THE AGA KHAN UNIVERSITY (AKU)

KARACHI, PAKISTAN

FACULTY OF HEALTH SCIENCES (FHS)

STANDARD OPERATING PROCEDURES REGARDING HUMAN SUBJECTS RESEARCH

Developed By: Associate Dean Research, AKU Medical College Approved By AKU, University Research Council (URC) CMO AKUH & Associate Dean Clinical Affairs, AKU Dean School of Nursing and Midwifery, AKU Dean Medical College, AKU	Effective Date : January 1, 2018 Revision Dates : July 2021 Revision No : 0 Total Pages : 70 *Note: This document will replace existing ERC Guidelines 2015 and Research Scope Document 2015*

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1.0 OVERVIEW AND INTRODUCTION

The Aga Khan University (AKU) is fully supportive of advancing scientific inquiry through high quality, ethical research, which extends across diverse subjects including health sciences, basic sciences, education, culture and society. The AKU wide Ethics Review Policy was approved by the University Research Council (URC) in December 2017 and further endorsed by the Academic Council in March 2018. The ethics review system in the Faculty of Health Sciences at AKU Pakistan (see section 3.0 below) is in compliance with the policy approved by URC.

Faculty of Health Sciences, which includes AKU Medical College and School of Nursing and Midwifery along with its affiliated clinical facilities, is committed towards human research subjects' protection, and therefore requires all the human subject researchers and the related staff members to ensure compliance to the following institutional research processes:

- Ethics Review Committee (ERC) approvals;
- Compliance to research ethics;
- Compliance to research informed consent policy and procedure;
- Compliance to research regulations;
- Financial coverage to compensate patients for adverse events due to the research protocol;
- Compliance to Good Clinical Practice (GCP) standards of research;
- Compliance of research sponsors to applicable hospital policies and procedures;
- Management of research based conflicts of interest;
- Reporting of human research subjects related adverse drug reactions or adverse events at relevant forums (in case of hospital based studies, this should include hospital's adverse drug reactions and incident reporting system);
- Close supervision of medical trainees' research studies by designated research supervisors.

2.0 REQUIREMENTS FOR CONDUCTING HUMAN SUBJECTS RESEARCH AT FHS, AKU, PAKISTAN

1.0 Qualification requirements of Principal Investigators and other members of research teams.

1.1 To be a principal investigator, the researcher must be:

1.1.1 A full time faculty member at the AKU;

1.1.2 Must be trained in Good Clinical Practices (GCP) in case of clinical trials;

1.1.3 Preferably trained in research ethics.

1.2 Qualification of the other members of research teams must have:

1.2.1 These are attached as Appendix 2.

2.0 Conditions for hospital staff members to serve as research subjects.

2.1 The hospital staff members may serve as research subjects, provided:

2.1.1 The study is approved by hospital ERC and the Medical Director Office;

2.1.2 Consent process follows the policy;

2.1.3 There are no conflicts of interest;

2.1.4 Staff members participation is voluntary.

3.0 The Scope of Clinical Trials Unit.

3.1 Clinical Trials Unit (CTU) is a GCP compliant facility designed to provide the following services:

3.1.1 Clinical services;

3.1.2 Trial management services;

3.1.3 Clinical trials review and approval;

3.1.4 Clinical trial drug management services;

3.1.5 Capacity building.

4.0 The Scope of Human Subjects Research in Clinical Departments.

4.1 The twelve clinical departments viz. medicine, surgery, obstetrics & gynaecology, paediatrics, radiology, emergency medicine, family medicine, anaesthesiology, pathology & microbiology, oncology and psychiatry are all involved in human subjects research.

4.2 Each clinical department has a defined research track for its faculty members that defines all the necessary research requirements that their faculty members are expected to meet.

4.3 Few clinical departments have a dedicated research faculty as well as research administrative staff and few have departmental research committees.

4.4 Each clinical department facilitates its post graduates (fellows and residents) in completing their research dissertations as a post-graduate training requirement.

4.5 All the departments follow the standard institutional research policies.

5.0 The Role of AKU Research Council (URC).

The URC has the responsibility for research policy and management, allocation of resources for research, and strengthening of research capacity throughout the University's academic units. The URC is chaired by the Associate Vice Provosts Research and Graduate Studies and the membership is drawn from all academic units of the University representing various geographical locations. The core responsibilities of the URC include:

5.1 To approve allocation of available resources for research within the policy framework of the University.

5.2 To develop policies and make recommendations in areas such as:

5.2.1 Strengthening, promoting and institutionalizing the capacity for research;

5.2.2 Establishing institutional priorities for research;

5.2.3 Coordinating research linkages with graduate studies;

5.2.4 Promoting partnerships within AKU and with institutions;

5.2.5 Periodic review and assurance of research quality; Access and use of core research facilities;

5.2.6 Ethical consideration of research, including involvement of animals, humans as individuals and communities, genetic engineering, reproductive technology, and stem cell research;

5.2.7 Annual review of the University's research achievements of AKU.

6.0 The Role of AKU Ethics Review System at AKU.

6.1 The Ethic Review Board (ERB) is an AKU wide body responsible for policy-making, governance, oversight of the ethics review process across AKU and for hearing of appeals. It sits in the office of Associate Vice Provosts Research and Graduate Studies. The ERB reports to the University Research Council (URC). To ensure quality and due diligence in the review process, the ERB reserves the right to review a random selection of applications approved by the ERCs. All the ERCs report to the ERB through their respective chairs.

6.2 The ERB has devolved the power to approve ethics clearance to Ethics Review Committees (ERCs) created as sub-committees of the ERB. ERCs are responsible for provision of ethical clearance to all university-wide (hospital included) internally and externally funded research projects before commencement of the research study.

6.3 The office of Associate Vice Provost ensures systematic monitoring and compliance of ethics in research through the office of Research Ethics and Integrity.

6.4 ERC members consist of clinicians, researchers, public health professionals, lawyers and lay persons. There are academicians from others institutions as well. Gender balance is also maintained while selecting committee members.

7.0 AKU Institutional Bio-Safety Committee.

7.1 Responsibilities:

7.1.1 Raise awareness about laboratory biohazards, risk management and risk mitigation among the faculty, students, research assistants and other lab staff of AKU.

7.1.2 Develop policies and procedures to guide decisions of AKU-IBC for conduct of research proposals involving use of biohazard material.

7.1.3 Evaluate research proposals and lab based teaching activities that involve use of hazardous material. The evaluation will include but is not limited to: type of hazardous material being used such as biological, radiological recombinant DNA, toxin, human tissues/body fluid etc. mode of acquisition of this material, amount of the material, use of vertebrate animals or plants, categorization of the biological material and use of appropriate facility design, training experience.

7.1.4 Ensure adequate teaching and training of bio-risk management for AKU faculty, staff and students.

7.1.5 Oversight of the compliance to AKU policies and protocols.

7.1.6 Maintain record of any shortfalls, hazardous exposure, mitigation reports, and laboratory acquired infections.

8.0 The Role of AKU Research Office.

8.1 Support and enhancement of scholarly activity of research related faculty.

8.2 Supports research governance including the University Research Council, Ethics Review Board and the Institutional Bio-Safety Committee.

8.3 Development of a university-wide information management system for research activities.

8.4 Monitoring and benchmarking research achievements (Publications, Impact Factor, Research grants).

8.5 Coordination of research collaboration and partnerships.

8.6 Acting as a hub for electronically signing-off grant applications that are submitted online to funding agency.

8.7 Organizing training sessions for faculty/students on grant writing and management to enhance their skills in developing competitive proposals.

8.8 Identification of potential funding opportunities.

8.9 Intellectual property and commercialization including the setting up of an Office of Research Innovation and Commercialization (ORIC).

8.10 Custodian of research related policies on authorship, research misconduct, intellectual property rights, code of good research practice and mechanism for change of principal investigator.

8.11 Ensuring compliance in research in accordance with the national regulatory bodies such as the Higher Education Commission Pakistan (HEC).

9.0 The Role of Hospital's (AKUH) Leadership.

The Hospital's leadership is fully supportive to advance scientific inquiry through its human research subjects program. Keeping Patient Safety as hospital's top priority, the hospital's leadership is also committed to protect human research subjects from any sort of injury, harm or adverse events that may arise as a result of research protocol.

In order to deliver that commitment for human research subjects' protection, the hospital's leadership strongly recommends all the human subject researches and the related staff members to ensure full compliance to the following institutional research processes:

9.1 Ethics Review Committee (ERC) approvals;

9.2 Compliance to research ethics;

9.3 Compliance to research informed consent policy and procedure;

9.4 Compliance to research regulations;

9.5 Financial coverage to compensate patients for adverse events due to the research protocol;

9.6 Compliance to Good Clinical Practice (GCP) standards of research;

9.7 Compliance of research sponsors to applicable hospital policies and procedures

9.8 Management of research based conflicts of interest;

9.9 Reporting of human research subjects related adverse drug reactions or adverse events through hospital's adverse drug reactions and incident reporting system;

9.10 Close supervision of medical trainees' research studies by designated research supervisors.

3.0 INTRODUCTION TO RESEARCH ETHICS REVIEW SYSTEM AT FHS, AKU, PAKISTAN

Responsibility for Establishing The Research Ethics Review System

As per University Research Council (URC) of the Aga Khan University, approved recommendations of the working group to review research ethics system at AKU, a multi- tiered ethics review system has been introduced to ensure rigour, efficiency and relevance in the geographical and disciplinary context. This ethics review system consists of a central Ethic Review Board (ERB) which is an AKU wide body responsible for policy making, governance and oversight of the ethics review process across AKU. The ERB has created eight Ethics Review Committees (ERC's) as its sub-committees and have empowered these to approve ethical clearance to proposed research studies. The eight ERCs include four ERCs specific to FHS Pakistan, one for FHS Kenya, one for FHS and Tanzania, one for Social Sciences, Humanities and Arts and one for animal care and use.

Composition of Ethical Review Committee

Each of the four FHS Pakistan ERCs will have a multidisciplinary and multisector membership, their composition will be gender balanced and reflect the social and cultural diversity. The members will include individuals with backgrounds relevant to the areas of research that these committees will most likely to review. The following factors should be taken into consideration:

1. Members will include individuals with **scientific expertise, including expertise in behavioral or social sciences; health care; legal matters; ethics;** and lay people whose primary role will be to share their insights about the communities from which participants are likely to be drawn.
2. Lay people and other members, whose primary background is not in health research with human participants, are appointed in sufficient numbers (2-3) to ensure that they feel comfortable voicing their views.
3. In order to enhance independence, committee membership includes 2-3 members who are not affiliated with organizations that sponsor, fund, or conduct research reviewed by the ERC.
4. There will be at least 9 members to ensure that multiple perspectives are brought into the discussion.
5. Quorum requirements provide that at least five people, including at least one lay member and/or one non-affiliated member, are present to make decisions about the proposed research.

Ethical Review Committee Resources

There should be adequate resources, including staffing, facilities, and financial resources to allow ERC to effectively carry out its responsibilities. These include:

1. One to two fulltime staff with adequate training to enable the committees to carry out their technical and administrative responsibilities.
2. Adequate resources for the staff to fulfill their assigned functions, including office space and equipment and supplies (e.g. computers, stationery, telephones, photocopying machines, shredding machine) to conduct administrative business, to store committee files, and to keep documents secure and confidential.
3. Access to appropriate space for the committee to meet and adequate means for members to communicate as needed between meetings.
4. Financial resources to permit the committee to produce high-quality work.

