GUIDE FOR HUMAN SUBJECTS RESEARCH (UoH)

The University of Hail (UoH) Research Ethics Committee (REC), is a standing committees that serves as the Institutional IRB and is charged with evaluating the religious and ethical aspects of all research undertaking by members of the UoH 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.

GENERAL FOLLOWED PROCEDURE IN THE CONDUCT OF LIVING CREATURES SUBJECT RESEARCH:

1. If the research project is a scholarly work for one of the postgraduate students and its one of the postgraduate studies (program and courses) requirements, the post-graduate student will be considered as the main investigator and the supervising faculty member will be included in the research project as a co-investigator when applying for obtaining approval from the Research Ethics Standing Committee (REC) in UoH.

2. Prior to beginning any research activities, investigators shall submit "Application for Obtaining Approval from the Research Ethics Standing Committee (REC) in UoH" with all relevant documents for research proposals involving living creatures for review by the REC.

Note: Be careful to complete all items in the application form in order to receive final approval by REC.

3. Principal investigator must provide REC committee with the following documents:
   - 3.1. Research proposal (see research proposal guidelines).
   - 3.2. Data collection tool(s)
   - 3.3. Accomplished Informed Consent Form approved by REC, or other forms related forms that can replace it based on the nature of the study (see Informed Consent
   - 3.4. Updated CV for the researchers

4. Approval decision letter officially dated with the inclusive REC approval dates must be used in the conduct of living creatures' subject studies:
   - 4.1 Once the research proposal is approved by REC, the approval decision letter including period of the study will be issued and sent in an electronic form from the REC to the Principal Investigator.
   - 4.2. For sponsored research studies where funding is needed before the start of the project, approval letters will not be released to the investigators until official notification of funding is received by Deanship of Research (DoR) 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 Deanship of Research (DoR), as well).

4.4. Approval letters may not be used beyond their expiration date under any

5. It is the responsibility of the principal investigator to obtain approvals from outside the University of Hail for research studies that require obtaining approval by external institutions or ethics committees for scientific research of the institution in which the study will be applied and sample will be taken

6. No research involving living creatures' subjects shall be initiated without REC approval.

7. If you have any questions, please contact the Research Ethics Standing Committee email, research.ethics@uoh.edu.sa.

HUMAN SUBJECTS RESEARCH

Research projects involving human subjects require review and approval by a Research Ethics Standing Committee. REC is an ethics committee of scientists and non-scientists who advocate for human subjects in research. The REC is responsible for reviewing and overseeing human subjects research conducted by UoH or with UoH faculty.

The first question a researcher should consider with respect to REC review is whether the research project fits the definition of "human subjects and research".

When in doubt, **the investigator should err on the side of caution and consult the REC staff to clarify whether a study is human subjects research or not.**

RESEARCH DEFINED

Research is defined as **"any systematic investigation** (i.e., the gathering and analysis of information)**, including development, testing, and evaluation, designed, in whole or in part, to develop or contribute to generalizable knowledge"**.

The term "Generalizable knowledge" is information where the intended use of the research findings can be applied to populations or situations beyond that studied.

The term "research" means an activity designed to test a hypothesis. Research is usually described in a formal protocol that includes an objective and a set of procedures to reach that objective.

"Research" generally does **not** include **operational activities** such as defined practice activities in public health, medicine, psychology, and social work (e.g., routine outbreak investigations and disease monitoring) and studies for internal management purposes such as program evaluation, quality assurance, quality improvement, fiscal or program audits, marketing studies or contracted-for services. Research generally does not include journalism or political polls. However, some of these activities may include or constitute research in circumstances where there is a clear intent to contribute to generalizable knowledge.

HUMAN SUBJECTS DEFINED

A **human subject** is defined by Federal Regulations as **"a living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information."**

The Department of Defense defines "Research Involving a Human Being as an Experimental Subject" as: "An activity, for research purposes, where there is an intervention or interaction with a human being for the primary purpose of obtaining data regarding the effect of the intervention or interaction. Examples of interventions or interactions include, but are not limited to, a physical procedure, a drug, a manipulation of the subject or subject's environment, the withholding of an intervention that would have been undertaken if not for the research purpose.

Living individual – The specimen(s)/data/information must be collected from live subjects. Cadavers, autopsy specimens or specimens/information from subjects now deceased is not human subjects.

"About whom" – a human subject research project requires the data received from the living individual to be **about** the person.

