative, you can learn how to avoid becoming infected in the future. If your results are positive, you can learn how to avoid infecting other individuals, and if you are pregnant, or are thinking about having children, you can learn how being HIV positive will affect your decision to have children. Additionally, we can offer you enrollment in a

wide variety of research projects for the treatment of AIDS or refer you to a doctor for non-experimental treatment.

This is a voluntary procedure, and all results, either positive or negative, are confidential. Information about your HIV antibody test can only be released to people who you designate by signing a release form, or to those people listed below:

- a) You (or a person authorized by law who consented to the test for you);
- b) To a health care facility (such as a hospital, blood bank, or clinical laboratory) or a health care provider (such as a physician, nurse, or mental health counselor) providing care to you or your child, and anyone working for such a facility or provider who reasonably needs the information to supervise, monitor or administer health care;
- c) To a person whom your doctor believes is at significant risk for HIV infection, if you do not notify that person after being counseled to do so;
- d) To a committee or organization responsible for reviewing or monitoring a health facility;
- e) To a government agency, when the agency needs the information to supervise, monitor, or administer a health or social service;
- f) By a physician to someone who may consent to health care for you if you have been counseled and won't inform such person and disclosure is medically necessary to provide timely care and treatment. Disclosure must not be against your best interest.

If you do not want anybody to know your tests results or that you have been tested, you can go to an anonymous test site. This is a place where you can have your blood tested and receive counseling without having to tell anybody your name or address.

Authorization for HIV testing

Patient Name and Unit # _____

1. As part of my participation in a research project I authorize Dr. _____ and his/her associates at King Faisal Specialist Hospital & Research Centre to perform **HIV Antibody Testing, provide Pre-Test Counseling and Post-Test Counseling and draw less than one teaspoon of blood, one time from me.**
2. I acknowledge that I have read, or had explained to me in a language I understand, the attached consent document and that Dr. _____ has explained to me the nature and purposes of the described procedures, as well as any benefits, associated discomforts and risks reasonably to be expected. I have had the opportunity to ask questions with respect to such procedures and all questions I asked were answered to my satisfaction.
3. I voluntarily accept the risks associated with the performance of the above-mentioned procedures.
4. I understand that I am free to withdraw this consent and to discontinue the above-mentioned procedures at any time. The consequences and risks, if any, which might be involved have been explained to me.
5. I confirm that I have read the foregoing authorization and that all blanks or statements requiring completion were properly completed before I signed.

Research Subject/Surrogate: _____ Date: _____
(signature)

Name: _____ Time: _____

Relationship: _____ (print)
_____ (If signed by surrogate)

For subjects who are not able to read this consent document themselves, the following must be completed:
I confirm that I have accurately translated and/or read the information to the subject:
Witness:

(Signature)
Name:

(Print)
Address:

(Number & Street) (City) (Postcode)

ATTESTATION OF PRINCIPAL INVESTIGATOR/DELEGATE

I have fully explained to the above volunteer/relative/surrogate the nature and purposes of the foregoing procedures, the benefits reasonably to be expected, the associated discomforts and risks involved. I believe that the above volunteer/relative/surrogate understands the nature, purposes, benefits, and risks of participation in this research. I have also offered to answer any questions the above volunteer/relative/surrogate might have with respect to such or procedures and have fully and completely answered all such questions.

Signature of Principal Investigator/Delegate Date

Name of Principal Investigator/Delegate (print) Title

2 Studies Only Involving Blood Drawing:

There are a number of research projects in which the drawing of blood is the only research activity, which involves human subjects. In these projects, one of two situations may exist. In the first, an additional sample may be obtained at the time of venipuncture for clinically indicated reasons. Signed consent for the

drawing of additional blood may be waived and investigators proposing such protocols should refer to the guidelines for waiver of signed consent prior to submitting their proposal to the ORA.

Venipuncture may also be performed independent of any clinical procedure, such as occurs when obtaining samples from normal controls. A sample consent, intended to be used as a model for all studies involving independent venipuncture, except those studies in which blood is drawn for HIV-antibody testing, is detailed below. Investigators are strongly urged to make use of this model, as it will hopefully prevent the need for revisions.

NOTE: If banking or genetic testing is involved, see Sections XI. 7 & 8 above.

Model Consent For Blood Drawing

You are being asked to participate in a research study. The purpose of this study is _____. You qualify for participation in this study because you have _____/ you are a normal, healthy individual. There will be _____ subjects enrolled in this study in the upcoming year.

Your participation in this study will involving drawing a blood sample from a vein in your arm. The total amount drawn will not exceed _____teaspoons/tablespoons/ounces each time. We will draw blood _____ times, approximately once every _____days/weeks/months.

The blood will be used for determining/measuring . You will/will not be informed of the results of these tests. You may experience some minor pain and may develop a black and blue mark as a result of the blood drawing. You will not incur any costs/will be charged SR_____ for your participation. You will receive SR_____ for your time and expenses incurred as a result of participating/ will not receive any financial compensation for participating.

While there is no direct benefit to you, it is hoped this study will yield more information about _____. You may withdraw from this study at any time by informing the individual drawing your blood or by contacting the investigator.

3 Donation Of Fetal Tissue For Use In Therapeutic Transplantation Research

Several attestations are required; one from the woman who will donate the tissue, one from the attending physician who will obtain the tissue, and one from the investigator who will carry out the research with the fetal tissue. Three model attestations are provided. A separate consent form that explains all aspects of the research (the transplantation) will have to be written by the investigators for subjects who are asked to participate as recipient of the fetal tissue. Model consents and attestations follow.

A. Model Attestation For Women Who Will Donate Fetal Tissue For Therapeutic Transplantation Research To Be Obtained By The Attending Gynecologist

- 1) You have decided to have an abortion and have given your informed consent to the abortion. Your decision to have the abortion was made independent of and prior to reading this statement. Your decision to have the abortion is not related to your decision to donate the fetal tissue obtained during the abortion for medical research. This

research involves transplantation of some of the tissue that will be obtained during the abortion into another human being for therapeutic purposes.