Independence of Ethics Review Committees

ERCs should maintain independence in their operations, in order to protect decision making from influence by any individual or entity that sponsors, conducts, or hosts the research it reviews. ERC members (including the Chair) should remove themselves from the review of any research in which they or close family members have a conflicting interest.

To ensure that the ERC cannot be influenced to approve or disapprove particular protocols, the following should be ensured:

1. The ERC membership includes at least one person with no connection to the organization that sponsors or conducts the research under review.
2. Researchers, sponsors, and funders may attend an ERC meeting to answer questions about their research protocols and associated documents.
3. They should not be present when the ERC reaches decisions about their proposed research.
4. Senior members responsible for creating the ERC should not serve as members of the ERC or its Chair.
5. Entities that established the ERCs must ensure that members are protected from retaliation based on positions taken with respect to ERC-related matters or review of research projects.

Training the Ethics Review Committee

Training on the ethical aspects of health-related research with human participants, ethical considerations that apply to different types of research, and guidance on how ERC conducts its review of research, is provided to ERC members when they join the committee and periodically during their committee service.

The training provided to ERC members, either directly by the appointing entity or through cooperative arrangements with other ERCs and/or organizations that provide education on research ethics focuses on:

1. The role and responsibilities of the ERC, and its role vis-à-vis other relevant entities, according to relevant international guidelines (e.g. the Council for International Organizations of Medical Societies [CIOMS] International Ethical Guidelines for Biomedical Research, CIOMS International Ethical Guidelines for Epidemiological Research, International Council on Harmonization [ICH] Good Clinical Practice [GCP] guidelines in the case of clinical trials), national laws, and institutional policies.
2. The full range of ethical considerations relevant to research with human participants.
3. The application of such ethical considerations to different types of research.
4. Basic aspects of research methodology and design (for members who lack such background).
5. The impact of different scientific designs and objectives on the ethics of a research study.
6. The various approaches for ERC recognizing and resolving the tensions that can arise among different ethical considerations and modes of ethical reasoning. When training is supported by research sponsors, mechanisms are in place to ensure that the sponsor has no control, directly or indirect, over the content of the training.

Transparency, Accountability and Quality of the Research Ethics Committee

Mechanisms should exist to make ERC operations transparent, accountable, consistent, and of high quality. The entity establishing the ERCs should employ reliable means to evaluate whether the staff and members of the ERC routinely follow the ERC's policies, rules, and written procedures, with special attention to whether the ethical considerations articulated in international guidelines and national standards are being considered and applied consistently and coherently.

1. Such evaluations are conducted by knowledgeable and unbiased people at regular, pre-defined intervals using a pre-defined format; internal assessments are supplemented periodically by independent external evaluations.
2. The entity establishing the ERC should be committed to consider and, when appropriate, follow up on the findings and ERC recommendations of the internal and external evaluations.
3. The results of the evaluation should be of a type that can aid the ERC in reviewing its practice and appraising performance (rather than apportioning blame), while also assuring the public that research is being reviewed according to established standards.
4. Researchers, research participants, and other interested parties should have a means of lodging complaints about the ERC; such complaints should be reviewed by an entity other than the ERC itself, and appropriate follow-up actions should be taken.
5. Researchers have a means of discussing concerns with ERC members, both on general matters and in response to ERC decisions on particular research studies.

ERC decisions, excluding confidential information, should be made publicly available, through mechanisms such as clinical trial registries, web sites, newsletters, and bulletin boards.

Written Policies and Procedures

Written policies and procedures specify the ERC's membership, committee governance, review procedures, decision making process, communication, follow-up, monitoring, documentation and archiving, training, Quality assurance, and procedures for coordination with other ERCs.

ERC Policies

The Associate Dean Research, Medical College, while working with the chairs of the FHS ERCs will establish the necessary protocols in line with the URC approved policies to govern the FHS Pakistan ERCs; The Associate Dean Research will:

1. Provide ERCs with a secretariat whose staff have the necessary training, knowledge and experience to support the ERC in:
    - Performing its review function and;
    - Record keeping and archiving function.
2. Membership of the ERC.
    - Members and Chairperson will be appointed by the chair, URC upon the recommendation of the Dean/Associate Dean Research.
    - In order that, over time, an increasing number of individuals experience the processes of decision making involved in the conduct of ERC business,
        - the initial term of appointment will be for two years, extensible to three or four years;
        - Staggered finite terms of appointment will be patterned to allow both continuity as well as the consideration of new members. Therefore in the initial appointments some may be for a period of two years and some for a period of one year.
    - There will be at least one lay (non-scientist) member;
    - At least one member will be a nonaffiliated member (from outside the institution);
    - It is expected that ERC members will attend at least 60% of all meetings.

Checklist for Review of Applications by the FHS ERCs

The checklist is included as an Appendix 6 and will serve as a guide for the members in their review of the application.

Governance of ERCs

Each committee will have a Chair and a Vice Chair. The Vice chair will be responsible for assuming the position of Chair in her/his absence and will conduct the review of granting ERC extensions to existing approved projects, as all ERC approved projects will come for review in

one year. The accepted quorum will be a majority or 50% attendance of members. The roles of the staff and chair are as outlined in the following sections.

The designated ERC staff will be responsible for

1. Identifying and screening out proposals where research protocol, language, science or statistics requires further attention of the departmental review committee. These will be returned without detailed review.
2. Ensuring that at least two reviewers are sent the project, preferably, a week before the meeting for a written review to be received by the committee before the meeting.
3. Recording and informing the Chair of the quorum, the changes in the quorum at voting time; and the recording of recusals because of conflict of interest.
4. Recording the voting for each submission as
    a. Approved;
    b. Returned for clarification/modification;
    c. Disapproved, giving reason.

Inviting special experts at *the request of the Chair*, in situations where the Chair/reviewer indicates the need for specialized information, scientific or other, essential for full comprehension of the research.

The Chair will be responsible for ensuring

1. Appropriate conduct of the meetings, and ensuring a wide understanding by all members of the modus operandi of the meetings (viz, the encouragement of free discussion, stating all concerns, followed by voting; and including an understanding that the role of the chair is a non-supervisory relationship; and the options for members when they vote on a proposal).
2. That all members have taken appropriate courses to familiarize themselves with ERC procedures.
3. That cooperative review arrangements are implemented ***when applicable***, such as joint review, reliance on the review of another qualified ERC, or similar arrangements aimed at avoiding duplication of effort.
4. The appropriate use of consultants by the ERC, ensuring the recording of the process to identify the need for a consultant, select a consultant, and document the consultant's participation and role in the review of research.

Ancillary members /independent consultants

Independent consultants can only be called in with the express approval of the Chair when this may be thought necessary for specific research proposals, research subjects or topics.

1. Consultants will be informed well in advance of the context and the need for their opinion;
2. Appropriate arrangements will be made by the staff to ensure that the consultant is called in only for the appropriate case and has comfortable seating before the case.

Submissions and documents required

Submissions should be made on the standard AKU ethics proposal review by ERC form. The application is to be submitted online using the customized software available at https://www.aku.edu/mcpk/research/Pages/ethical-review.aspx

Communicating a decision to the Principal investigator

A decision of acceptance will be sent to the PI within eight days of the committee meeting. The communication will clearly state whether the project is

a. Approved;
b. Disapproved;
c. Requires modifications or clarifications, after which final decision will be made by the chair.

Documentation and Archiving

1. The staff is responsible for documentation and archiving.
2. All of the ERCs documentation and communication will be dated, filed, and archived according to the committee's written procedures. This will include the original and revised submissions of the research projects.
3. Records will be kept electronically.
4. Sufficient safeguards are established (e.g. locked cabinets for hard copy files, password protection and encryption for electronic files) to maintain confidentiality.
5. Members of staff are sufficiently trained to understand their responsibilities related to record-keeping, retrieval, and confidentiality.
6. The chair will be informed about the procedures to safeguard the files.

4.0 CODE OF GOOD ETHICAL CONDUCT FOR RESEARCHERS

This code also emphasizes on the ethical conduct for human subjects research program applies to all University employees (viz. faculty, residents, students and staff) and also those affiliated with the University Hospital (such as, trainees, technicians, students, fellows, clinicians, visiting researchers, collaborators, and other staff members) who are engaged in research conducted at or by the University, regardless of the source of funding.

The following are the codes of ethical conduct:

1. Ensuring that the research subjects take part voluntarily, free from any coercion or undue influence, and their rights, dignity and (when possible) autonomy is respected and appropriately protected.
2. Obtaining ERC approval prior to commencing any human subjects research.
3. Complying with all applicable policies and procedures of AKU Research Office.
4. Disclosing all actual or perceived conflicts of interest regarding their research.
5. Conducting research according to the ERC approved protocol.
6. Ensuring that risks to participants are minimized.
7. Ensuring that informed consent is sought from each participant, using an ERC approved consent form or procedure, and that the consent is appropriately documented.
8. Ensuring that an ongoing research review function monitors all studies to ensure human subjects safety and confidentiality of the data.
9. Ensuring that additional safeguards are in place for vulnerable populations.
10. Submitting all proposed changes to previously approved protocols to ERC for review and approval and ensuring that changes to approved research are not initiated without prior ERC approval, unless they are necessary eliminate immediate hazards to participants.
11. Ensuring financial coverage to compensate patients for adverse events due to the research protocol.
12. Ensuring compliance to Good Clinical Practice (GCP) standards of research.
13. Ensuring compliance of research sponsors to applicable hospital policies and procedures.
14. Reporting of human research subjects related adverse drug reactions or adverse events at relevant forums (e.g. through hospital's adverse drug reactions and incident reporting system in hospital based studies).
15. Providing close supervision to medical trainees' research studies by designated research supervisors.

16. In case if the research study includes use of medications, the investigator should ensure to include the hospital's Medication Management and Use (MMU) program by involving hospital's pharmacy services in the study.
17. In case if the research study includes use of medical equipment, the investigator should ensure to include hospital's Equipment Management Program by involving hospital's Biomedical services in the study.
18. In case if the research study includes use of any Hazardous Material, the investigator should ensure to include hospital's Hazardous Material (HAZMAT) Management Program by involving hospital's HAZMAT sub-committee of Safety Committee.

Researchers Responsibilities

Research should be performed only by persons with scientific, clinical, or other relevant qualifications appropriate to the project, who are familiar with the ethical standards applicable to their research, who submit the necessary information to the ERC for review (including both the research protocol and disclosures of any conflicting interests), and who carry out the research in compliance with the requirements established by the ERC.

The person conducting research should fulfill the following criteria in the conduct of ethical research:

1. Submitting an application for review.
    1.1 An application or review of the ethics of proposed health-related research should be submitted by a researcher qualified to undertake the particular study, who is directly responsible for the ethical and scientific conduct of the research.
    1.2 Student applications should be submitted under the responsibility of a qualified advisor / faculty member involved in the oversight of the student's work or in the student's name, co-signed by the qualified faculty supervisor. In case of research involving medical students, a letter of approval from the UGME is needed.
    1.3 All information required for a thorough and complete review of the ethics of proposed research should be submitted, including disclosures about researchers' conflicting interests, if any.
2. Conduct of research.
    2.1 The research must be conducted in compliance with the protocol approved by the ERC.
    2.2 No deviation or changes may be made to the approved protocol or in following it, without prior approval of the REC, except where immediate action is necessary to avoid harm to research participants. In such a case, the ERC should be informed promptly of the changes/deviations made, and the justification for doing so.
    2.3 The ERC must be informed of any changes at the research site that significantly affect the conduct of the trial, and/or reduce the protections or decrease the benefits provided or increase the risk to participants (e.g. closing down of a health facility at

the research site or other impediments to obtaining access to health care that was originally available).

