##### Guidelines

**For**

**Researchers**

###### ETHICS REVIEW COMMITTEE

**The Aga Khan University**

# Karachi

## General Principles

1. All research projects involving human subjects, whether as individuals or communities, including the use of foetal material, embryos and tissues from the recently dead, supported and undertaken by AKU faculty, staff or students, wherever conducted, shall be reviewed by the Ethics Review Committee (ERC) before the study begins.
2. A research that does not involve interaction or intervention with human subjects may be exempted from the regulations requiring ERC approval. Examples include educational research, testing and survey procedures where no identifying information will be recorded that can link subjects to the data, and disclosure of the data could not reasonably place the subjects at risk of civil or criminal liability or be damaging to the subjects financial standing, employability, or reputation. Such exemption would be conditional to:
* The use of existing data, documents or specimens, where no identifying information will be recorded that can link subjects to the data. Examples:
1. Literature review and theoretical analysis; in such cases, the only ethical concern would be acknowledgement of sources.
2. Analysis of data, documents, specimen, not linked to individual subjects.
3. Evaluation studies of intervention programmes/projects, especially by those who were partners in planning the intervention.

All researchers must give the subject participants the option of sharing the results and specify how this will be done.

3. Every 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.

1. The human subjects in the project must participate willingly, having been informed about the research. All relevant information must be provided that is likely to affect the person irrespective of age, sex, or literacy level of the subjects. If the human subjects in your project are part of a vulnerable (See appendix 1) population, such as prisoners, children or mentally handicapped then the researcher should clearly state why is it necessary to have such groups as their research subjects and how do they plan to administer the informed consent.

**Essentials of informed consent are:**

 4.1 **Comprehension:** Investigator must ensure that the informed consent is in first person language, clearly comprehended by the subject / guardian

* 1. **Purpose of research** must be clearly explained.
	2. **Procedure** that the subjects would be expected to undergo must be described in simple words. Identify any procedures that are experimental/ investigational/ non-therapeutic. Indicate type and frequency of monitoring during and after the study.
	3. **Length of time** subject is expected to participate. If subject’s participation is expected to continue over a period of time, please indicate that any new information that develops during the study and may affect the subjects’ willingness to continue participation will be communicated to them. This would apply even when the intervention/investigation phase of the study has ended but monitoring continues.
	4. **Benefits** of the research must be shared with/communicated to:

a. Subjects

1. Other study participants
2. Society

 In studies evaluating drugs or other products the subjects should be advised as to the availability of the product after discontinuation of the study. Please indicate whether drug would be available to the patients free of cost. If not, kindly specify expected local cost.

* 1. Please specify **financial burden** to be incurred by the research subject while participating in the study.
	2. **Explain all foreseeable risks or discomforts** to the subjects. This includes physical injury, psychological, social, economic harm, discomfort, and inconvenience. If risk is unknown, it should be stated.
	3. **Treatment for adverse experiences** Explain what therapeutic measures would be available to the subjects in case of adverse reactions or injury as a result of being a participant in the study. All research related adverse reactions are the financial responsibility of the researchers. CIOMS guideline states, “Research subjects who suffer physical injury as a result of their participation are entitled to such financial or other assistance as would compensate them equitably for any temporary or permanent impairment or disability. In the case of death, their dependants are entitled to material compensation. The right to compensation may not be waived.”
	4. **Confidentiality** Describe the extent to which confidentiality of records will be maintained.
	5. **Person to contact** for answers to questions, or in event of research related injury or emergency.
	6. Statement that **participation is voluntary** and that refusal to participate will not result in any penalty or any loss of benefits that the person is otherwise entitled to receive.
	7. Subject’s **right to withdraw** from the study at any time.
	8. How sharing of results with subjects will occur.
	9. No abbreviations will be used.

Consent document must be clearly written and/or verbally explained so as to be understandable to subjects (local language wherever applicable). The language must be non- technical (comparable to the language in a newspaper or general circulation magazine), and scientific, technical or medical terms must be plainly defined. It is the Principal Investigator’s responsibility to ensure quality of consent procedure.

1. The researcher should submit to the committee for review information regarding funding, sponsors, institutional affiliations, potential conflicts of interest and incentives for subjects.
2. Specify the cost of management directly related to the study and indicate what portion of the cost would be incurred by the study participants.
3. The researcher should also declare any personal and institutional benefits (monitory or otherwise including travel) accrued through study participation. A statement has to be submitted describing any compensation (including expenses and access to medical care) to be given to research participants.
4. Please also specify benefits of the study to the funding agency or sponsors, if any.
5. The research protocol should indicate that there is compliance with the principles of Helsinki Declaration (Appended). In case of conflict, kindly specify the particular clause, which is being contravened.
6. a) **Medical research** involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person.

b) **Non-medical research** should be conducted by suitably qualified persons.

1. The right of research subjects to safeguard their integrity must always be respected. Every precaution should be taken to respect the privacy and confidentiality of the patient’s information and to minimize the impact of the study on the subject’s physical, psychological and social integrity.
2. In the conduct of research, the investigator must at all times respect the personality, rights, wishes, beliefs, consent and freedom of the individual subject.
3. Volunteers and patients should be reimbursed for travel and any out of pocket expenses e.g. any wage loss if applicable.