Intervention includes physical procedures, manipulations of the subject, or manipulations of the subject's environment for research purposes. **Interaction** includes communication between the investigator and the subject. Interaction also includes face-to-face, mail, and phone interaction as well as other modes of communication.

Identifiable private information "includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation is taking place," (such as a public restroom) "and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be shared or made public (for example, a health care record)."

Researchers must take caution since disclosure of private information may place the subjects at risk of criminal or civil liability and/or damage their financial standing, employability, or reputation.

"Identifiable" means the information contains one or more data elements that can be combined with other reasonably available information to identify an individual (e.g. Social Security #).

Observational studies of public behavior (including television and internet chat rooms) do **not** involve human subjects as defined when there is no intervention or interaction with the subjects and the behavior is not private. Studies based on data collected for

non-research purposes may **not** constitute human subjects research if individuals are not identifiable (e.g. data such as service statistics, school attendance data, crime statistics, or election results).

Studies based on data that are individually identifiable but are also publicly available may **not**
constitute human subjects research. However, the term "publicly available" is intended to refer
to record sets that are truly readily available to the broad public, such as census data, federal and health, labor, or educational statistics. An investigator should **not** assume information qualifies as "publicly available" merely because it has been posted on an electronic website and can be accessed without authorization.

IDENTIFYING HUMAN RESEARCH STUDIES

Certain studies may have the characteristics of human subjects research but may not meet the regulatory definition. Studies which meet the definition require IRB review. There are three categories to consider:

- **Studies that <u>are</u> human subjects research**
- **Studies that <u>may be</u> considered human subjects research (gray area)**
- **Studies that <u>do not</u> qualify as human subjects research**

Any investigator who is unsure of whether his/her proposal constitutes "human subjects research" should contact the REC office. The REC staff, Chair and/or designee will determine if the study is human subjects research.

STUDIES THAT <u>ARE</u> HUMAN SUBJECTS RESEARCH

1. Studies that utilize test subjects for new devices, products, drugs, or materials.
2. Studies that collect data through intervention or interaction with individuals. Examples of this type of research include drug trials, internet surveys about alcohol consumption, studies that involve deception, research involving risky behaviors or attitudes, and open- ended interviews with minors that contribute to generalizable knowledge.
3. Studies using private information that can be readily identified with individuals, even if the information was not collected specifically for the study in question.
4. Studies that use bodily materials such as cells, blood, urine, tissues, organs, hair, or nail clippings, even if one did not collect these materials for the study. However, such research may be considered exempt or not human subjects research if the materials/data are coded and the investigator does not have access to the coding systems.
5. Studies that produce generalizable knowledge about categories or classes of subjects from individually identifiable information.

6. Studies that use human beings to evaluate environmental alterations, for example, weatherization options or habitat modifications to their living or working space or test chamber.

STUDIES THAT ARE NOT HUMAN SUBJECTS RESEARCH

Studies that fit any of the categories below do not need REC review.

1. **Data collection** for internal departmental, school, or other University administrative purposes. Examples: teaching evaluations, customer service surveys.

2. Service surveys issued or completed by University personnel for the intent and purposes of improving services and programs of the University or for developing new services or programs for students, employees, or alumni. This would include surveys by professional societies or University consortia.

   Note: If at a future date, an opportunity arose to contribute previously collected identifiable or coded survey data to a new study producing generalizable knowledge, IRB review may be required before the data could be released to the new project.

3. **Information-gathering interviews** with questions focused on things, products, or policies rather than people or their thoughts/ personal opinions. Example: canvassing librarians about inter-library loan policies or rising journal costs.

4. **Course-related activities** designed specifically for educational or teaching purposes, where data is collected from and about human subjects as part of a class exercise or assignment, but are **not** intended for use outside of the classroom. Example: instruction on research methods and techniques.
   Note: The IRB does not review classroom studies.

5. **Biography or oral history research** involving a living individual that is not generalizable beyond that individual.

6. **Independent contract for procedures** carried out for an external agency. Examples: personnel studies, cost-benefit analyses, customer satisfaction studies, biological sample processing (for a fee and not authorship or other credit), public park usage, IT usage, and software development.

7. **Research involving cadavers,** autopsy material or bio-specimens from deceased individuals.
   Note: Some research in this category, such as genetic studies providing private or medical information about live relatives, may need IRB review. Please contact the IRB for further information.