3. Safety reporting.

   3.1 All serious, unexpected adverse events related to the conduct of the study/study product or unanticipated problems involving risks of harm to the participants or others should be promptly reported to the ERCs and/or other relevant authorities.

   3.2 Any recommendations provided by the ERC in response to such reporting must be immediately implemented.

4. Ongoing reporting and follow-up.

   4.1 The researcher must submit written summaries of the research status to the ERC annually, or more frequently, if requested by the ERC.

   4.2 Researchers must inform the ERC when a study is completed or prematurely suspended/terminated.

   4.3 In the case of the early suspension/termination by the researcher or sponsor, the researcher should notify the ERC of the reasons for suspension/termination; provide a summary of results obtained prior to prematurely suspending or terminating the study; and describes the manner by which enrolled participants will be notified of the suspension or termination and the plans for care and follow-up for the participants.

   4.4 If the ERC terminates or suspends its approval of a study, the researcher must inform the institution under whose authority the research is being conducted, the sponsor of the research, and any other applicable organizations.

5. Information to research participants.

   a. Researchers have a responsibility to keep the research participants and their communities informed of the progress of research by appropriate means, at suitable time-frames in simple and non-technical language, for example, when:

   b. The research study is terminated or cancelled.

   c. Any changes occur in the context of the research study that alter the potential benefits or risks.

   d. The research project is completed.

   e. Results of the research are available.

6. Researcher should ensure that patients and families should be identified and informed about how to gain access to clinical research, clinical investigations, or clinical trials relevant to their treatment needs through any of the following means:

   a. AKU website;

   b. Flyers and posters in clinics;

   c. Short Message Service (SMS) on mobile phones;

   d. AKUH Facebook postings.

7. Researchers should ensure safeguards to protect the safety, rights, and well-being of vulnerable patients, including children, prisoners, pregnant women, persons who are mentally disabled, persons who are economically or educationally disadvantaged, and others who may be at risk for coercion or undue influence.
8. Researchers should ensure safeguards to protect the safety, rights, and well-being of hospital staff who may be at risk for coercion or undue influence.

5.0 PROCEDURE FOR INFORMED CONSENT

Please refer to Appendix 6 for the sample Informed Consent.

Informed consent from the subject should be taken in accordance with the following:

1. Investigator must ensure that the informed consent is clearly comprehended by the subject/ guardian.
2. Purpose of research must be clearly explained.
3. In simple word describe the procedure that the subjects would be expected to undergo. Identify any procedures that are experimental/ investigational/ non-therapeutic. Indicate type and frequency of monitoring during and after the study.
4. Length of time subject is expected to participate. If subject's participation is expected to continue over a long 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.
5. 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.
6. Please specify financial burden to be incurred by the research subject while participating in the study.
7. Explain expected benefits, potential risks, and alternative treatments and procedures to the subjects. Note this not only includes physical injury, but also possible psychological, social, or economic harm, discomfort, or inconvenience. If risk is unknown, state so.
8. 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 and the institution.
9. Describe the extent to which confidentiality of records identifying the subject will be maintained.
10. Identify the person to contact for answers to questions, or in event of research related injury or emergency.

11. 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.
12. Subject's right to withdraw from the study at any time.
13. How sharing of results with subjects will occur.
14. No abbreviations shall be used on the informed consent form.
15. 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 PI's responsibility to ensure quality of consent procedure.
16. Provide a copy of the informed consent to the subject, file original in PI file and a copy to the sponsor if required as part of the contract.

6.0 STUDIES QUALIFYING EXEMPTION FROM ETHICAL REVIEW

Please refer to Appendix 3 for the criteria for exemption studies.

7.0 PROCEURE FOR APPROVAL OF INITIAL RESEARCH PROTOCOLS

Ethical Basis For Decision-Making In Ethical Review Committee

The primary task of an ERC is the ethical review of research protocols and their supporting documents. Approval or disapproval is based on the ethical acceptability of the research, including its social value and scientific validity, an acceptable ratio of potential benefits to risks of harm, the minimization of risks, adequate informed consent procedures (including cultural appropriateness and mechanisms to ensure voluntariness), measures to ensure protection of vulnerable populations, fair procedures for selection of participants, and attention to the impact of research on the communities from which participants will be drawn, both during the research and after it is complete. The review take into account any prior scientific reviews and applicable laws.

The ERC should base its decisions about research that it reviews on a coherent and consistent application of the ethical principles articulated in international guidance documents and human rights instruments, as well as any national laws or policies consistent with those principles. The ERC should make clear the specific ethical guidelines on which it relies in making decisions and makes them readily available to researchers and the public. When an ERC develops reliance

agreements for review of research under its jurisdiction by another ERC, it is the responsibility of the delegating ERC to assure that the same ethical principles serve as the basis of the other ERC's decision-making. To aid in determining the ethical acceptability of research protocols, an ERC may utilize a checklist to ensure that all relevant criteria are considered during review and that, as a general rule, similar protocols are treated similarly. When an ERC determines that an approach it has taken on a particular ethical issue in the past is no longer appropriate, it should provide an explicit rationale for its change in position. In communicating decisions about particular protocols to researchers, the ERC should explain its analysis of any significant ethical issues that arose in the review.

The checklist for review of applications is included in Appendix 6. Key criteria for review should include, but are not limited to, the following:

1. **Scientific design and conduct of the study**

   Research is ethically acceptable only if it relies on valid scientific methods. Research that is not scientifically valid exposes research participants or their communities to risks of harm without any possibility of benefit. ERCs should have documentation from the Departmental Review Committees that the research methods are scientifically sound, have appropriate research design and methodology, adequacy of provisions made for monitoring and auditing, as well as the adequacy of the study site (e.g. availability of qualified staff and appropriate infrastructures).

2. **Risks and potential benefits**

   In ethically acceptable research, risks have been minimized (both by preventing potential harms and minimizing their negative impacts should they occur) and are reasonable in relation to the potential benefits of the study. The nature of the risks may differ according to the type of research to be conducted. ERC members should be aware that risks may occur in different dimensions (e.g. physical, social, financial, or psychological), all of which require serious consideration. Further, harm may occur either at an individual level or at the family or population level.

3. **Selection of study population and recruitment of research participants**

   Ethically acceptable research ensures that no group or class of persons bears more than its fair share of the burdens of participation in research. Similarly, no group should be deprived of its fair share of the benefits of research; these benefits include the direct benefits of participation (if any) as well as the new knowledge that the research is designed to yield. Thus, one question for ERC review to consider is whether the population that will bear the risks of participating in the research is likely to benefit from the knowledge derived from the research. In addition, ethically acceptable research includes recruitment strategies that are balanced and objectively describe the purpose of the research, the risks and potential benefits of participating in the research, and other relevant details.

4. **Inducements, financial benefits, and financial costs**

It is considered ethically acceptable and appropriate to reimburse individuals for any costs associated with participation in research, including transportation, child care, or lost wages. Many ERCs also believe that it is ethically acceptable to compensate participants for their time. However, payments should not be so large, or free medical care or other forms of compensation so extensive, as to induce prospective participants to consent to participate in the research against their better judgment or to compromise their understanding of the research.

5. **Protection of research participants' privacy and confidentiality**

Invasions of privacy and breaches of confidentiality are disrespectful to participants and can lead to tangible harms such as social stigma, rejection by families or communities, or lost opportunities such as employment or housing. ERCs should therefore examine the precautions taken to safeguard participants' privacy and confidentiality.

6. **Informed consent process**

The ethical foundation of informed consent is the principle of respect for persons. Competent individuals are entitled to choose freely whether to participate in research, and to make decisions based on an adequate understanding of what the research entails. Decisions for children or adults who lack the mental capacity to provide informed consent should be made by an authorized surrogate decision-maker. ERCs should examine the process through which informed consent will occur, as well as the information that will be provided. ERCs may waive the requirement of informed consent only when doing so is consistent with international guidelines and national standards. While informed consent to research is important, the fact that a participant or surrogate may be willing to consent to research does not, in itself, mean that the research is ethically acceptable.

7. **Community considerations**

Research has impacts not only on the individuals who participate, but also on the communities where the research occurs and/or to whom findings can be linked. Duties to respect and protect communities require examining by the ERC and, as far as possible, are aimed at minimizing any negative effects on communities such as stigma or draining of local capacity, and promoting, as relevant, positive effects on communities, including those related to health effects or capacity development.

8. **Decision Making Procedures for ethical review committee**

Decisions on research protocols designated for review by the convened ERC should be based on a thorough and inclusive process of discussion and deliberation. Expedited

Review- Protocols involving no more than minimal risk and burden to research participants may be reviewed on an expedited basis by one or more members (rather than the full committee). During meetings of the ERC, members should engage in discussions to elicit all concerns and opinions related to the protocols and the associated documents under consideration. The ERC's rules ensure that the discussions are respectful of all opinions and allow for varied beliefs to be aired. The Chair should foster a respectful and inclusive tone and allows adequate time for deliberation, during which only ERC members participate, and decisions are made only by those who were present during the entire discussion. The Chair is responsible for the decision-making process, in particular for determining when consensus is needed to achieve the decision. *Researchers, funders, or others directly associated with the protocol in question should not be present during committee deliberations.*

ERC members should recognize the limitations of their knowledge and seek external input when necessary, particularly in relation to research that involves people whose life experiences may differ significantly from those of the committee members.

Decisions should be arrived at through either a vote or consensus. Consensus does not require that all ERC members support the decision, but that all members consider the decision at least acceptable and no member considers the decision unacceptable. A pre-defined method should determine when votes will be taken and how many favourable votes will be needed for a proposed research to be approved.

8.0 PROCEDURE FOR ONGOING RESEARCH REVIEW

The ERC forms Ad hoc Research Review Committees with a mandate to review designated ongoing studies using a review tool (Appendix 7&8 attached) that contains the following criteria:

a) ERC approvals/exemptions.

b) ERC renewals with any subsequent changes in protocols or consent forms.

c) Study protocols.

d) Sponsors contract containing evidence of:

- Insurance to cover adverse events;
- Compliance with hospital policies on reporting adverse events, involvement of institutional medical equipment, hazardous material, medication management and ethics programs;
- Use of qualified research teams;
- Protection of the privacy and confidentiality of data;

- Reliability and validity of data and accurate reporting;
- Prohibition of incentives compromising research integrity.

e) Evidence of required qualifications of PI, Co-PIs and other staff.

f) Evidence of compliance to Good Clinical Practices (GCPs).

g) Evidence of compliance to regulatory requirements, e.g., DRAP.

h) Coverage of indemnity insurance to compensate patients who experience an adverse event.

i) Safeguards to protect the safety, rights and well-being of vulnerable patients, including children, pregnant women, mentally disabled, economically or educationally disadvantaged and others who may be at risk for coercion or undue influence.

j) Documentation of all above in the review tool and finally in the consolidated ERC Research Review Report.

The ERC office compiles all the review data and turns it into a brief annual report to be reported to the University Research Council (URC) as well as the hospital's Joint Staff Committee.

9.0 PROCEDURE FOR SPONSORS AND CONTRACT RESEARCH ORGANIZATIONS (CRO'S)

In case the sponsor is a commercial organization or a contract research organization (CRO) involved in the clinical research, the sponsor shall work together with the university to ensure:

- Compliance with the university and hospital's policies and processes for monitoring and evaluating the quality, safety, and ethics of the research.
- Research teams used by the sponsor are trained and qualified to conduct the research.
- Privacy and confidentiality of subject data is maintained.
- Research data are reliable and valid and the results and reporting are statistically accurate, ethical, and unbiased.
- Patient or researcher incentives do not compromise the integrity of the research.