- 2) A blood sample drawn from you at the time of the abortion and the tissue obtained may be tested for infections such as human immunodeficiency virus (HIV), the virus that carries AIDS. Such tests are important for transplant purposes. You will be asked to sign a separate consent for HIV testing of your blood.
- 3) You have not been informed of the identity of any potential tissue recipient. Your agreement and consent to donate the fetal tissue are made without any restrictions regarding the identity of any potential recipient of the tissue.
- 4) You have been informed that the physician performing the abortion procedure has no financial interest in the tissue that will be obtained from the abortion procedure. Your physician may be included as an author in any published scientific studies that arise out of discoveries made in connection with the fetal tissue research.
- 5) We are required to disclose any known medical risks to you or risks to your privacy that might be associated with your donation of the tissue. At this time, no such medical risks or risks to your privacy are known. Your identity and any information relating to your donation of this tissue will remain completely confidential.
- 6) You have read this document and have been given the opportunity to ask questions. By signing this document you agree to the donation of the fetal tissue that was obtained at the abortion for therapeutic transplantation research. You have been informed that you may refuse to sign this form without penalty.

Patient's Signature

Date

Name (Please Print)

B. Model Attestation Of Attending Gynecologist Who Has Obtained Fetal Tissue For Therapeutic Transplantation Research

I affirm that the human fetal tissue obtained from my patient () has been obtained in accord with her signed statement consenting to its use for therapeutic transplantation research. I have disclosed to her any interest I may have in the research to be conducted with the human fetal tissue that I obtained from her. I have advised her of any medical risks associated with this procedure including (insert risks of procedure), which are in addition to her clinical care. Additionally, I have advised her of any possible risks to her privacy which are associated with the donation of the tissue.

I further affirm that in cases of induced abortion, the donor's consent for the abortion was obtained prior to requesting or obtaining consent for the donation of fetal tissue. The abortion was also conducted in accord with Kingdom Islamic Law, and no alteration of the

timing, method, or procedures used to terminate the pregnancy was made solely for the purposes of obtaining the tissue.

Signature

Date

Name (please print)

C. Model Attestation Of The Principal Investigator Who Will Receive Fetal Tissue For Use In Therapeutic Transplantation Research

As the Principal Investigator of the above referenced study, for which study I have received human fetal tissue, I am aware that the tissue was donated for research purposes and was obtained pursuant to a spontaneous abortion, an induced abortion, or a still birth. I have provided this information to other individuals with responsibilities regarding this research. I have had no part in any decisions as to the timing, method, or procedures used to terminate the pregnancy.

I will obtain from any recipient of this tissue written acknowledgment that the above information regarding the tissue was given to her/him, prior to obtaining his/her consent to be a recipient of the tissue.

Signature

Date

Name (please print)

4 Donation Of Fetal Tissue and/or Placenta For Use In In-Vitro Studies

Consent for use of fetal tissue and/or placenta in research must be obtained after the patient has consented to an abortion or has undergone a spontaneous abortion. The individual who requests and obtains consent for fetal tissue or placenta (The P.I., Co-P.I. or delegate) must be different from the individual who obtained consent and/or performed the abortion. See model consent below.

Model Consent For Donation Of Fetal Tissue and/or Placenta For Use In In-Vitro Studies

You are being asked to participate in a research study. You qualify for participation in this study because....., and you are now pregnant, and have, (e.g. elected to undergo an interruption of pregnancy; had a spontaneous abortion; had a still birth). You are asked to donate the fetus and placenta after interruption of your pregnancy. The purpose of this study is

Performance of this research requires the use of products of conception, (e.g. specifically fetal tissues, blood and/or placenta). These tissues/blood/or placenta will be obtained at the time of your interruption of pregnancy. There are no risks to you, since the studies will be carried out on the fetal tissue/ blood/or placenta following the interruption of pregnancy.

The studies on the fetal tissues/blood/or products of conception will be performed at no cost to you. You will not receive any compensation for your participation.

There is no direct benefit of these studies to you; however, we hope that the information gained may expand our knowledge of.

5 Model Statement for Risks of Lumbar Puncture

All studies that involve lumbar puncture must incorporate the following statement in the consent form under Potential Risks and Discomforts:

"There is a remote possibility of an infection at the puncture site. You might develop a headache after the procedure. This is usually mild, but rarely might be severe and prolonged for several days, or very rarely, longer. These risks will be minimized by use of experienced personnel. More serious adverse effects such as infection or damage to the nervous system have been reported, but usually when there is a pre-existing neurologic illness in symptomatic neurologic patients, which we attempt to rule out prior to this study. This will be accomplished by a neurologic physical examination before the procedure."

6 Model Statement for Risks of Administration of Radioactive Substances

The risks of administration of radioactive substances have often been compared to "x" number of x-rays. According to experts, this is not an appropriate comparison. The following description of potential risks and discomforts of administering radioactive substances has been approved by the REC and should be incorporated under the Potential Risks and Discomforts section when radioactive compounds are used in research protocols.

"The possible discomforts associated with this study include local pain during the needle insertion. The likelihood of an allergic reaction to the injected radioactive compound is extremely low. The risks associated with the administration of _____mCi of radioactivity into the body cannot be absolutely determined. However, the amount of radiation subjects will be exposed to will be _____ (high, modest, low). The amount of radioactivity injected is comparable to the amount generally used for routine diagnostic nuclear medicine studies."

"The dose of radioactivity injected into your body is _____mCi of _____ (name of isotope). Various organs in the body such as the liver, kidney, bones retain different amounts of radioactivity while some of the radioactivity is excreted from the body. Therefore, the dose to your

body is expressed as "total effective dose equivalent (TEDE)". This value was estimated to be () mrem for this protocol. The critical organ (the organ receiving the highest dose) is, and will receive ()mrem. Both of these doses are (well below, equal to, or greater than) the safe limits established by the Nuclear Regulatory Commission (NRC), an organization which determines the safety of radiation exposure. (If dose is greater than the established safe limits indicate how much greater)

7 Model Statement for Risks of Sedation/Anesthesia

Incorporate the applicable section of the following for any procedures that involve sedation/anesthesia:

You/your child's participation in this research project involves the performance of a test(s) or procedure(s) called (). This test (procedure) may require the use of drugs which produce sedation or in some cases general anesthesia. This may be necessary to minimize any discomfort to you/your child. In some cases, especially young children, general anesthesia may be necessary if it is important that you/your child must remain very still for some period of time while the test or procedure is being done.