8. **Innovative therapies** except when they involve "research" as defined by the above criteria. (An innovative clinical practice is an intervention designed solely to enhance the well-being of an individual patient or client. The purpose of an innovative clinical

practice is to provide diagnosis, preventative treatment, or therapy to particular individuals.)

9. **Quality improvement** projects are generally **not** considered research unless there is a clear intent to contribute to generalizable knowledge ***and*** use the data derived from the project to improve or alter the quality of care or the efficiency of an institutional practice.
10. **Case histories** which are published and/or presented at national or regional meetings are **not** considered research if the case is limited to a description of the clinical features and/or outcome of a single patient and do not contribute to generalizable knowledge.
11. **Publicly available data** do **not** require REC review. Examples: census data, labor statistics.
12. **Coded private information or biological specimens** that were **not** collected for the currently proposed projects do not need IRB review as long as the investigator cannot link the coded data/specimens back to individual subjects.

If the data/specimen provider has access to the identity of the subjects (e.g. subjects' names, addresses, etc.), the investigator must enter into an agreement with the data/specimen provider that states under no circumstances will the identity of the subjects be released to the investigator.

Note: Investigators are not allowed to make this determination. These projects require verification from the REC.

GUIDELINES FOR STUDIES DOES NOT QUALIGY AS HUMAN SUBJECTS RESEARCH

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 considered not human participant research IF the information is recorded in such a manner that the participants cannot be identified, either directly or through a code linked to the participant (i.e. the identity of the participant may NOT be readily ascertained or associated with the information).

2. It is also important to note that the types of research that can be considered not human participant research must pose NO risks to the participants.

3. Research involving the collection or study of EXISTING data, documents, records, pathological specimens, or diagnostic specimens if:
3.1. These sources are publicly available OR
3.2. If the information is recorded by the investigator in such a manner that PARTICIPANTS CANNOT BE IDENTIFIED, DIRECTLY OR THROUGH IDENTIFIERS LINKED TO THE PARTICIPANTS.

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

4.1. The information obtained is recorded in such a manner that human participants can be identified, directly or through identifiers linked to the participants.

4.2. Any disclosure of the human participants' responses outside the research could reasonably place the participants at risk of criminal or civil liability or be damaging to the participants' financial standing, employability, or reputation.

5. The research is conducted in established or commonly accepted educational settings, involving normal educational practices, such as:

5.1. Research on regular and special education instructional strategies, OR

5.2. Research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

6. Research and demonstration projects which are designed to study, evaluate, or otherwise examine:

6.1. Public benefit or service programs

6.1.2. Procedures for obtaining benefits or services under those programs

6.1.3. Possible changes in or alternatives to those programs or procedures OR

6.1.4. Possible changes in methods or levels of payment for benefits or services under those programs.

7. Research involving the following are qualify as human participants research:

7.1. PRISONERS

7.2. FETUSES

7.3. PREGNANT WOMEN OR

7.4. HUMAN IN VITRO FERTILIZATION MINORS

7.5. SURVEYS INTERVIEW PROCEDURES OR OBSERVATION OF PUBLIC BEHAVIOR

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 confidentially 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.

RACIAL DISCREIMINATION

Research with negative impacts on society may not be conducted, especially research reinforcing racial discrimination.

Conducting research on diseases that are particular among a certain group for the purpose of treatment and understanding of mechanisms of transmission of said diseases may not be construed as promoting racial discrimination.

Scientific results shall not be leaked to the media if this could lead to promoting discrimination on the basis of race or family or tribal affiliation.

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 its 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.

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.

7. There are three types of Consent that an Investigator may obtain for his/her Research:
7.1. Informed Consent

7.2 Waiver of Signed consent (Verbal Consent) with documentation of the verbal consent process in the research subjects/Investigators records
7.3 Waiver of Informed Consent

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 form "Request for Modification in Documentation of Informed Consent" form 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.
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 which include Research Participation Information sheet is read to the subject 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. 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 and contact information of the person who obtained the consent.

*Investigators must be aware that procedures which 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 "REQUEST FOR MODIFICATION OF INFORMED CONSENT" form must be completed and submitted with the research proposal application form.

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 REC 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 (Recruitment Methods for Research) 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

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

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).