In case the sponsor is transferring its duties, functions and responsibilities to the contract research organization, the investigator will ensure following requirements should be met:

- A written contract clearly delineating this transfer of responsibilities.

- The contract should specify that the contract research organization or sponsor is also responsible for monitoring and evaluating the quality, safety, and ethics of the research.
- The sponsor should be responsible for monitoring the contract.

The investigators must ensure that all of the above requirements are defined in the contracts between the university and the sponsors or CRO's, whenever applicable.

10.0 GLOSSARY

Adverse Event: An unanticipated, undesirable, or potentially dangerous occurrence in a health care organization.

Benefit: A favorable consequence arising from a study, for example the demonstration that a vaccine is effective in a randomized controlled trial or the identification of a workplace hazard in an observational study.

Bioethics: A field of ethical enquiry that examines ethical issues and dilemmas arising from health, health care, and research involving humans.

Clinical Trial: Testing of drugs, devices, or techniques in three or sometimes four stages depending on the purpose, size, and scope of the test. "Phase I" trials evaluate the safety of diagnostic, therapeutic, or prophylactic drugs, devices, or techniques to determine the safe dosage range (if appropriate). They involve a small number of healthy subjects. The trial usually lasts about one year. "Phase II" trials are usually controlled to assess the effectiveness and dosage (if appropriate) of the drugs, devices, or techniques. These studies involve several hundred volunteers, including a limited number of patients with the target disease or disorder. The trial usually lasts about two years. "Phase III" trials verify the effectiveness of the drugs, devices, or techniques determined in Phase II studies. Phase II patients are monitored to identify any adverse reactions from long-term use. These studies involve groups of patients large enough to identify clinically significant responses. The trial usually lasts about three years. "Phase IV" trials study the drugs, devices, or techniques that have been approved for general sale. These studies are often conducted to obtain more data about a product's safety and efficacy.

Compensation: That which is given in recompense, as an equivalent rendered, or remuneration.

Confidentiality: The obligation to keep information secret unless its disclosure has been appropriately authorized by the person concerned or, in extraordinary circumstances, by the appropriate authorities. The restricted access to data and information to health care practitioners and clinical staff who have a need, a reason, and permission for such access. An

individual's right to personal and informational privacy, including for his or her medical records.

Conflict of interest: In the research context, scientists have a conflict of interest if they stand to achieve personal gain (money or the equivalent) by failing to discharge professional obligations, either to protect the welfare of participants or to uphold the integrity of the scientific process.

Consent form: An easily understandable written document that documents a potential participant's consent to be involved in research which describes the rights of an enrolled research participant. This form should communicate the following in a clear and respectful manner: research time-frame; title of research; researchers involved; purpose of research; description of research; potential harms and benefits; treatment alternatives; statement of confidentiality; information and data to be collected; how long the data will be kept, how it will be stored and who can access it; any conflicts of interest; a statement of the participant's right to withdraw from participation at any point; and declarative statement of understanding that the potential participant agrees to and signs. The consent form should be in a language that the potential participant understands. For potential participants with limited literacy, the verbal communication of the consent document details should be provided along with proper documentation of consent, if it be given.

Data: Facts, clinical observations, or measurements collected during an assessment activity. Data before they are analyzed are called *raw data*.

Ethical guidelines: Guidance documents which assist with decisions relating to the responsibility to adhere to established and relevant standards of ethical principles and practice.

Expedited review: Review of proposed research by the REC chair or a designated voting member or group of voting members rather than by the entire REC.

Human Subjects Research: Research involving living individuals about whom an investigator obtains data through intervention or interaction with individuals and/or identifiable personal information. Research protocols involving human subjects are reviewed by an Institutional Review Board (ERC) or other research ethics review mechanism and receive ongoing oversight as necessary.

Informed consent: Is a decision to participate in research, taken by a competent individual who has received the necessary information; who has adequately understood the information; and who, after considering the information, has arrived at a decision without having been subjected to coercion, undue influence or inducement, or intimidation.

Medical Research: Basic, clinical, and health services research that includes many types of research studies, such as clinical trials, therapeutic interventions, development of new medical technologies, and outcomes research, among others.

Multi-site research: A clinical trial conducted according to a single protocol but at more than one site, and, therefore, carried out by more than one investigator.

Personal data: Data that relate to a living person and contain personally identifying information.

Principal investigator (PI): The main researcher overseeing or conducting the research process.

Privacy: The state or condition of being alone, undisturbed, or free from public attention, as a matter of choice or right; seclusion; freedom from interference or intrusion; absence or avoidance of publicity or display; secrecy, concealment, discretion; protection from public knowledge or availability.

Protocol: A scientific medical treatment plan or study outline for a new or experimental procedure or treatment with the intent of measuring human applications (**for example**, management of diabetes mellitus type 2). Protocols frequently include components such as types of participants, scheduling, procedures used, types of medications and dosages, among others.

Reimburse: To repay (a sum of money which has been spent or lost).

Voluntary: (1) Performed or done of one's own free will, impulse, or choice; not constrained, prompted, or suggested by another; (2) free of coercion, duress, or undue inducement. Used in the health and disability care and research contexts to refer to a consumer's or participant's decision to receive health or disability care or to participate (or continue to participate) in a research activity.

Vulnerable (research) participants: Vulnerable persons are those who are relatively (or absolutely) incapable of protecting their own interests. More formally, they may have insufficient power, intelligence, education, resources, strength, or other needed attributes to protect their own interests. Individuals whose willingness to volunteer in a research study may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate may also be considered vulnerable. Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental, and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention. Other vulnerable persons include patients with incurable diseases, people in nursing homes, unemployed or impoverished people, patients in emergency situations, ethnic minority groups, homeless people, nomads, refugees, minors, and those incapable of giving consent, and women.

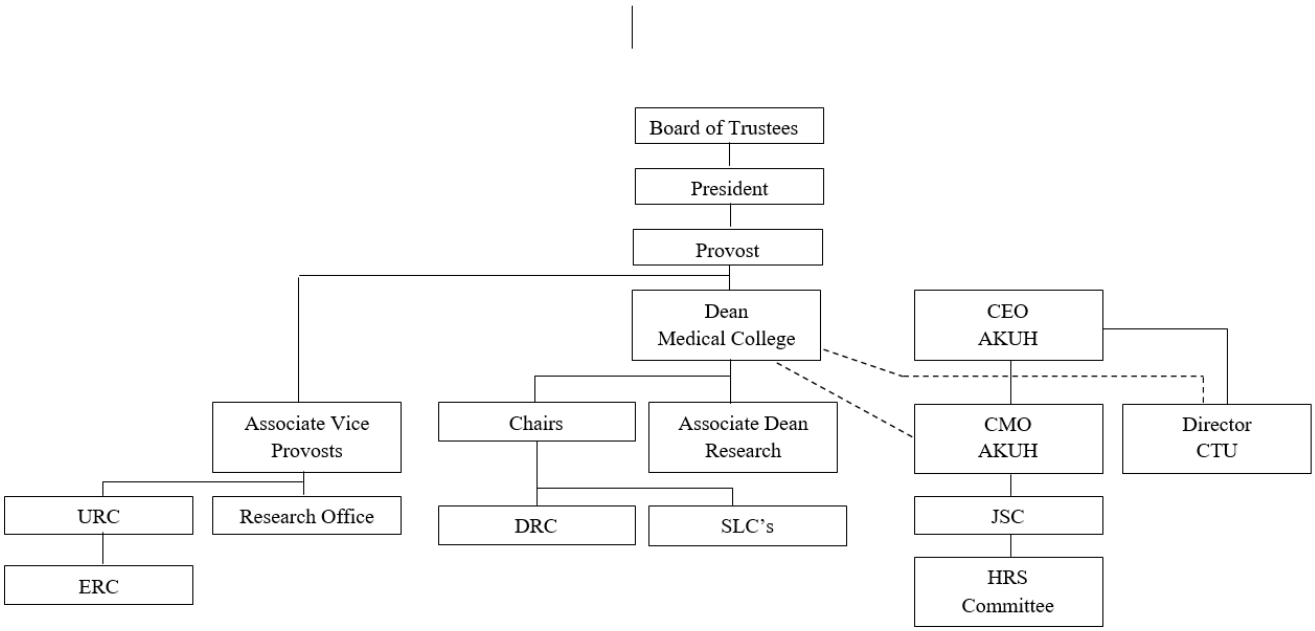
11.0 REFERENCES

1. World Medical Association Declaration of Helsinki.
2. International Conference on Harmonisation (ICH) / World Health Organization (WHO) Good Clinical Practice (GCP) standards.
3. Human Subjects Research Program (HRP), Joint Commission International Accreditation Standards for Academic Medical Centers, 6th Edition.
4. AKU Research Policy ORGS/008-2018 on Research Ethics Review System.
5. AKU ERC Guidelines for Researchers 2015.
6. AKU Research Policy ORGS/003-2014 on Intellectual Property Rights.
7. AKU Research Policy RGS2013/001 on Research Misconduct.
8. AKU Research Policy on studies qualifying exemption from ethical review.
9. AKU Research Policy ORGS/2013-005 on Code of Good Research Practice and Access to Patient Data.
10. AKU Research Policy ORGS/001-2013 on Research Authorship.
11. AKU Research Policy ORGS/007-2018 on submitting extramural grants applications and requirements for sponsors and contract research organizations.
12. AKU HR Policy HR/ER-07 on Conflict of Interest.
13. AKUH Scope of Research Services 2015.
14. CTU Policy CTU/TM-03 on Informed Consent in Clinical Trials.
15. AKU Research Insurance Coverage Policy.

12. APPENDICES

Appendix No.1: AKU/AKUH Research Organogram

Human Subjects Research Structure at AKU & AKUH, Karachi



Appendix No. 2: Qualification of Researchers

This document is the modified version of URC's research staff file. The document has been further modified by Research Office and CTU based on JCIA recommendations.

Proposed Definition of Research Staff

Research staff can be defined as those employees hired by the university as permanent research staff or on contract to undertake or assist research for a funded project. Staff hired to support research can be categorized under the title of Research Assistant, Research Medical Officer, Research Officer, Research Associate, Research Fellow, Post-doctoral Research Fellow and Research Coordinator.

All individuals with these titles shall be engaged in:

1. Providing professional and technical support and/or assistance to the faculty directly engaged in research;
2. Conducting research and experimental studies in the field or laboratory, or providing professional, technical and administrative support or assistance to senior research staff;
3. Providing professional and/or technical guidance to students undertaking graduate level research;
4. Development and organization of short research courses and graduate research courses; at the same time, teaching similar courses;
5. R&D activities including development and upgrading of new technology to be used for diagnosis and research;
6. Clinical trials: staff engaged in clinical trials must demonstrate sound working knowledge & proficiency in human clinical trials processes, good clinical practices (ICH-GCP), research ethics and human research regulatory requirements. Staff in clinical trials must be GCP and BLS/ALS and IATA certified;
7. Compliance with the University policies relating to biosafety, data management and research conduct.