Sedative drugs and tranquilizers like valium, are used to help you/your child remain calm and to lessen any anxiety you/your child may experience. These drugs cause drowsiness and sometimes sleep. They often also produce short periods of amnesia so that you/your child may not remember some of the events which occur after you/your child are given the medication. If the test or procedure is expected to cause any pain, pain relieving medication or narcotics like morphine, may be given. The narcotics help to relieve pain but may also cause drowsiness and can sometimes have an effect on you/your child's breathing. The most common side effect of sedatives and narcotics are drowsiness, which lasts for some time after the test or procedure, slow heart rates or allergic reactions. It is also possible that these drugs can depress your/your child's breathing. All of these side effects can be treated and in most instances will not cause any permanent injury. However, although it is very rare, the possibility of severe injury including death or permanent brain damage cannot be excluded. You/your child will be closely watched for any side effects when given these medications, and any problems will be rapidly treated.

General anesthesia requires the use of powerful drugs which affect many of the functions of the body. These drugs are used to produce unconsciousness and prevent pain and movement. They are administered by highly trained physicians who are experts in their use and the treatment of any complications which may occur. You/your child will be closely watched throughout the procedure and any problems which may occur will be rapidly treated. The most common side effects of general anesthesia include nausea, vomiting, sore throat, damage to teeth or dental appliances (caps, bonding, and bridges) , and drowsiness which may last for some time after the procedure. These side effects can either be treated or will go away on their own and usually do not cause any serious problems. Low blood pressure, high blood pressure, fast or slow heart rates or irregular heart rates can also occur, but are usually quickly and easily treated with other medications. The modern practice of anesthesia is generally considered to be very safe. However, on rare occasions, unforeseen problems can occur even when all the proper precautions have been taken to protect you/your child. Serious possible complications associated with anesthesia include irritation of the lungs which may cause difficulty with breathing, or aspiration (stomach contents entering you/your child's lungs) which may require that a breathing tube be placed in you/your child's trachea (windpipe) and a machine (ventilator) used to help you/your child to breath for some time. Rarely these problems can result in permanent brain damage or death. On very rare occasions, unpredictable allergic type reactions can occur which may result in liver damage, liver failure or death.

The risks of anesthesia are increased by the presence of any diseases or medical conditions which may be present in any individual. If any additional risks or considerations exist, these will be discussed with you/your child by an anesthesiologist before the test or procedure.

APPENDIX 1. INFORMED CONSENT FOR RESEARCH INVOLVING THE ADMINISTRATION OF DRUGS, USE OF DEVICES OR PERFORMANCE OF PROCEDURES

Title of Proposal: [See 5.1.5.1 and 5.1.5.2 signature lined consent forms](#)

Part I – Research Participant Information Sheet: [See 7.2 REC guidelines and policies manual Consf.doc](#)

A. Purpose of the Research:

B. Description of the Research:

C. Potential Risks and Discomforts:

D. Potential Benefits:

E. Alternative to Participation (where applicable):

F. Cost/s Reimbursements:

G. Termination of Participation (where applicable):

H. Compensation / Treatment:

In the event of injury resulting from participation in the research study, KFSH&RC will make available to you, including admission, if required, its hospital facilities and professional attention. Financial compensation from KFSH&RC is not available.

I. Voluntary Participation:

Participation in this study is voluntary. You will suffer no penalty nor loss of any benefits to which you are otherwise entitled should you decide not to participate. Withdrawal from this research study will not affect your ability to receive alternative methods of medical care available at KFSH&RC.

Significant new findings developed during the course of the research study which might be reasonably expected to affect your willingness to continue to participate in the research study will be provided to you.

J. Confidentiality:

Your identity and medical record, as a participant in this research study, will remain confidential with respect to any publications of the results of this study. Furthermore, your medical record may be reviewed by the Research Advisory Council or the agency sponsoring this research in accordance with applicable laws and regulations.

K. Contact Person(s):

You may call the Section of Assurance & Compliance, Office of Research Affairs at _____ or _____ pager # _____ for general questions concerning research at KFSH&RC or research subjects' rights. For any specific questions with regard to this study, or in the event of a research-related injury, please contact Dr. _____ telephone # _____ Ext. _____, Pager # _____.

A signed copy of the consent form will be given to you.

PART II - Authorization for Administration of certain drugs, use of devices or performance of certain procedures to:

Patient _____ Name: _____

MRN #: _____

1.a I authorize Dr. _____ and his/her associates at KFSH&RC to administer the following drugs, use the following devices or perform the following procedures during my treatment (or the treatment of the person named above for whom I am responsible):

1.b I also agree that the following body fluids and tissues may be sampled for research analyses and related purposes (include volume and frequency of each):

2. I understand that the above-mentioned drugs, devices or procedures are being studied to determine the extent to which they may be of value in treating my illness or condition (or the illness or condition of such patient named above, as the case may be).

3. I acknowledge that I have read, or had explained to me in a language I understand, the attached Research Participant Information sheet and that Dr. _____ has explained to me the nature and purposed of the drugs, devices or procedures described in the Research Participant Information Sheet as well as any benefits reasonably to be expected, possible alternative methods of treatment, the attendant discomforts and risks reasonably to be expected and the possibility that complications from both known and unknown causes may arise as a result thereof. I have had the opportunity to ask any questions I had with respect to such drugs, devices or procedures and all questions I asked were answered to my satisfaction.