Economically or Educationally Disadvantaged Persons

Economically or educationally disadvantaged persons are those persons placed at special risk by socioeconomic and educational background. Economically disadvantaged persons include those persons who struggle to provide basic necessities for themselves and their families or communities. Therefore, the use of financial incentives for research participation is a special issue with economically disadvantaged persons. Medical care, remedial education, and financial remuneration are common incentives in research. To a person who is economically disadvantaged, seemingly nominal inducements may be powerfully coercive. Incentives cannot be so strong that they take away a person's voluntary choice to participate in research. Educationally disadvantaged persons may have educational deficits, learning disabilities, or cultural backgrounds that limit communication with a researcher. It is the responsibility of the researcher to ensure that a subject is fully informed. This includes presenting material at an

appropriate level, in an appropriate language, and via an appropriate medium (e.g., verbal or visual).

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".

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 (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. 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.

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.

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.

RESEARCH ON INMATES (PRISONERS)

Prisoners, including those sentenced to death, shall be treated like other persons as regards conducting medical research on them. The Regulations shall specify ethical controls for conducting research on prisoners.

When serving as subjects in medical research, inmates, even if sentenced to death, shall not be treated differently. Their confinement may not be exploited to compel them to consent to be research subjects.

The local committee may not approve research on inmates unless said research aims to achieve any of the following:

1- Study the criminal behavior of inmates, provided the research does not expose them to more than the minimal potential risk;

2- Study conditions of prisons and inmates as well as prevailing diseases and

identify the circumstances leading to crime;
3- Study administrative rules and operational procedures applicable in prisons, so as to improve health and living conditions of inmates;
4- Inmates may not be subject to clinical research whether by coercion or inducement or for any purposes other than those set forth in this Article.

DEALING WITH GENETIC MATERIAL AND ITS BANKS

A written approval shall be obtained from the National Committee in all matters related to gene therapy research.

Results of the research on genetic material shall be the property of the GOVERNMENT.

Neither the researcher nor the institution may provide said results to any internal or foreign body without permission from the National Committee, provided the material and scientific rights of the researcher or research team and the research subject are preserved.

The investigator shall maintain the confidentiality of research conclusions, and not identify their source.

When conducting research on genetic material, the following shall be observed:
1- Islamic values, local culture and environmental safety;
2- Applicable and internationally recognized practices relating to conducting research on genetic material.

RESOURCES

- **King Abdulaziz City for Science and Technology**
  https://www.kacst.edu.sa/eng/Pages/default.aspx

- **Implementing regulations of the law of ethics of research on living creatures**
  https://prod.kau.edu.sa/Med/ali/files/Publications/Guide/National_Committe_of_BioEthics-Regulations_of_the_Law_of_Ethics_of_Research_on_Living_Creatures.pdf
  &
  https://laws.boe.gov.sa/BoeLaws/Laws/LawDetails/fad7b0d1-e536-46ea-8202-a9a700f28b03/1

- **The research ethics committee (REC) guidance in the conduct of research at King Faisal Specialist Hospital & Research Center (KFSH & RC)**
  https://www.kfshrc.edu.sa/store/media/8bo.pdf

- **Saudi Food and Drug Authority**
  https://www.sfda.gov.sa/en/drug/Pages/default.aspx

- **Federal Policy for the Protection of Human Subjects**
  https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html

- **Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans – TCPS 2 (2018)**
  https://ethics.gc.ca/eng/policy-politique_tcps2-eptc2_2018.html

- **Council of Europe. Convention on Human Rights and Biomedicine (1997)**
  https://www.coe.int/en/web/conventions/full-list/-/conventions/rms/090000168007cf98

- **World Medical Association Declaration of HelsinkiEthical Principles for Medical ResearchInvolving Human Participants**
  https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-participants/

- **The Belmont Report**
  www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html

- **The Nuremberg Code (1947)**
  https://history.nih.gov/research/downloads/nuremberg.pdf

- **Office for Human Research Protections (OHRP)**
  United States Department of Health & Human Services
  www.hhs.gov/ohrp/

- **Chart for determining if a project is human participants research**
  Office of Human Research Protections (OHRP)
  www.hhs.gov/ohrp/regulations-and-policy/decision-trees/index.html
  Select: Chart 1: Is an Activity Research Involving Human Participants?

- **Engagement of Institutions in Research**
  https://www.hhs.gov/ohrp/regulations-and-policy/guidance/guidance-on-engagement-of-institutions/index.html

- **United States Food and Drug Administration**
  www.fda.gov

- **Guidance on Research with Coded Private Info or Bio Specimens**
  www.hhs.gov/ohrp/policy/cdebiol.html