Involvement restricted just to the following activities should not be considered as research specific:

1. Preparation and support for undergraduate teaching and lab exercise.
2. Providing scientific and technical support and information services without being involved in active research process.
3. Dealing study medications in Pharmacy (not directly involved with the research subjects)

4. General purpose or routine data collection and entry.
5. Standardization and routine laboratory testing with no intellectual input.
6. Regular computer programming, systems work and data entry.
7. Facilitation of the logistic arrangements or core facilities required for research projects and labs.

Proposed classification of non-faculty Research Staff

These employees are hired either against regular budgeted positions or are paid from grants. Each individual appointed to one of the positions below should be given a clearly written statement of terms of his/her appointment, including the approved Job Description on the approved format. Any reference to benefits in the statement of terms must be in accord with current University HR policies and procedures.

Remunerations

Salary and benefits offered to research staff should be in line with the University's policies and salary scales (when applying for the grant funding, the total cost for salary and benefits for the incumbent should be considered and funds should be requested accordingly).

Research Assistant (Grade 7)	**EDUCATIONAL/EXPERIENCE /PROFESSIONAL QUALIFICATIONS & LICENSURE** Works under supervision of principal investigator and research coordinator • Must possess a BScN degree with one year clinical experience OR Bachelor in sciences with at least 3 years' experience in any research work • Must have a current registration (RN license for BScN) • Must have BLS and GCP certification with validity within 2 years (for clinical trials) • Demonstrate some knowledge of research work and regulations
Research Associate (Grade 8)	**EDUCATIONAL/EXPERIENCE /PROFESSIONAL QUALIFICATIONS & LICENSURE** Works under supervision of principal investigator and research coordinator • Must possess a degree in MBBS or BScN with at least 2 years research experience OR Master in any discipline (with two years of graduation) with at least 3 to 4 years' research experience • Must have a current registration (PMDC &PNC) & be in good standing with their professional association

	• Must have BLS and GCP certification with validity within 2 years (for clinical trials) • Demonstrate sound working knowledge & proficiency in human clinical trials processes, good clinical practices (ICH-GCP), research ethics & human research regulatory requirements (By exception, an incumbent holding a Bachelor's degree with research related experience can be appointed/ promoted at this level. But his/ her career growth will be limited since at grade 9 & above, a Master's degree or an M.B.B.S. is an essential requirement).
Research Officer (Grade 9 to 11)	**EDUCATIONAL/EXPERIENCE/PROFESSIONAL QUALIFICATIONS & LICENSURE** This individual should have additional skills and knowledge regarding various tools of research which he or she is expected to have acquired after spending at least two to three years as Research Associates (Grade 8) or equivalent. S/he should be able to supervise the work of juniors and provide support to specific research programs. • If Research Officer has to manage specimen shipment or handling, then s/he must be IATA certified. • Must have BLS and GCP certification with validity within 2 years (for clinical trials). • Demonstrate sound working knowledge & proficiency in human clinical trials processes, good clinical practices (ICH-GCP), research ethics & human research regulatory requirements. **Senior Research Officer** (in addition to work experience, must have Masters in Epidemiology & Biostatistics /MPH/HPM/MScN or M.Ed.)
Research Fellow (Grade 12)	**EDUCATIONAL/EXPERIENCE /PROFESSIONAL QUALIFICATIONS & LICENSURE** • Must have 4 years post M.B.B.S research experience or four years research experience with MSc in Epi & Bio/ HPM/ MScN/MPH or M.Ed.) Incumbent in this position normally have a double Master's degree, or an M.B.B.S and Master's degree in a related discipline, with 4 to 5 years research related experience (Master's degree should be thesis based). • Must have a current registration & be in good standing with their professional association • If research fellow has to manage specimen shipment or handling, then s/he must be IATA certified

Post-doctoral Fellow **(Grade 12 / 13** depending on incumbents experience and responsibilities associated with the position)	• Must have BLS and GCP certification with validity within 2 years (for clinical trials) • Demonstrate sound working knowledge & proficiency in human clinical trials processes, national and international regulatory guidelines (GCP, CIOMS, CFR, Helsinki, HIPPA, NBC, DRAP and ERC etc.), research ethics & human research regulatory requirements Non-faculty position to engage in advanced study and research in collaboration with members of the faculty. This position will be suitable for fresh PhD who intends to start a career in research and teaching. (The incumbent would normally move up to the position of Assistant Professor within 2 to 3 years). *Note: Fellows in Clinical departments are part of the PGME programme and would not be included in # 5 and # 6.*
Research Coordinator (Grade 12) **Senior Research Coordinator (Grade 13)**	**EDUCATIONAL/EXPERIENCE /PROFESSIONAL QUALIFICATIONS & LICENSURE** This position would require individuals with considerable experience in managing and coordinating specific activities of a research programme or a project. Individual aiming for this position should have experience relevant to the objectives of the research projects. • Masters (MSc. Epi & Bio, MPH, MScN, or M.Ed.,) with 5 to 6 years research related experience OR M.Phil. with 4 to 5 years research • Must have a current registration & be in good standing with their professional association • Must have BLS and GCP certification with validity within 2 years (for clinical trials) • If research coordinator has to manage specimen shipment or handling, then s/he must be IATA certified • Demonstrate sound working knowledge & proficiency in human clinical trials processes, national and international regulatory guidelines (GCP, CIOMS, CFR, Helsinki ,HIPPA, NBC, DRAP and ERC etc.), research ethics & human research regulatory requirements The incumbent shall have responsibility of coordinating and managing research programme or a research unit of a department. Individual at this position should have exceptional understanding of research project management and skills to train juniors on research management as well as the ability to independently supervise and carry forward research projects.

Appendix 3: Criteria for Exemption Studies

AGA KHAN UNIVERSITY FACULTY OF HEALTH SCIENCES (FHS)

EXEMPT RESEARCH UNDER THE REVISED 2018 COMMON RULE

In line with the revised 2018 US guidelines of ethical review of research studies that are known as COMMON RULES, the Ethical Review Committees (ERCs) of FHS, AKU have updated their criteria for classifying research studies as exempt from review. These criteria are listed below.

Even when research is exempt from further requirements of review and reporting, basic ethical standards still apply.

- Except in the case of chart reviews or database research, potential subjects must be provided enough information to be able to choose whether or not to participate. The information would typically include the voluntariness of their participation, the purpose of the research, the nature of the subject's involvement, time commitments, and contact information for the investigator.
- Research data must be handled and stored securely, in compliance with university policy.
- Access to research data must be limited to study team members and other authorized personnel.
- All members of the research team must be current on human subjects training and must have a current conflict of interest disclosure.

Please note that the researcher CANNOT himself or herself decide if the research project is exempt. The application for exemption still must be made via Infonetica and the ERC chair will decide if the project is exempt or not.

Each exempt category is described below. The regulatory text is in blue, and clarifications follow.

EXEMPT CATEGORY 1

Research, conducted in established or commonly accepted educational settings, that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

Most educational research on regular and special educational instructional strategies, and research on the effectiveness of, or comparison among, instructional techniques, curricula, or classroom management methods may be exempt under this category.

There must not be any impact of subject's opportunity to learn or any negative impact if the research involves an evaluation of the instructors. If the research involves significant

time and attention away from the delivery of regular curriculum or withholding of standard educational content, this exemption would not apply. Also, there must be protection against negative impact on employment if instructors are being evaluated. Research involving randomization to a unproven educational technique, or research conducted by supervisors involved in employment decisions may not be approvable under this exemption.

Applicability to vulnerable populations:

- Pregnant women may be included in this type of research.
- Research that targets a prisoner population is not eligible for this exemption. The exemption is allowable if the research is aimed at a broader population and only incidentally includes prisoners.
- Research involving children is eligible for this exemption.

EXEMPT CATEGORY 2

Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met:

(i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

(ii) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

(iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an ERC conducts a limited ERC review.

This category involves interactions (verbal and written responses) and data collection only. The data collection can include audio or video recordings. Research involving "interventions" would not be approvable under this category. Interventions include manipulation of the environment or physical procedures to collection information, such as a cheek swab.

Applicability to vulnerable populations

- Pregnant women may be included in this type of research.
- Research that targets a prisoner population is not eligible for this exemption. The exemption is allowable if the research is aimed at a broader population and only incidentally includes prisoners.
- Research involving children is eligible for this exemption only when it related to educational tests or observations in which the investigators don't participate in the

activities being observed. Additionally, children are not eligible for this exemption if the project requires limited ERC review.

EXEMPT CATEGORY 3

Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

(i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

(ii) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

(iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an ERC conducts a limited ERC review.

For the purpose of this provision, benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.

If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

Applicability to vulnerable populations:

- Pregnant women who are adults may be included in this type of research
- Research that targets a prisoner population is not eligible for this exemption.
    - Research that could include children is not eligible for this exemption. The exemption is allowable if the research is aimed at a broader population and only incidentally includes prisoners.
- Research involving decisionally-impaired persons is not eligible for this exemption.

EXEMPT CATEGORY 4

Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

(i) The identifiable private information or identifiable biospecimens are publicly available;

(ii) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;

(iii) The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is for health care operations or for public health activities and purposes

- The requirement that all study data be existing at the time of ERC submission has been eliminated. Data under this exemption may be both retrospective and prospective. • The requirement that the study involves data only has been eliminated. The research may also involve the use of specimens.

It is important to note the Exemption Category 4 only applies to the re-use of data and specimens that were or will be collected for non-research purposes or from research studies other than the proposed research study. The research materials typically will be publicly available materials, medical records or existing repositories of clinical specimens. No contact between investigator and subject is allowed. If an investigator wants to collect information/specimens directly from research subjects, then another approval path would be required.

Applicability to vulnerable populations:

- Data/specimens from pregnant women would be allowed
- Data/specimens from prisoners could be allowed as long as the research wasn't designed to recruit prisoners and prisoners were only incidental subjects of the research.
- Data/specimens from children would be allowed
- Data/specimens from persons with decisional impairment would be allowed

EXEMPT CATEGORY 5

Research and demonstration projects that are conducted or supported by a governmental department or agency, and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs. Such projects include, but are not limited to, internal studies by governmental employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Each governmental department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible

website or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.

EXEMPT CATEGORY 6

Secondary research for which broad consent is required: Research involving the use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met:

(i) Broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained

(ii) Documentation of informed consent or waiver of documentation of consent was obtained

(iii) An ERC conducts a limited ERC review and makes the determination that the research to be conducted is within the scope of the broad consent

(iv) The investigator does not include returning individual research results to subjects as part of the study plan. This provision does not prevent an investigator from any legal requirements to return individual research results.

Research with vulnerable populations may be approvable with this exemption:

- Pregnant women may be included in this type of research.
- Research that targets a prisoner population is not eligible for this exemption. The exemption is allowable if the research is aimed at a broader population and only incidentally includes prisoners.
- Research involving children is eligible for this exemption.

Acknowledgement: ERC FHS Pakistan gratefully acknowledges the permission of University of Kansas Medical Center to use their following document as a resource used to draft this AKU FHS ERC document. http://www.kumc.edu/Documents/hrpp/Topical%20Guidance/KUMC%20Guidance%20Document%20for%20Exempt%20Research%202018%20Common%20Rule%20Changes.pdf

V. July 17, 2018

Appendix No. 4: ERC Consent Form

Sample Informed Consent

This is a generic sample form to help you address most situations. Please adapt as appropriate for your research protocol and institution. *Pending rulemaking for classified human subject research will require additional elements of consent.*

Project Information	
Project Title:	Project Number:
ERC Ref No:	Sponsor:
Principal Investigator:	Organization:
Location:	Phone:
Other Investigators:	Organization:
Location	Phone:

Consent document must be clearly written and understandable to subjects. The language must be non-technical (comparable to the language in a newspapers or general circulation magazine), and scientific, technical or medical terms must be plainly defined.