4. I understand that I am entitled for reimbursement for expenses incurred as a result of my participation in this study

5. I voluntarily accept the risks associated with the use of the above-mentioned drugs, devices or the performance of the above-mentioned procedures with the knowledge and understanding that the extent to which they may be effective in my treatment (or the treatment of the patient named above, as the case may be) has not been established, that there may be side effects and complications from both known and

unknown causes and that these drugs, devices, or procedures may not result in cure or improvement.

6. I understand that I am free to withdraw this consent and discontinue treatment with the above-mentioned drugs, devices or procedures at any time. The consequences and risks, if any, which might be involved in the event I later decide to discontinue such treatment have been explained to me. I understand that such withdrawal will not affect my ability to receive any medical care made necessary by the performance of such studies or to which I might be otherwise entitled.

7. I confirm that I have read, or had read to me, the foregoing authorization and that all blanks or statements requiring completion were properly completed before I signed.

Patient/Surrogate: _____
_____ Signature _____ Date

Print _____ Name: _____

Relationship: _____
(If signed by Surrogate)

8. I confirm that I have accurately translated and/or read the information to the subject or his/her surrogate.

Witness: _____

Print _____ Name: _____
_____ Signature _____

KFSH&RC ID #: _____

Date: _____

9. I have fully explained to the above patient/ relative/ guardian the nature and purpose of the foregoing drugs, devices or procedures, possible alternative methods of treatment which might be advantageous, the benefits reasonably to be expected, the attendant discomforts and risks involved, the possibility that complications may arise as a result thereof and the consequences and risks, if any, which might be involved in the event the patient/ relative/ guardian hereafter decides to discontinue such treatment. It is my understanding that the above patient/ relative/ guardian understands the nature, purposes, benefits, and risks of participation in this research before signing of this informed consent. I have also offered to answer any questions the above patient/ relative/ guardian might have with respect to such drugs, devices or procedures and have fully and completely answered all such questions.

(Signature of Principal Investigator/ Delegate):

Print

Name:

Title:

Date: _____

APPENDIX 2. INFORMED CONSENT FOR RESEARCH WITH NO DIRECT BENEFITS TO PARTICIPANT

Title of Proposal:

Part I – Research Participant Information Sheet:

A. Purpose of the Research:

B. Description of the Research:

C. Potential Risks and Discomforts:

D. Potential Benefits:

E. Alternative to Participation (where applicable):

F. Cost/s Reimbursements:

G. Termination of Participation (where applicable):

H. Compensation / Treatment:

In the event of injury resulting from participation in the research study, hospitalization and professional attention, if these are required, will be provided at KFSH at no cost to you. Financial compensation from KFSH&RC is not available.

I. Voluntary Participation:

Participation in this study is voluntary. You will suffer no penalty nor loss of any benefits to which you are otherwise entitled should you decide not to participate. Withdrawal from this research study will not affect your ability to receive alternative methods of medical care available at KFSH&RC.

Significant new findings developed during the course of the research study which might be reasonably expected to affect your willingness to continue to participate in the research study will be provided to you.

J. Confidentiality:

Your identity and medical record, as a participant in this research study, will remain confidential with

respect to any publications of the results of this study. Your medical record in connection with this study will be kept confidential to the extent permitted by the law. Furthermore, your medical record may be reviewed by the Research Advisory Council or the agency sponsoring this research in accordance with applicable laws and regulations.

A signed copy of the consent form will be given to you.

PART II: Authorization of Voluntary participant who is not expected to obtain any direct benefit:

Participant _____ Name:

MRN # (or address): _____

1.a I hereby volunteer to participate in a research program under the supervision of Dr. _____ and his/her associates at KFSH&RC which will involve the following conditions, drugs or procedures:

1.b I also agree that the following body fluids and tissues may be sampled for research analyses and related purposes (include volume and frequency of each):

2. I acknowledge that I have read, or had explained to me in a language I understand, the attached Research Participant Information sheet and that Dr. _____ has explained to me the nature and purpose of these studies, including the extent, if any, to which they are experimental, the possible attendant discomforts, symptoms, side effects and risks reasonably to be expected, and the possible complications, if any, which may arise from both known and unknown causes as a result of these studies. I have had the opportunity to ask any questions I had with respect to this study and all questions I asked were answered to my satisfaction.

3. I understand that these studies are not intended to be of any direct therapeutic benefit to me and I voluntarily accept the risks and discomforts associated with these studies.

4. I understand that I am entitled for reimbursement for expenses incurred as a result of my participation in this study

5. I understand that, in order to provide the data by which to measure the effectiveness of these studies, Dr. _____ and his/her associates may carry out certain routine preliminary diagnostic procedures which have been fully described and explained to me. Should these indicate any abnormality, my participation in the aforementioned studies may be terminated. I am unaware of any preexisting medical or emotional problem which would make it unwise for me to participate in these studies.

6. I understand that I am free to withdraw this authorization and discontinue participation in these studies at any time. The consequences and risks, if any, of such withdrawal during the course of the studies have been explained to me. I understand that

such withdrawal will not affect my ability to receive any medical care made necessary by the performance of such studies or to which I might be otherwise entitled.

7. I grant this consent as a voluntary contribution in the interest of medical research.

8. I confirm that I have read, or had read to me, the foregoing authorization and that all blanks or statements requiring completion were properly completed before I signed.

Patient/Surrogate Signature:

Date: _____

Print Name:

Relationship:

(If signed by Surrogate)

9. I confirm that I have accurately translated and/ or read the information to the subject:

Witness:

Signature

Print

name: _____

KFSH&RC ID#: _____

I have fully explained to the above volunteer/ relative/ surrogate the nature and purpose of the above-mentioned research program (including the fact that the studies will not result in any direct therapeutic benefit and the extent, if any, to which the studies are experimental), the possible complications which may arise from both known and unknown causes as a result thereof and the consequences and risks, if any, if the volunteer decides to discontinue participation. It is my understanding that he/she understands the nature, purposes, and risks of these studies before he signs this informed consent. I have also offered to answer any questions relating to these studies and have fully and completely answered all such questions.