### Application

1. The researcher responsible for the ethical and scientific conduct of the research should submit the application form electronically along with required attachments for review of the ethics of proposed research. A signed **hard copy** of the application form only should be sent to:

Ms. Gulshan Kalani

Secretary ERC

Research Office

Juma Building

The Aga Khan University

Stadium Road

P.O. Box 74800

Karachi, Pakistan.

Fax: (92 21) 4934294, 4932095

Tel: (9221) 3486-4880.

E-mail: gulshan.kalani@aku.edu

1. ERC meets second Friday of every month.
2. The deadline for submission of the application is **3rd Friday of each month**.
3. Applications will be acknowledged and researchers shall be informed of the review date. The researchers shall also be communicated regarding the incompleteness of an application. This will obviously delay the review process.
4. The outcome of review shall be communicated to the researchers within 2 weeks after the ERC meeting.
5. In cases where the ERC requests supplementary information or changes to documents from the applicant, such information should be provided as requested.
6. In cases where clarification is sought and researchers fail to respond within 3 months, the file will be abandoned. For ethics approval of such studies, researchers need to resubmit the entire study and attach the previous ERC letter of recommendation for the Committee review.
7. Researcher may be asked to present the case in the meeting if required.

a) Follow-up (of the research)

 b) End-report

### Documents for submission

1. The ERC application form (see annexure) should be submitted. Information in the form should be typed. All questions in the form must be adequately answered without reference to attachments.

1. Research protocol (clearly identified and dated), together with supporting documents and annexes. This should always include description of the arrangements for insurance coverage for research participants, if applicable and all ethical considerations involved in the research.
2. Questionnaire (if applicable) intended for research participants should be included along with its translation in Urdu or local language of the study’s population.
3. If research involves a study product (such as a pharmaceutical or device under investigation), an adequate summary of all safety, pharmacological, pharmaceutical, and toxicological data available on the study product, together with a summary of clinical experience with the study product to date (e.g. recent investigator’s brochure, published data, a summary of the product’s characteristics) must be provided.
4. Flyer or document used for the recruitment process of subjects.
5. Informed consent form (clearly identified and dated) in English and Urdu or the language(s) understood by the potential research participants.
6. Official signed and stamped permission letters from the Administrator of the Institutions participating in the study
7. All significant previous decisions (e.g. those leading to a negative decision or modified protocol) by other ERCs or regulatory authorities for the proposed study (whether in the same location or elsewhere) and an indication of modification(s) to the protocol made on that account. The reasons for previous negative decisions should be provided.

#### CONDITIONS for APPROVAL to amendments

1. Approval is given for a period of one year. If the project takes longer than the specified period to complete, a request for an extension of the ethics clearance should be sought along with the ERC annual progress report.
2. Approval is given on condition that any alterations proposed to the approved protocol are submitted to the Committee for approval prior to the alterations being effected along with the ERC progress report.
3. Approval is given for therapeutic trials subject to the Principal Investigator notifying the Committee within seven (7) days of any adverse event or occurrence that takes place during that trial.
4. Research could be audited by ERC during the research period to ensure compliance with guidelines.

**References:**

1. International Ethical Guidelines for Biomedical Research Involving Human Subjects Prepared by the Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO), Geneva 1993.

* 1. Institutional Review Board Guidebook, National Institutes of Health, USA Year 2000.
	2. Operational Guidelines for Ethics Committees that Review Biomedical Research, World Health Organization, Geneva 2000.

# Appendix 1

# Vulnerability/Vulnerable Patients

For the purpose of definition, vulnerability is operationally defined as 'the potential risks associated with the physical and mental status of an individual which might reasonably be anticipated irrespective of the context in which care is provided'.

Increasingly, vulnerability is being described in terms of potential for exposure to deliberate maltreatment (active) and unintentional or thoughtless acts (passive). There are many risks involved, which mean that the potential for a breach of care is always present and is not restricted to specific care contexts.

All people are potentially vulnerable but, by concentrating on those groups considered to be most at risk of abuse and on raising awareness about vulnerability amongst all carers, it is anticipated that all population groups will benefit. Individuals in the following population groups are considered to be at greatest risk. They apply across all care settings, including the home, and are relevant irrespective of age and/or severity.

 people with limited physical mobility

 people with impaired mental function

 people with learning disabilities

 people with impaired communication

 people with reduced levels of consciousness

 people participating in research

 people with a heightened emotional state

 people caring for individuals in any of the above groups.

The above categories are not mutually exclusive and it is possible that an individual may belong to more than one grouping, even if only temporarily.

**Appendix 2**

Initiated: 1964 17.C

 Original: English

# 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**

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

11. 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.

12. 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.

13. 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.

14. 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.

15. 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.

1. 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.
2. 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.

18. 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.

19. 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.

20. The subjects must be volunteers and informed participants in the research project.

21. 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.

22. 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.

23. 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.

24. 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.

25. 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.

26. 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.

27. 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.

**C. ADDITIONAL PRINCIPLES FOR MEDICAL RESEARCH COMBINED WITH MEDICAL CARE**

28. 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.

1. 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.

30. 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.

31. 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.

32. 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.

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