Informed Consent, whether oral or written, may not include language that appears to waive subjects' legal rights or appears to release the investigators or anyone else from liability for negligence.

It must begin with the introduction of the person seeking consent. For example: "I am Dr [SAK] from Department of _ _ _, Aga Khan University and doing a research on _ _ _."
It must also include some background information on the topic of study. For example:
"Disease X (Malaria) is a common disease in Pakistan, Asia and Africa, caused by a germ (parasite) spread by mosquito. It causes high grade fever. Some patients may have complications and even die. The commonly used drugs are losing their effectiveness and germs are getting resistant to it. A new drug known as [A] is supposed to be effective in treatment of disease (malaria) but there is not enough evidence that it is as good as other drugs used for treatment of disease (malaria)."

It should then state the following:

1. PURPOSE OF THIS RESEARCH STUDY

- Include 3-5 sentences written in nontechnical language. “You are being asked to participate in a research study designed to...”

2. PROCEDURES

- Describe procedures: “You will be asked to do...”
- Identify any procedures that are experimental/investigational/non-therapeutic.
- Define expected duration of subject's participation.
- Indicate type and frequency of monitoring during and after the study.

3. POSSIBLE RISKS OR DISCOMFORT

Note that these include not only physical injury, but also possible psychological, social or economic harm, discomfort, or inconvenience.

- Describe known or possible risks. If unknown, state so.
- Indicate if there are special risks to women of child bearing age; if relevant, state that study may involve risks that are currently unforeseeable, e.g., to developing fetus
- If subject's participation will continue over time, state: “any new information developed during the study that may affect your willingness to continue participation will be communicated to you.”
- If applicable, state that a particular treatment or procedure may involve risks that are currently unforeseeable (to the subject, embryo or fetus, for example.)

4. POSSIBLE BENEFITS

- Describe any benefits to the subject that may be reasonably expected. If the research is not of direct benefit to the participant, explain possible benefits to others.

5. FINANCIAL CONSIDERATIONS

- Explain any financial compensation involved or state: “There is no financial compensation for your participation in this research.”
- Describe any additional costs to the subject that might result from participation in this study.
- Please indicate any financial benefits to the subjects including therapeutic or diagnostic costs being covered by the study.

6. AVAILABLE TREATMENT ALTERNATIVES

- If the procedure involves an experimental treatment, indicate whether other non-experimental (conventional) treatments are available and compare the relative risks (if known) of each.

7. AVAILABLE MEDICAL TREATMENT FOR ADVERSE EXPERIENCES

- "This study involves (minimal risk) (greater than minimal risk)." In the event that greater than minimal risk is involved, provide the subject with the following information.
- If you are injured as a direct result of taking part in this research study, emergency medical care will be provided by [name] medical staff or by transporting you to your personal doctor or medical center. Indicate who will pay for this treatment.

8. CONFIDENTIALITY

- Describe the extent to which confidentiality of records identifying the subject will be maintained.

  "Your identity in this study will be treated as confidential. The results of the study, including laboratory or any other data, may be published for scientific purposes but will not give your name or include any identifiable references to you."

  "However, any records or data obtained as a result of your participation in this study may be inspected by the sponsor or by AKU ERC members".

  In addition, list steps to protect confidentiality such as codes for identifying data.

9. TERMINATION OF RESEARCH STUDY

You are free to choose whether or not to participate in this study. There will be no penalty or loss of benefits to which you are otherwise entitled if you choose not to participate. You will be provided with any significant new findings developed during the course of this study that may relate to or influence your willingness to continue participation. In the event you decide to discontinue your participation in the study,

- These are the potential consequences that may result: (list)
- Please notify (name, telephone no., etc.) of your decision or follow this procedure (describe), so that your participation can be orderly terminated.

In addition, your participation in the study may be terminated by the investigator without your consent under the following circumstances. (Describe) It may be necessary for the sponsor of the study to terminate the study without prior notice to, or consent of, the participants in the event that (Describe circumstances, such as loss of funding.)

10. AVAILABLE SOURCES OF INFORMATION

- Any further questions you have about this study will be answered by the Principal Investigator:
  Name:
  Phone Number:
- Any questions you may have about your rights as a research subject will be answered by:
  Name:
  Phone Number:
- In case of a research-related emergency, call:
  Day Emergency Number:
  Night Emergency Number:

11. AUTHORIZATION

I have read and understand this consent form, and I volunteer to participate in this research study. I understand that I will receive a copy of this form. I voluntarily choose to participate, but I understand that my consent does not take away any legal rights in the case of negligence or other legal fault of anyone who is involved in this study.

Name of participant (Printed or Typed):
Date:

Signature of participant:
Date:

Signature of Principal Investigator:
Date:

Name and Signature of person obtaining consent:
Date:

Appendix No. 5: CTU Consent Form

Appendix 1: Sample Informed Assent Form Template for Children

This informed assent form is for children between the ages of 12 - 16 who attend clinic4 and who we are inviting to participate in malaria vaccine research.

Name of Principal Investigator: Dr XXX

Name of Organization: Aga Khan University

Name of Sponsor: Pharma B

Name of Proposal and version: MP4– version 1

This Informed Consent Form has three parts:

• Information Sheet (to share information about the research with you)

• Certificate of parents' consent (for signatures if you agree to allow your child to take part)

• Certificate of Consent (for signatures if you agree to take part)

You will be given a copy of the full Informed Consent Form

PART I: Information Sheet

Introduction

My name is Dr XXX and my job is to research and test vaccines to see which work best to stop malaria before it makes someone sick .We want to know if this new vaccine will stop children from getting sick and we think this research could help us about that.

I am going to give you information and invite you to be part of a research study. You can choose whether or not you want to participate. We have discussed this research with your parent(s)/guardian and they know that we are also asking you for your agreement. If you are going to participate in the research, your parent(s)/guardian also have to agree. But if you do not wish to take part in the research, you do not have to, even if your parents have agreed.

You may discuss anything in this form with your parents or friends or anyone else you feel comfortable talking to. You can decide whether to participate or not after you have talked it over. You do not have to decide immediately.

There may be some words you don't understand or things that you want me to explain more about because you are interested or concerned. Please ask me to stop at anytime and I will take time to explain.

Appendix 6: Checklist for ERC Reviewers

Ethical basis for decision-making in research ethics committees.

ERC template of questions- For reviewers

Approval or disapproval is based on

- the ethical acceptability of the research, including its social value and scientific validity,
- an acceptable ratio of potential benefits to risks of
- harm, the minimization of risks,
- adequate informed consent procedures (including cultural appropriateness and mechanisms to ensure voluntariness),
- measures to ensure protection of vulnerable populations,
- fair procedures for selection of participants, and
- attention to the impact of research on the communities from which participants will be drawn, both during the research and after it is complete.
- The review take into account any prior scientific c reviews and applicable laws.

The ERC bases its decisions about research that it reviews on a coherent and consistent application of the ethical principles articulated in international guidance documents and human rights instruments, as well as any national laws or policies consistent with those principles. The ERC makes clear the specific ethical guidelines on which it relies in making decisions and makes them readily available to researchers and the public. When an ERC develops reliance agreements for review of research under its jurisdiction by another ERC, it is the responsibility of the delegating ERC to assure that the same ethical principles serve as the basis of the other ERC's decision-making.

CHECKLIST FOR ETHICAL SOUNDNESS

	YES	NO	N/A
Protocol			
Have any risks to participating in the research been identified and does the protocol state how these will be minimized?			
If the research involves treatment /new drugs/technical equipment/technique or vaccines- is it justified			
If an intervention study, is a plan for adverse event reporting included in the protocol? If yes the provision of managing and payment mentioned			
Does the protocol include a discussion of ethical issues?			
Have consent forms been prepared? Are these included? Is translated consent form included			
Have assent forms been prepared for children aged 12 - 18 years? Are these included?			
Risks and benefits			
Have individual risk vs. the potential benefits from the study been adequately addressed?			
Does the protocol describe whether and how communities from which the participants are to be drawn are likely to benefit from the research?			
Is the research outcome also likely to benefit communities beyond the research population?			
Study population			
Is a vulnerable population being studied (i.e. any of the following - pregnant women, children, adolescents, elderly people, people with mental or behavioral disorders, prisoners, refugees, those who cannot give consent (unconscious), others)?			
If a vulnerable population is being studied, is the justification adequate?			
Have adequate provisions been made to ensure that the vulnerable population is not being exploited?			
Autonomy/Incentives/Coercion			
Does the design of the study include inducements (financial or free medical care, etc) to participate in the research?			
If yes, is the rationale described in the protocol?			
Are the research participants free not to participate or to leave the research at any time without penalty?/ voluntary participation			
Privacy/Confidentiality			
Does the study outline the procedures for the protection of the privacy?			
Are there mechanisms to ensure the confidentiality of the data?			
Monitoring safety/protection			

When appropriate, do provisions exist for counseling research participants prior to, during and after the research? Shift to scientific portion			
Are there issues that may affect the safety of the researchers involved in the study? How are these being addressed?			
Process for gaining informed consent			
Is the process, through which informed consent will be obtained, described?			
Where written consent from participants is not possible, have you explained the reasons for this and how the agreement of participants will be recorded?			
Is this a cluster randomized controlled trial?			
If so, has the process of taking consent for clusters to be included in the trial described?			
If this is not possible, is information provided to all communities participating in the trial?			
Is the process of taking consent from individuals in the clusters before they participate in any study procedures or data collection described? *			

ETHICAL CONSIDERATION FOR REVIEWING INFORMED CONSENT

	YES	**NO**	**N/A**
General format and content of the ICF			
Does the informed consent form make it clear that the participant is being asked to participate in research?			
Is the information sheet free of technical terms & written in lay-person's language, easily understandable & appropriate to the educational level of the community concerned?			
Does it describe why the study is being done & why the individual is asked to participate?			
Does it provide participants with a full description of the nature, sequence and frequency of the procedures to be carried out, including the duration of the study?			
Does it explain the nature and likelihood of anticipated discomfort or adverse effects (including psychological and social risks) if any, and what has been done to minimize these? Does it state the action to be taken should these occur?			
Does it outline the procedures to protect the confidentiality of data, and if confidentiality is not possible due to the research design, has this been conveyed to all relevant persons?			
Does it inform the research participants that their participation is voluntary and they are free to decide whether or not to participate, or to withdraw at any time and for any reason without further penalty either personal or professional or affecting their future medical care?			
Does it describe the nature of any compensation or reimbursement to be provided (in terms of time, travel, man-days lost from work, etc)?			
Does it outline how participants will be informed of the progress & outcome of the research?			

Does it provide the name and contact information of a person who can provide more information about the research project at any time?			
Has a provision been made for subjects incapable of reading and signing the written consent form?			
Questionnaires			
State that the participant is free to not answer any question?			
Where applicable, make it clear that the interviews (in-depth or focus group discussions) are likely to be audio or video taped?			
Where applicable, mention how and for how long are the tapes going to be stored?			
Human biologic materials (tissues, cells fluids, genetic material or genetic information)			
If human biologic materials are to be collected, does the information sheet and consent form describe in simple language the nature, number and volume of the samples to be obtained and the procedures to be used to obtain them?			
Indicate if the procedures for obtaining these samples are routine or experimental and if routine, are more invasive than usual?			
Describe the use to which the samples will be put both in the study & in the longer term?			
Does it include a provision for the subject to decide on the use of left over specimens in future research of a restricted, specified or unspecified nature?			
State for how long the specimens can be kept and how they will finally be destroyed?			
Mention that genetic testing/genomic analysis will be carried out on the human biologic materials, where applicable?			
Participant Recruitment Material (If you plan to use participant recruitment material (e.g. advertisements, notices, media articles, transcripts of radio messages) please review the material in light of the following questions)			
Is the information provided in both English and in the local language?			
Does the material make promises that may be inappropriate in the research setting (e.g. provide undue incentives, emphasize remuneration)?			

Appendix 7: Ongoing Research Monitoring Form (Observational Studies)

THE AGA KHAN UNIVERSITY
RESEARCH OFFICE
AUDIT CHECKLIST FOR HUMAN SUBJECTS RESEARCH
OBSERVATIONAL STUDIES

Study Title:	
Principal Investigator:	
Co-Investigator(s):	
Department:	
Date of ERC Approval:	
ERC number:	
Date of Commencement	
Date of Completion	

Please mark (✓) the appropriate Box. NA = Not Applicable

A.	REGULATORY APPROVALS	Yes	No	NA	Comment, if any
1.	Has ERC approval been obtained?	☐	☐	☐	
2.	Has ERC approval been obtained for any amendments in the protocol?	☐	☐	☐	
3.	Has ERC renewal been obtained?	☐	☐	☐	
4.	Has ERC approval ever got lapsed?	☐	☐	☐	
5.	If yes, did any recruitment take place during the lapsed period?	☐	☐	☐	
6.	Has the progress report been submitted to the ERC in a timely manner?	☐	☐	☐	
7.	Has the study completion report been submitted to ERC?	☐	☐	☐	

8.	Is a complete record of correspondence with ERC available?	☐	☐	☐	
9.	In case of any protocol deviation, have the ERC and sponsor been informed?	☐	☐	☐	
10.	Has an NBC approval been obtained in case of a multicenter/ multi-province study?	☐	☐	☐	

B.	INVESTIGATOR/ STAFF QUALIFICATION AND DOCUMENTATION	Yes	No	NA	Comment, if any
11.	Are the PI(s), Co-PI(s), and other research staff trained in research methodology, ethics, and GCP?	☐	☐	☐	
12.	Is an updated CV (signed and dated within 2 yrs.) of the PI available in the master file?	☐	☐	☐	
13.	Is Delegation of Authority (Responsibility) Log maintained?	☐	☐	☐	
14.	Is there evidence of study team training regarding study protocol?	☐	☐	☐	
15.	Does the PI maintain a complete study master file containing protocol, regulatory approvals, contracts and agreements, consent forms and questionnaire?	☐	☐	☐	
C.	**INVESTIGATORS'/ INSTITUTION'S RESPONSIBILITIES**	**Yes**	**No**	**NA**	**Comment, if any**
	Is there evidence of commitment to each of the following either in the study protocol or sponsor contract:				
16.	Insurance to cover adverse events and harm	☐	☐	☐	
17.	Reporting of adverse events using hospital's incident reporting system	☐	☐	☐	
18.	Storage, ordering, dispensing and administration of medications under study follow hospital's medication system standards	☐	☐	☐	

19.	Medical equipment used in study is handled as per hospital's medical equipment program standards	☐	☐	☐	
20.	Hazardous material used in study is handled as per hospital's HAZMAT program standards	☐	☐	☐	
21.	Protection of the privacy and confidentiality of data	☐	☐	☐	
22.	Prohibition of incentives compromising research integrity	☐	☐	☐	

D.	PARTICIPANT INFORMATION SHEET AND CONSENT FORM	Yes	No	NA	Comment, if any
	Does the consent form(s) include explanation/a statement of each of the following:				
23.	Purpose of the research, expected duration of participation, and procedures to be followed	☐	☐	☐	
24.	Expected benefits, potential discomforts and risks	☐	☐	☐	
25.	Alternative treatments and procedures that might also be beneficial if applicable	☐	☐	☐	
26.	Extent to which confidentiality of records will be maintained	☐	☐	☐	
27.	Compensation or medical treatment coverage in case if injury occurs	☐	☐	☐	
28.	Participation is voluntary and refusal will not impact care and access	☐	☐	☐	
29.	Whom to contact for answers to pertinent questions about the research and research participants' rights	☐	☐	☐	
30.	Identity of the person taking consent with date and time	☐	☐	☐	
E.	**CONSENT PROCESS**	**Yes**	**No**	**NA**	**Comment, if any**

31.	Is the consent obtained from the subject or his/her legally authorized representative?	☐	☐	☐	
32.	Is the consent form appropriately signed by the subject?	☐	☐	☐	
33.	In case of illiterate or mentally incapacitated, is the impartial witness obtained?	☐	☐	☐	
34.	Is the consent form appropriately signed by the PI or his/her designee?	☐	☐	☐	
35.	Is a copy of consent form provided to the subject?	☐	☐	☐	

F.	CONFIDENTIALITY AND PRIVACY	Yes	No	NA	Comment, if any
36.	Are study data kept in lock and key?	☐	☐	☐	
37.	Are data de-identified using participants' IDs and initials instead of Name, MR numbers or other identifiable information?	☐	☐	☐	
38.	Are electronic data password protected?	☐	☐	☐	
39.	Are only authorized users allowed to access the data?	☐	☐	☐	
G.	**DATA INTEGRITY**	**Yes**	**No**	**NA**	**Comment, if any**
40.	Do the case report forms and source data match?	☐	☐	☐	
41.	Do the electronic data and case report forms match?	☐	☐	☐	
Overall comments					

Name of Reviewer _____ Designation _____ Date _____

Appendix 8: Ongoing Research Monitoring Form (CTU)

AGA KHAN UNIVERSITY

CLINICAL TRIALS UNIT

Clinical Trials Monitoring/Audit Checklist

GENERAL INFORMATION

Protocol Title		
Principal Investigator		
Acronym/ Protocol Number		
Name of Individual Completing Checklist/ Auditor		
Funding Sources/sponsor		
Phase of Clinical Trial	☐ Phase II ☐ Phase III	☐ Phase IV ☐ Other
Study Status	☐ On-going ☐ Recruitment closed, follow-up only	☐ Last patient last visit completed, Data Analysis in process ☐ Completed
Has the PI or Co- investigators declared any direct or indirect conflict of interest in the research? Yes ☐ No ☐ If Yes, please clarify: _____		

Reviewed by,

_____ _____ _____

(SIGNATURE) (PRINT NAME) (DATE)

SECTION A: REGULATORY DOCUMENTATION:

1.	**ERC INITIAL REVIEW**	YES	NO
1.1	Is the initial ERC approval letter on file? Date of approval:_____	☐	☐
1.2	Version of initial approved protocol.	_____	
1.3	Version of initial approved informed consent form.	_____	
1.4	Does the consent form(s) include explanation/a statement of each of the following:	☐	☐
a)	Trial involves research	☐	☐
b)	Purpose of the trial	☐	☐
c)	Trial treatment (s) and random assignment to Treatment if it is RCT	☐	☐
d)	Trial procedures to be followed, including invasive procedures including invasive procedures	☐	☐
e)	Subject's responsibilities	☐	☐
f)	Experimental aspects of the trial	☐	☐
g)	Description of foreseeable risks or discomforts	☐	☐
h)	Expected benefits	☐	☐
i)	Alternative procedure(s)/ treatment(s) available	☐	☐
j)	Subject compensation in trial-related injury	☐	☐

k)	Anticipated prorated payment, if any, to subject	☐	☐
l)	Anticipated expenses, if any, to subject	☐	☐
m)	Participation in the trial is voluntary and that may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the subject is otherwise entitled	☐	☐
n)	Direct access to subject's original medical records without violating confidentiality	☐	☐
o)	Records identifying the subject will be kept confidential	☐	☐
p)	Will be updated if new information becomes available	☐	☐
q)	Person(s) to contact for further information and in the event of trial-related injury	☐	☐
r)	Circumstances for trial termination	☐	☐
s)	Duration of participation in trial	☐	☐
t)	Number of subjects involved in the trial	☐	☐
u)	Impartial witness for illiterate or mentally incapacitated subjects	☐	☐
v)	Subject thumb impression in case of Impartial witness	☐	☐
2.	**CONTINUING REVIEW**	YES	NO
2.1	Has this study undergone Continuing Review? (If no, go to Question 3)	☐	☐

2.2	Expiry Date	Project Progress Report Date	Renewal Date		
	_____	_____	_____		
	_____	_____	_____		
	_____	_____	_____		
2.3	Was each Project Progress Report submitted on time?			☐	☐
2.4	Was there any lapse between expiry date and continuing review approval date? (If no, go to 3) If yes, state reason:_____			☐	☐
2.5	Was any subject enrolled during this lapse period? If yes, was a protocol violation submitted to the ERC?			☐ ☐	☐ ☐
2.6	Were any study procedures done during the lapse period? If yes, were they approved by the ERC?			☐ ☐	☐ ☐
3	**PROTOCOL/CONSENT FORM AMENDMENT**			YES	NO
3.1	Have there been any amendments to the protocol? (If no, go to section 4)			☐	☐
3.2	Do all amendments have ERC's documented approval?			☐	☐
3.3	Has protocol amendments incorporated in consent form as well?			☐	☐

3.4	If yes, has been approved by ERC.		☐	☐
3.5	Version No. / Date of Protocol and Consent form Amendment	Date submitted	Date approved	
	_____	_____	_____	
	_____	_____	_____	
	_____	_____	_____	
4.	**STUDY COMPLETION**		YES	NO
4.1	Has the study been completed? (If no, skip to question 4.2) If yes, has the ERC/ regulatory bodies been informed?		☐ ☐	☐ ☐
4.2	Have there been a premature termination / suspension of the study? If no, skip to Section 5. If yes, please give reason: _____		☐	☐
1.	If there has been a termination / suspension, have the subjects/ institution/ sponsor/ regulatory bodies/ ERC been informed? If no, please give reason: _____		☐	☐

2.	Is there a protocol for follow up of subjects after termination/ suspension? If yes, has this protocol been approved by ERC?	☐ ☐	☐ ☐
5.	**SAEs/ AE REPORTING**		
5.1	All SAEs/AEs reported to the sponsor within timelines as defined in the protocol	☐	☐
	Are SAEs/AEs reported to ERC, OIR (online incident report) and Pharmacy (online ADR if applicable) and CTU Pharmacist according to institutional guidelines?	☐	☐
5.2	AEs/SAEs reported to DRAP(if applicable)	☐	☐
	AEs/SAEs reported to NBC (if applicable)	☐	☐
Please use this space for additional explanation/comments			

SECTION B - OTHER REGULATORY APPROVALS

FOR INVESTIGATIONAL PRODCUT ONLY		YES	NO
1.	Has study been approved by NBC if applicable?	☐	☐

2.	Has the trial medication approved by DRAP if applicable	☐	☐
3.	Has renewal obtained from NBC and DRAP (if applicable i.e., imported or new drug)?	☐	☐
Please use this space for additional explanation/comments			

SECTION C - SUBJECT RECRUITMENT PROCEDURES:

1.	**SUBJECTS**	
1.1	No of subjects targeted as approved by ERC:	_____
	No of subjects screened:	_____
	No of subjects enrolled:	_____
	No of subjects randomized(If applicable)	_____
	No of subjects completed:	_____
	No of subjects discontinued :	_____
	No of lost to follow up /drop out	/
2.	**RECRUITMENT**	
2.1	How are potential subjects identified? (check all that apply)	

	☐ Investigators: ☐ Medical record review ☐ Database ☐ Clinical practice ☐ Referrals by treating physician or other ☐ Subject response to recruitment materials ☐ Other, specify : _____		
2.2	Will recruitment materials be used in this study? If no, go to section D	Yes ☐	No ☐
2.4	If recruitment materials are used, specify: (check all that apply) ☐ Advertisements ☐ Flyers ☐ Web posting ☐ Letter ☐ Pre-Screening form ☐ No recruitment materials used; go to Item 4 ☐ Other, specify:_____		
2.5	Are recruitment methods and material approved by ERC?	☐	☐
	Are all approved recruitment materials on file?	☐	☐
		☐	☐
	Please use this space for additional explanation/comments		

SECTION D – DRUG/ DEVICE ACCOUNTABILITY:

(If the study does not involve drug/ device check here ☐ and go to Section E)

Collect this information from CTU pharmacy		YES	NO
1.	Is a drug/device dispensing and accountability log being maintained?	☐	☐
2.	Is there proper documentation on drug storage? (Temperature, accessibility by team members?)	☐	☐
3.	Is there proper documentation on the receipt/ return/ destruction of drug/ device?	☐	☐
Please use this space for additional explanation/comments			

SECTION E – GENETIC RESEARCH:

(If the study does not involve genetic research check here ☐ and go to Section F)

		YES	NO
1.	Are subject identifiers maintained?	☐	☐
1.1	If yes, are identifiers stored and maintained in a secure location with limited access?	☐	☐
2.	Are samples coded?	☐	☐

3.	Is there any secondary use of samples?	☐	☐
3.1	If yes, is there ERC approval for these uses?	☐	☐
4.	Are there procedures in place to remove samples?	☐	☐
4.1	If yes, are these procedures described in the ERC approved consent form?	☐	☐
5	Are samples being sent to 3rd parties?	☐	☐
5.1	If yes, are these samples de-identified?	☐	☐
6	Are there provisions in place for dealing with sample/storage failure?	☐	☐
Please use this space for additional explanation/comments			

SECTION F – BIOLOGICAL SAMPLES:

(If the study does not involve collection of biological samples check here ☐ and go to Section G)

		YES	NO
1.	Are samples collection methods in compliance with protocol?	☐	☐
2	Are samples being stored?	☐	☐

	2.1 Is the storage area secure with access control?	☐	☐
	2.2 Are samples stored at the correct temperature?	☐	☐
	2.3. If refrigeration is required, is a temperature log maintained?	☐	☐
3.	If samples are being shipped- are shipping records on file?	☐	☐
4.	If protocol states that samples will be destroyed after study, are destruction records being maintained?	☐	☐
5.	If sample are shipped out of the study site then MTA has maintained?	☐	☐
Please use this space for additional explanation/comments			

SECTION G – DATABASE:

(If the study does not involve creation of a database check here ☐ and go to Section H)

1.	Where electronic data has stored? _____		
		YES	NO
2.	Is there a list of individuals who have access to the database?	☐	☐
3.	Is the database password protected?	☐	☐
4.	Are patient identifiers being stored together with the data? (If yes, measures should be taken to store them separately).	☐	☐

Please use this space for additional explanation/comments

SECTION H - CASE REVIEW:

This section can be completed for subjects randomly selected for verification. Choose the number of at least 10% of the total number of subjects enrolled to date or 2 charts, whichever is greater. Ensure that there is adequate source documentation for all research data.

Subject ID and initials: _____

1	**INFORMED CONSENT FORM (ICF)**	YES	NO
1.	Was correct version of the consent document signed?	☐	☐
2.	Did Subject / Legally Acceptable Representative sign the ICF? Date signed : _____	☐	☐
3.	Did a witness sign the ICF (if applicable)? Date signed : _____	☐	☐
4.	Did the person obtaining consent sign and date the ICF?	☐	☐
5.	Has PI counter signed the consent form?	☐	☐

6.	Did anyone not listed on study responsibility log to consent subjects sign?	☐	☐
7.	Documentation of consent in medical records?	☐	☐
8.	Is there documentation that a copy of the consent was given to the subject?	☐	☐
9.	Indicate location of signed ICF :		

Please use this space for additional explanation/comments

2. SUBJECT SELECTION CRITERIA

		YES	NO
1.	Is there a checklist to assess the eligibility of the subject?	☐	☐
2.	Is the subject appropriately enrolled?	☐	☐
3.	Was any protocol violation detected?	☐	☐
4.	If yes, was the protocol violation reported to ERC?		

Please use this space for additional explanation/comments

3. ADVERSE EVENT (AE) REPORTING

(If there have been no AEs reported for this subject check here □ and go to 4)

		YES	***NO***
1.	Are all AE/SAEs reported to ERC?	□	□
2.	Are the reports, correspondences in Trial Master File (TMF)?	□	□

Please use this space for additional explanation/comments

4. DRUG/DEVICE DISPENSING ACCOUNTABILITY

(If this is not a drug/device study, check here □ and go to section 5)

		YES	NO
1.	Are there discrepancies in the dispensing of drug/device for this subject?	□	□
2.	Are drug/ device dispensed by the authorized personnel?	□	□

Please use this space for additional explanation/comments

5. DATA COLLECTION & SOURCE DOCUMENTS

		YES	NO
1.	Is source documentation available to support data entry?	☐	☐
2.	Is data entry/ cross outs performed according to GCP guidelines?	☐	☐
3.	Are there discrepancies noted during source document verification? If yes specify :	☐	☐

Please use this space for additional explanation/comments

Trial Master File checklist

1. Is there a Trial Master File? Yes □ No □

2. If no, state where the essential documents are stored in the remarks column.

Action items

Monitor's Name	**Signature**	**Date**
Investigator's/SC's Name	**Signature**	**Date**

SITE INFORMATION	
Study Title:	**Study number/ acronym:**
Name of Clinical Site:	**Site Number:**
Principal Investigator (PI):	**Study Coordinator (SC):**
Other Investigators:	**Sponsor:**

Section	Study documents	Version	Y	N	NA	Comments
1.	**Protocol**					
1.1.	Protocol and signed protocol signature page					
1.2.	Protocol Amendments and signed protocol amendments signature page					
1.3.	Investigator brochure (final version)					
1.4.	Manual of operation					
1.5.	Any other protocol associated document/ material					
2.	**Contracts & Agreements/ Finance/ Indemnity**					
2.1.	Signed confidentiality agreement					
2.2.	Signed financial disclosure form					
2.3.	Signed participating center agreement(clinical trial agreement)					
2.4.	Contract / Financial Agreement					
2.5.	Contract / Contract Addendums with sub-contractors / third parties					
2.6.	Banking detail forms					
2.7.	Payment information and records					
2.8.	Certificate of Insurance/indemnity.					
2.9.	Acknowledgement of receipt					
2.10.	Funding / Grant application(s) and approval(s)					
2.11.	Reports / communication with Funding / Grant Provider					
2.12.	other i.e. interdepartmental contracts, MOUs etc.					
3.	**Ethics Review committee (ERC)**					
3.1.	Application to Ethics Committee for trial approval					
3.2.	Correspondence & Approval from Ethics Committee					
3.3.	Interim/Annual Reports (as required)					
3.4.	ERC notification of Trial Termination					
3.5.	Study close out report					
3.6.	ERC members composition list					
4.	**Other Regulatory documents**					
4.1.	National Bioethics Committee application correspondences and approvals					
4.2.	DRAP application, correspondences and approvals					
4.3.	Other relevant regulatory documentation “Data Safety Monitoring Board Correspondence” if available					
5.	**Registration of Clinical Trial**					

5.1.	Application for registration					
5.2.	Response notification					
5.3.	Unique Study identifier					
6.	**Investigator/Staff Qualification and documentation**					
6.1.	Curriculum Vitae (Signed/ dated within 2 year)					
6.2.	ICH-GCP or other site training certificate s and medical licenses etc.					
6.3.	Authorized Signature Sheet					
6.4.	Personnel & Delegation of Duties Log					
6.5.	Meeting agendas and minutes					
6.6.	Meeting attendance sheet					
6.7.	Presentation material					
7.	**Monitoring**					
7.1.	Site monitoring visit log					
7.2.	Site feasibility Documentation					
7.3.	Pre Trial Monitoring Report, site confirmation and follow up report					
7.4.	Initiation Visit Report & Confirmation & Follow- Up letters					
7.5.	Monitoring & Close out Visit/s Confirmation and Follow up Letters					
7.6.	Protocol deviation forms					
7.7.	Data correction and query resolution correspondence					
8.	**Subject Information Sheet and Consent Forms**					
8.1.	Subject Identification List (Maintained only at the site)					
8.2.	Subject screening log					
8.3.	Subject enrollment log					
8.4.	Subject visit log					
8.5.	Master Randomization list					
8.6.	ERC approved versions of consent forms and participant information sheets (blank forms both in Urdu and English)					
8.7.	ERC approved versions of assent forms and participant information sheets (blank forms both in Urdu and English) if applicable					
8.8.	Blank approved Diary cards					
8.9.	*Signed informed consent forms.(if filed elsewhere, please provide memo stating the location of the signed forms) 1 copy should be given to the subject					
9.	**Laboratory**					
9.1.	Local or central Laboratory Reference Ranges					
9.2.	Local or central Laboratory Accreditation Documents					
9.3.	Biological specimen sampling, labeling, storing and shipping procedure					
9.4.	Biological specimen log					
9.5.	Shipping records (if central lab is used)					
9.6.	Specimen transfer logs (if local lab is used)					

9.7.	Temperature Logs/Sample Storage Condition Log					
9.8.	Laboratory correspondences					
9.9.	Specimen labels					
9.10.	Laboratory Manual					
9.11.	Relevant lab SOPs					
10.	**Pharmacy**					
10.1.	Import/Export License Application for investigational product					
10.2.	Temperature monitoring logs (including temperature deviation reports), if applicable					
10.3.	Documentation of drug /device receipt (shipping records)					
10.4.	Documentation of drug/ device quarantine / return / destruction					
10.5.	Sealed unblinding envelopes (or location)					
10.6.	Individual treatment codes (or location)					
10.7.	Notification of Unblinding					
10.8.	Retrieval of Code-Break Envelopes					
10.9.	Drug Accountability logs					
10.10.	Pharmacy Correspondence					
10.11.	Pharmacy SOPs relevant to the study i.e. randomization, code breaking, investigational product management, Instructions for handling of IMP etc.					
11.	**Safety Reporting**					
11.1.	AEs/SAEs reports to Sponsor					
11.2.	Pregnancy reporting					
11.3.	Correspondences with Ethics Committee regarding AEs/SAEs & Safety Reports					
11.4.	ERC acknowledgments					
12.	**Study Materials**					
12.1.	Inclusion/exclusion Pocket cards (sample)					
12.2.	Inclusion poster (sample)					
12.3.	Patient File/ CRF (sample)					
12.4.	Sample specimen/ drug labels					
12.5.	Recruitment materials i.e., flyers, advertisement etc.					
13.	**Correspondences**					
13.1.	General Correspondences					
14.	**Data management**					
14.1.	CRF/ eCRF entry guidelines					
14.2.	*Completed CRFs (May include but are not limited to documentation, subject diaries, questionnaires, laboratory reports etc.). Mention in comments if kept somewhere else.					
14.3.	File notes					
14.4.	Data query resolution Forms					
15.	**Miscellaneous**					

15.1.						
15.2.						

* This could be maintained in individual study subject files.