Signature of Principal Investigator/ Delegate:

(Print Name):

Date: _____

APPENDIX 3. GLOSSARY OF LAY TERMS FOR USE IN PREPARING INFORMED CONSENT DOCUMENTS

1.	ABSORB	Take up fluids, take in	
2.	ACIDOSIS	Condition when blood contains more acid than normal	
3.	ACUITY	Clearness, keenness, esp. of vision airways	
4.	ACUTE	New, recent, sudden	
5.	ADENOPATHY	Swollen lymph nodes (glands)	
6.	ADJUVANT	Helpful, assisting, aiding	
7.	ADJUVANT TREATMENT	Added treatment	
8.	ANTIBIOTIC	Drug that kills bacteria and other germs	
9.	ANTIMICROBIAL DRUG	Drug that kills bacteria and other germs	
10.	ADVERSE EFFECT	Side effect	
11.	ALLERGIC REACTION	Rash, trouble breathing	
12.	AMBULATE –ATION –ORY	Walk, able to walk	
13.	ANAPHYLAXIS	Serious, potentially life threatening allergic reaction	
14.	ANEMIA	Decreased red blood cells; low red blood cell count	
15.	ANESTHETIC	A drug or agent used to decrease the feeling of pain or eliminate the feeling of pain by putting you to sleep	
16.	ANGINA	Pain resulting from insufficient blood supply to the heart, same as angina pectoris	
17.	ANTIBODY	Protein made in the body in response to foreign substance; attacks the foreign substance and protects us from infection	
18.	ANTICONVULSANT	Drug used to prevent seizures	
19.	ANTILIPEMIC	A drug that counteracts fat in the blood	
20.	ANTITUSSIVE	A drug used to relieve coughing	

21.	ARRHYTHMIA	Any change form the normal heartbeat (abnormal heartbeat)	
22.	ASPIRATION	Fluid entering lungs following vomiting	
23.	ASSAY	Lab test	
24.	ASSESS	To learn about	
25.	ASYMPTOMATIC	Without symptoms	
26.	AXILLA	Armpit	
27.	BENIGN	Not malignant, without serious consequences	
28.	BINDING/ BOUND	Carried by to make to stick together, transported	
29.	BIOAVAILABILITY	The extent to which a drug or other substance becomes available to the body	
30.	BLOOD PROFILE	Series of blood tests	
31.	BOLUS	A large amount	
32.	BRADYCARDIA	Slow heartbeat	
33.	BRONCHOSPASM	Breathing distress caused by narrowing of the airways	
34.	CARCINOGENIC	Capable of causing cancer	
35.	CARCINOMA	Type of cancer	
36.	CARDIAC	Pertains to the heart	
37.	CARDIOVERSION	Restoration of normal heartbeat by electric shock	
38.	CATHETER	A tube for withdrawing or introducing fluids	
39.	CATHETER	A tube placed near the spinal cord used for anesthesia indwelling epidural during operations	
40.	CEREBRAL TRAUMA	Damage to the brain	
41.	CHD	Coronary heart disease	
42.	CHEMOTHERAPY	Treatment of disease, usually cancer, by chemical agents	
43.	CHRONIC	Continuing for a long time	
44.	CLINICAL	Pertaining to medical care	
45.	CLINICAL TRIAL	An experiment in patients	
46.	COMPLETE RESPONSE	Total disappearance of disease	

47.	CONSOLIDATION PHASE	Treatment phase intended to make a remission permanent, follows induction	
48.	CONTROLLED TRIAL	Study in which the experimental treatment or procedure is compared to a standard (Control) treatment or procedure	
49.	COOPERATIVE GROUP	Association of multiple institutions to perform clinical trials	
50.	CORONARY	Pertains to the blood vessels that supply the heart	
51.	CT SCAN (CAT)	Computerized series of x-rays (computerized tomography)	
52.	CULTURE	Test for infection or organisms that could cause infection	
53.	CVA STROKE	Cerebrovascular accident	
54.	DIASTOLIC	Lower number in blood pressure reading	
55.	DISTAL	Toward the end, away from the center of the body	
56.	DIURETIC	“Water pill” or drug that causes increase in urination	
57.	DOPPLER	Sound waves	
58.	DOUBLE BLIND	Study in which neither in which investigators nor subjects know what drug the subject is receiving	
59.	DYSPLASIA	Abnormal cells	
60.	ECHOCARDIOGRAM	Sound wave test of the heart	
61.	EDEMA	Increased fluid	
62.	EEG	Electric brainwave tracing (electroencephalogram)	
63.	EFFICACY	Effectiveness	
64.	ELECTRO CARDIOGRAM	Electrical tracing of heartbeat (ECG or EKG)	
65.	ELECTROLYTE IMBALANCE	Imbalance of minerals in the blood	
66.	EMESIS	Vomiting	
67.	EMPIRIC	Based on experience	

68.	ENDOSCOPIC EXAMINATION	Examination of an internal part of the body with a lighted tube; looking at a part of the body with a lighted tube	
69.	ENTERAL	By way of the intestines	
70.	EPIDURAL	Outside the spinal cord	
71.	EXPEDITED REVIEW	Rapid review of a protocol by the IRB chair without full committee approval, permitted with certain low risk research	
72.	EXTRAVASATE	To leak outside of a blood vessel	
73.	FDA	US Food and Drug Administration, the branch of Federal government which approves new drugs	
74.	FIBRILLATION	Irregular beat of the heart of other muscle	
75.	GENERAL ANESTHESIA	Pain prevention by induction of drugged sleep, as in surgery	
76.	HEMATOCRIT	Amount of red blood cells in the blood	
77.	HEMATOMA	A bruise, a black and blue mark	
78.	HEMODYNAMIC MEASURING	Measuring of blood flow	
79.	HEMOLYSIS	Breakdown in red blood cells	
80.	HEPARIN LOCK	Needle placed in the arm with blood thinner to keep the blood from clotting	
81.	HEPATOMA	Cancer or tumor of the liver	
82.	HOLDER MONITOR	A portable machine for recording heart beats	
83.	HYPERCALCEMIA	High blood calcium level	
84.	HYPERKALEMIA	High blood potassium level	
85.	HYPERNATREMIA	High blood sodium level	
86.	HYPERTENSION	High blood pressure	
87.	HYPOCALCEMIA	Low blood calcium level	
88.	HYPOKALEMIA	Low blood potassium level	

