THE AGA KHAN UNIVERSITY

POLICY FOR ADVERSE EVENT AND SERIOUS ADVERSE EVENT	
Contact Office:	Office of Research & Graduate Studies
Developed by:	Ethics Review Board
Approving Authority:	University Research Council
Approved on:	October 12, 2023
Related Policies/SOPs	This document should be read in conjunction with the University *SOPs regarding Human Subjects Research*

1. SCOPE

This policy is intended for all AKU faculty/staff, including individuals with honorary positions, and students carrying out research at, or on behalf of the University. AKU in this document, means the schools, colleges and hospitals of Aga Khan University operating across all campuses around the globe. The policy guides the researchers to comply with the reporting procedures.

2. RATIONALE

To support the ethical conduct of Clinical Trials, which evaluate new treatments/appliances and underpin the effective and safe progress of medicine:

- The AKU Ethics Review Board (ERB) recommends additional facilitatory measures for inclusion in policy for researchers and Ethics Review Committees (ERCs).

With the provision that any of the stipulations mentioned in this policy do not replace or override the country's laws and regulations or requirements for research.

3. PURPOSE

This policy document contains additional guidelines for the prevention and safety reporting of adverse events and serious adverse events in research.

Qualifier: This document does not address legal processes involved in compensation, or quantum or source of compensation.

4. DEFINITIONS

4.1. Adverse event (AE): An untoward and unfavourable medical occurrence in human subject, including any abnormal sign, symptom, or diseases, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research.

4.2. Serious adverse event (SAE): An adverse event or suspected adverse reaction is considered "serious", if it results in any of the following outcomes: death, a life-threatening adverse event, in-patient hospitalisation or prolongation of existing hospitalisation, a persistent and significant incapacity or substantial disruption of the ability to conduct normal life function, or a congenital anomaly/birth defect of a research participant or foetus of a research participant.

4.3. Suspected Unexpected Serious Adverse Reaction (SUSAR): Any fatal and life-threatening event or reaction due to medicines administered in a clinical trial that are unexpected and serious.

4.4. Data and Safety Monitoring Board (DSMB): An entity responsible for assessing at intervals the progress of a clinical trial, the safety data, and the critical efficacy endpoints, and to recommend to the sponsor whether to continue, modify, or stop a trial.

5. RECOMMENDATIONS FOR RESEARCHERS AND ERC MEMBERS

This document reinforces the existing foundation of Good Clinical Practice in research at AKU, which is assisted by the Clinical Trials Units, the ERC and ERB checkpoints, and principal investigator(s) and ERB-based monitoring and evaluation systems. The purpose is to provide additional facilitatory frameworks for the safe practice of clinical trials, assist principal investigator (PI) and research teams, protect research participants, and guide ERCs.

5.1. Consent

An adequate understanding of the project by the research subject prior to signing the consent should be assured and may require that:

5.1.1. Other than PI/busy clinician/nurse, the consent should be taken by trained persons and by individuals.

5.1.2. A shorter version of the consent form be available for review and reflection by the research participant at home especially when the consent form is long and complex.

5.2. Recruitment of research subjects

5.2.1. Prior approval of ERC is required before any flyer/advertisement is used for recruitment.

5.2.2. Special care must be exercised to exclude persons at potential risk for the specific clinical trial, and permission should be sought where necessary and possible, for access to personal medical hospital records.

5.3. Data Safety Management Board (DSMB)

5.3.1. Until such time as a generic AKU DSMB is constituted, each proposal should state the composition of a research project (RP) DSMB, budgeted from the research funds, ensuring their training and availability and appropriate compensation as a team member.

5.3.2. The list of members (with qualifications and affiliation) of the sponsor's DSMB formed by the sponsor should be shared by the PI.

5.4. Reporting of SAEs

5.4.1. The PI should report SAEs to the ERC, sponsor, and DSMB within 24 hours of occurrence.

5.4.2. The sponsor should report SAEs to the AKU PI as they occur (or reported), in any country or entity as soon as possible.

5.4.3. The sponsor should periodically provide summary data that gives an indication of the proportion of research participants affected by the various SAEs.

5.4.4. Quantum of funds available to the PI from the sponsor, such as would be immediately available locally, to address SAE and SUSAR to be clearly indicated in the research budget/agreement.

5.5. Detection and management of SAEs

5.5.1. PIs will identify the team member (a medical professional) who will be responsible for directing the affected research participant to an appropriate care facility.

5.5.2. PIs will specifically train their team in the detection of s; and inform all members of the mode of contacting the Medical Professional on the team.

5.5.3. All SAEs will be reported within 24 hours to ERC.

5.5.3.1. Report to ERC IMMEDIATELY, if death of participant occurs.

5.5.4. A summary report of all SAE/AE will be sent quarterly to ERC.

5.6. Stop points!

5.6.1. The PI and sponsor should ensure that **"Stop points"** are predefined for each project, are clearly stated, and known to all team members.

5.6.2. The ERC/ERB has the right to halt and review trials if evidence indicates the need to do so, irrespective of whether stop points have been listed.

5.7. Psychosocial Side Effects

5.7.1. ERCs and PIs should consider the potential for harmful psychosocial side effects and physical and physiological harm. These should also be evaluated before declaring the SAEs as unrelated.

5.7.2. While conducting research with vulnerable populations, ERC should request the modification of the proposal from the PI (and by implication, by the sponsor), to comply with the ethics guidelines applicable to vulnerable populations. PIs should not resubmit a proposal to ERC without an agreement to the appropriate (explicit) modification by the sponsor/funding agency or explain why such recommendations of the ERC to the PI, regarding modification of the proposal are inappropriate.

5.8. ERC's responsibility for receiving SAE notifications

5.8.1. The ERC should study the report from the PI for each reported SAE, to note whether;

5.8.1.1. there is any protocol violation

5.8.1.2. the PI's/sponsor's evaluation indicates that the SAE can be attributed to the trial intervention

5.8.1.3. there is insufficient evidence to determine causality

5.8.1.4. the SAE brings to light a hitherto undiscovered medical condition

5.8.2. In case of the death of a participant, the PI should alert the ERC secretariat via email, in addition to the submission on ERC's online application portal. The secretariat will inform the chair of the respective ERC by email alert about the submission of this report.

5.8.3. The ERC may recommend an unmasking of blinding to the PI; but should use this judiciously, as every unmasking reduces the population size and strength of the results on which the value of the intervention will be assessed.

5.8.4. Mechanism for stopping a trial:

5.8.4.1. the ERC will check the 'stop points' listed in the proposal; and if the trial is being stopped in situations where the criterion used for stopping is not mentioned in the proposal,

5.8.4.1.1. the PI should be given an urgent opportunity to express his/her view.

5.8.4.1.2. the ERC will obtain further advice from ERB, which may constitute an independent AKU-DSMB, including ethics experts, to evaluate the situation and advise on stopping the trial, with immediate effect.

6. ROLE OF THE ERB

The ERB will conduct independent random six-monthly audits appointing an independent committee to review projects and take appropriate action.

References:

1. Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events: OHRP Guidance (2007): https://www.hhs.gov/ohrp/regulations-and-policy/guidance/reviewing-unanticipated-problems/index.html#Q2

2. US Food & Drug Administration Guidance Document (March 2018) - E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1): https://www.fda.gov/regulatory-information/search-fda-guidance-documents/e6r2-good-clinical-practice-integrated-addendum-ich-e6r1