89.	HYPONATREMIA	Low blood sodium level	
90.	HYPOTENSION	Low blood pressure	
91.	HYPOXEMIA	A decrease of oxygen in the blood	
92.	HYPOXIA	A decrease of oxygen in the blood	
93.	IATROGENIC	Caused by a physician or by treatment	
94.	IDE	Investigational device exemption, the license to test an unapproved new medical device	
95.	IDIOPATHIC	Of unknown cause	
96.	IMMUNOGLOBULIN	A protein that makes antibodies	
97.	IMMUNO SUPPRESSIVE	Drug which suppresses the body's immune response, used in transplantation and diseases caused by disordered immunity	
98.	IMMUNOTHERAPY	Giving of drugs to help the body's immune	
99.	IND	Investigational New Drug, the license to test an unapproved new drug	
100.	INDUCTION PHASE	Beginning phase or stage of a treatment	
101.	INDURATION	Hardening	
102.	INFARCT	Death of tissues because of lack of blood supply	
103.	INFUSION	Introduction of a substance into the body, usually into the blood	
104.	INGESTION	Eating; taking by mouth	
105.	INTRAMUSCULAR	Into the muscle; within the muscle	
106.	INTRATHECAL	Into the spinal fluid	
107.	INTRAVENOUS	IV, through the vein	
108.	INTRAVESICAL	Into the bladder	
109.	INTUBATE	The placement of a tube into the airway	
110.	INVASIVE PROCEDURE	Puncture, opening or cutting of the skin	
111.	ISCHEMIA	Decreased oxygen in a tissue (usually because of decreased blood flow)	

112.	LIPID CONTENT	A fat content in the blood	
113.	LOCAL ANESTHESIA	Creation of insensitivity to pain in a small, local area of the body.	
114.	LOCALIZED	Restricted to one area, limited to one area	
115.	LUMEN	The cavity of an organ or tube (eg blood vessels)	
116.	LYMPHANGIOGRAPHY	An x-ray of the lymph nodes or tissues after injection of dye in lymph vessels (eg in feet)	
117.	LYMPHOCYTE	A type of white blood cell important in immunity and defense against infection	
118.	LYMPHOMA	A cancer of the lymph nodes (or tissues)	
119.	MALAISE	A vague feeling of bodily discomfort, feeling bad	
120.	MALIGNANCY	Cancer or other progressively enlarging and spreading tumor, usually fatal if not successfully treated	
121.	MEDULLOBLASTOMA	A type of brain tumor	
122.	MELOBLASTOSIS	Change in red blood cells	
123.	METABOLIZE	A process of breaking down substances in the cells to obtain energy	
124.	METASTASES	Spread of cancer cells from one part of the body to another	
125.	MI	Myocardial infarction	
126.	MINIMUM	Slight	
127.	MINIMIZE	Reduce	
128.	MONITOR	Check on: keep track of; watch carefully	
129.	MOBILITY	Ease of movement	
130.	MORBIDITY	Undesired result or complication	
131.	MORTALITY	Death	
132.	MOTILITY	The ability to move	
133.	MRI	Magnetic resonance imaging, body pictures created using magnetic	

		rather x-ray energy	
134.	MUCOUS, MUCOUS MEMBRANE	Moist lining of digestive, respiratory, reproductive, and urinary tracts	
135.	MULTIPLE PROJECT	Agreement between institutions and OPRR ASSURANCE regarding institutional policies on the use of human subjects in research	
136.	MYOCARDIAL	Pertaining to the heart	
137.	NASOGASTRIC TUBE	Tube from the nose to the stomach	
138.	NCI	National Cancer Institute	
139.	NECROSIS	Death of the tissue	
140.	NEOPLASMA	Tumor, may be benign or malignant	
141.	NEUROBLASTOMA	A cancer or nerve tissue	
142.	NEUTROPENIA	Decrease in the main part of the white blood cells	
143.	NONINVASIVE	Not breaking, cutting or entering the skin	
144.	NOSOCOMIAL PNEUMONIA	Pneumonia acquired in the hospital	
145.	OCCLUSION	Closing; obstruction	
146.	ONCOLOGY	The study of tumors or cancer	
147.	OPHTHALMIC	Pertaining to the eye	
148.	OPTIMAL	Best, most favorable or desirable	
149.	OPRR	Office of Protection from Research Risks of the NIH, oversees IRBs and related matters	
150.	ORAL ADMINISTRATION	By mouth	
151.	ORTHOPEDIC	Pertaining to the bones	
152.	OSTEOPOROSIS	Softening of the bones	
153.	OSTEOPETROSIS	Rare bone disorder characterised by dense bone	
154.	PARENTERAL	Administration by injection	
155.	PATENCY	Condition of being open	
156.	PATHOGENESIS	Causative mechanism in a disease	
157.	PERCUTANEOUS	Through the skin	
158.	PHARMACO	The study of the way the	

	KINETICS	body absorbs, distributes and gets rid of a drug	
159.	PHASE I PHASE II PHASE III	Initial study of a new drug in humans to determine limits of tolerance. Second phase of study of a new drug intended to obtain initial information. Large scale trials to confirm and expand information on safety and usefulness of new drug.	
160.	PHLEBITIS	Irritation or inflammation of the vein	
161.	PLACEBO	A substance of no medical value; an inactive substance; a pill that contains no medicine	
162.	PLACEBO EFFECT	A phenomenon of improvement seen with the administration of a placebo	
163.	PLATELETS	Small particles in the blood that will help with clotting	
164.	POTENTIATE	Increase or multiply the effect of a drug or toxin by administration of another drug or toxin at the same time	
165.	POTENTIATOR	An agent that helps another agent to work better	
166.	PROPHYLAXIS	A drug given to prevent disease or infection	
167.	PER OS (PO)	by mouth	
168.	PRN	As needed	
169.	PROGNOSIS	Outlook, probable outcomes	
170.	PRONE	Lying on the stomach	
171.	PROSPECTIVE STUDY	Study following patients forward in time	
172.	PROTOCOL	Plan of study	
173.	PROXIMAL	Closer to the center of the body, away from the end	
174.	PULMONARY	Pertaining to the lungs	
175.	RADIATION	x-ray or cobalt treatment	

	THERAPY		
176.	RANDOM	By chance	
177.	RANDOMIZATION	Chance selection	
178.	RBC	Red blood cell	
179.	RECOMBINANT	Formation of new combination of genes	
180.	RECONSTITUTION	Putting back together the original parts or elements	
181.	REFRACTORY	Not responding to treatment	
182.	REGENERATION	Regrowth of a structure or of lost tissue	
183.	RELAPSE	The return of a disease	
184.	REMISSION	Disappearance of evidence of cancer of other disease	
185.	RENAL	Pertaining to the kidneys	
186.	REPLICABLE	Possible to duplicate	
187.	RESECT	Remove or cut out surgically	
188.	RETROSPECTIVE STUDY	Study looking back over past experience	
189.	SARCOMA	A type of cancer	
190.	SEDATIVE	A drug to calm or make less anxious	
191.	SEMINOMA	A type of testes cancer	
192.	SEQUENTIALLY	In a row	
193.	SEQUENTIALLY	In a row	
194.	STAGING	A determination of the extent of the disease	
195.	STENOSIS	Narrowing of a duct, tube or one of the valves in the heart	
196.	STRATIFY	Arrange in groups for analysis of results (eg by age, sex, etc)	
197.	SUBCLAVIAN	Under the collarbone	
198.	SUBCUTANEOUS	Under the skin	
199.	SUPINE	Lying on the back	
200.	SUPPORTIVE CARE	General medical aimed at symptoms, not intended to improve or cure underlying disease	
201.	SYMPTOMATIC	Having symptoms	
202.	SYSTOLIC	Top number in blood pressure, pressure during active contraction of the heart	

203.	TERATOGENIC	Capable of causing malformation fetuses	
204.	TESTES	Male sex glands	
205.	THROMBOSIS	Clotting	
206.	TITRATION	A method for deciding on the strength of a solution	
207.	T-LYMPHOCYTES	Type of white blood cells	
208.	TOPICAL	Surface	
209.	TOPICAL ANESTHETIC	Applied to a certain area of the skin and reducing pain only in the area to which applied	
210.	TRANSDERMAL	Through the skin	
211.	TRAUMA	Injury, wound	
212.	TREADMILL	Walking machine used to determine heart function	
213.	UPTAKE	Absorption and incorporation of a substance by living tissue, absorb and incorporate a substance, taking in of a substance by living tissues	
214.	VALVULOPLASTY	Plastic repair of valve, esp. of the heart	
215.	VARICES	Enlarged veins	
216.	VASOSPASM	Narrowing of the vessels	
217.	VECTOR	A carrier, usually an insect, that carries and transmits disease causing microorganisms	
218.	VENIPUNCTURE	Needle stick, entering the skin with a needle	
219.	WBC	White blood cell	

APPENDIX 4. CHECKLIST FOR CONSENT DOCUMENTS FOR INVESTIGATORS, REC MEMBERS, AND STAFF

All consent documents **must** include the following “**basic elements**” of informed consent and, when applicable “**additional elements**” of informed consent. This information **must** be written in a language that will be understandable to an individual with a sixth-grade education. The information **must** be incorporated into the specific sections of the consent document as indicated below:

A Purpose of the Research

- a statement that the study involves research.
[You (you/your child) are being asked to participate in a research project]
- a statement of the purpose of the research.
[The purpose of this research is _____.]
- a statement why the subject qualifies for participation in research.
[You qualify for participation because _____.]

B Description of the Research:

- a description of the study and all of the procedures to be followed.
- the identification of any procedures, drugs or devices which are experimental, and a statement that indicates whether they are approved by the Saudi Ministry of Health, or similar regulatory bodies in USA, UK, Canada, or Sweden for the purpose(s) they will be used for in the proposed study.
- when applicable, the identification of any procedures that will be performed for clinically indicated, non-research-related reasons.
- an indication of the expected duration of the subject’s participation.
- when applicable, an indication of the approximate number of subjects to be involved in the study.

C Potential Risks and Discomforts:

- a description of all potential-risks or discomfort to the subjects, and a statement of the reversibility of any potential adverse events.
- when applicable, a statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or foetus if the subject is, or may become, pregnant) which are currently unforeseeable.

D Potential Benefits:

- a description of potential benefits to the subjects or to others.

E Alternatives to Participation:

- a disclosure of alternative procedures or courses of treatment that might be beneficial.

F Costs/Reimbursements:

- a statement whether or not compensation will be made for time and expenses:
- a statement as to whether there will be any costs to the subjects as a consequence of participation in the study. When applicable, clarify that costs for clinically indicated tests and procedures will be the responsibility of the patient.

G Termination of Participation:

- a statement that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.
- when applicable, a statement of the consequences of a subject's decision to withdraw from the research, and procedures for orderly termination of participation by the subject
- when applicable, a statement of anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.

H Compensation and/or Treatment in the Event of Injury:

- a statement whether compensation and/or any medical treatment will be available if injury occurs,
- and if so, what they consist of, or where further information may be obtained.
- a statement of whom to contact in the event of a research-related injury to the subject:

I Voluntary Participation:

- a statement that participation is voluntary and refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled.
- when applicable, 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.

J Confidentiality of Identify of Participant:

- a statement describing how and the extent to which confidentiality of records identifying the subject will be maintained.

K Contact Person(s):

- a statement of whom to contact for answers to questions about the research (one or more of the investigators' team, including Hospital phone number and extension and pager) and the rights of the research subjects (Mr Mohamed Al Turki, Head Section of Assurance and Compliance, Office of Research Affairs, MBC 03, phone _____ ext _____ pager: _____).

APPENDIX 5. CHECKLIST FOR RESEARCH ETHICS COMMITTEE MEMBERS

1 Proposal and Proposal Summary:

1.1 Assessment of level of risk (check appropriate category):

- no risk
- Minimal risk. [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.]
- greater than minimal risk but has potential direct benefit
- greater than minimal risk and no direct benefit, but has potential to yield generalisable knowledge about the subjects disorder or condition

1.1.1 if risk is greater than minimal, are the risks reasonable in relation to the potential benefits? Yes No

1.2 have risks for all subjects been minimised via use of an appropriate research design?

- 1.2.1 is the subject population equitably distributed? Yes No
- 1.2.2 are inclusion and exclusion criteria appropriate? Yes No
- 1.2.3 does the study include vulnerable subjects? Yes No
- 1.2.4 Indicate (circle) vulnerable subjects to be enrolled: Yes No
Minors, pregnant women, prisoners, fetuses, mentally disabled individuals, educationally or socially disadvantaged persons.

1.3 are additional safeguards in place to protect vulnerable subjects?

- 1.3.1 are all subjects' rights and welfare protected? Yes No
- 1.3.2 if minors are to be enrolled in the study, is the assent category indicated? Yes No
- 1.3.3 will privacy and confidentiality of research records be adequately protected? Yes No
- 1.3.4 has safety been maximised for all subjects? Yes No

2 Consent Document:

- 2.1** are the eight basic elements of informed consent incorporated (see consent checklist)? Yes No
- 2.2** are the six additional elements of informed consent incorporated, when appropriate? Yes No
- 2.3** will the consent document be understandable to an individual with a sixth grade education? Yes No
- 2.4** will the consent document be understandable to an individual with a sixth grade education?
has the Principal Investigator (PI) requested a modification in the consent process (waiver of informed consent)? Yes No
does it fulfill all four requirements for a waiver? Yes No
- 2.5** has the (PI) requested a modification in the documentation of informed consent (waiver of signed consent)? Yes No
does it fulfill all four requirements for a waiver? Yes No

APPENDIX 6. REQUEST FOR MODIFICATION OF INFORMED CONSENT (WAIVER OF INFORMED CONSENT)

Request for Modification of Informed Consent (Waiver of Informed Consent)

Under specific circumstances, an investigator may request approval of a modification in the requirements for informed consent (waiver of informed consent). To request a waiver of informed consent, complete both Parts A and B.

Note: The Research Ethics Committee (REC) may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent (ie, a waiver of informed consent) if four very specific criteria are met. Your request will be considered on a case-by-case basis at a convened meeting of the REC.

A To determine if your request meets **ALL FOUR** of these criteria, you must answer the following questions:

- 1) does the research present more than minimal risk of harm to the subject? (Minimal risk is defined as the probability and magnitude of harm or discomfort not greater than those ordinarily encountered in daily life, or during the performance of routine physical or psychological tests). Yes No
- 2) will the waiver adversely affect the rights and welfare of the subjects? Yes No
- 3) can the research be practicably carried out without the waiver? Yes No
- 4) will the subjects be provided with additional pertinent information after participation, whenever appropriate? Yes No

B Indicate below why the research could not practicably be carried out without the waiver.

Name of Principal Investigator (print/type)

Signature:

Date:

**APPENDIX 7. REQUEST FOR MODIFICATION OF DOCUMENTATION OF INFORMED CONSENT
(WAIVER OF SIGNED CONSENT)**

**Request for Modification in Documentation of Informed Consent
(Waiver of Signed Consent)**

Under specific circumstances, an investigator may request a waiver of the usual requirement for research subjects to sign a consent form to document that informed consent has been given (waiver of signed consent). To request a waiver of signed consent, complete the following questionnaire.

Note: The Research Ethics Committee (REC) may consider the possibility of approving a consent procedure which does not require a subject's signature when at least one of two specific criteria are met. Your request will be considered on a case-by-case basis at a convened meeting of the REC.

To determine if your request meets **EITHER** of these criteria, you must answer the following questions:

- 1) would the consent document be the **ONLY** identifiable link between the subject and the research, **AND** would there be potential harm to the subject if the confidentiality of the consent form was breached?

Yes No

Indicate below how a breach of confidentiality would be harmful to the subject:

- 2) a) does the research present more than minimal risk?
(Minimal risk is defined as the probability and magnitude of harm or discomfort are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological tests).

Yes No

- b) **AND**, does the research involve any procedures for which written consent is normally required outside of the research context?

Yes No

<hr/>	
Name of Principal Investigator (print/type)	
<hr/>	
Signature:	Date:
<hr/>	<hr/>

APPENDIX 8. CERTIFICATION OF ASSENT OF MINOR

Project Title: _____

RAC #: _____

I hereby certify that Dr _____ has fully explained to _____ the nature of the study and its potential risks and benefits in a language that the child could understand. I also certify that the child was given the opportunity to ask questions and was informed that he/she could refuse participation in the study. I further certify that the child freely gave verbal assent and has, without coercion, agreed to participate in this study. I also certify that I have no personal relationship to the child or the research study in which the child has been asked to participate.

_____ Name of Witness: (print/type)	
_____ Signature of Witness:	_____ Date:

APPENDIX 9. ADVERSE EVENTS REPORT FORM

This form must be attached to all memos/reports describing the adverse event.

RAC #: _____ **Contact Person:** _____
PI: _____ **Extension** _____
Box: _____

The event was related to the subject's participation in the research in the following way:
(check one of the following):

- Definitely related:
- Probably related:
- Possibly related:
- Definitely not related:

If the adverse event is related to participation in this study, please check or complete one of the following:

- The consent form already includes a statement about the possibility of this adverse event and therefore does not need to be modified:
- The consent form has been modified and two copies are enclosed – one with all revisions highlighted, and one clean copy to be stamped with REC approval:
- Although the event was possibly related to participation in the study, we feel that the consent does not need to be modified at this time because:
