بسم الله الرحمن الرحيم

Kingdom of Saudi Arabia
Ministry of National Guard
Health Affairs

المملكة العربية السعودية
وزارة الحرس الوطني
الشؤون الصحية

APP

MINISTRY OF NATIONAL GUARD - HEALTH AFFAIRS
ADMINISTRATIVE POLICY AND PROCEDURES

NUMBER	:	**1426-02**
TITLE	:	**INSTITUTIONAL REVIEW OF RESEARCHES BY IRB**
ORIGINATING DEPT.	:	**KING ABDULLAH INTERNATIONAL MEDICAL RESEARCH CENTER (KAIMRC) (419801)**
ORIGINAL DATE	:	**APRIL 2005**
REVISED DATE	:	**MARCH 2019**

1. PURPOSE

To provide a process for ensuring ethical review of researches involving human subjects to ensure compliance with relevant rules and regulations, protect the rights and health of human subjects used in research investigations.

2. APPLICABILITY

To all staff involved in research with human subjects or social/behavioral research at the Ministry of National Guard - Health Affairs (MNG-HA) and all affiliated facilities.

3. RELATED REFERENCES

3.1 APP 1418-21: Committees Management Process

3.2 APP 1419-05: Research Proposal, Submission, Processing and Approval

3.3 APP 1419-08: Patient Informed Consent

3.4 APP 1423-05: Sentinel Events and Root Cause Analysis

3.5 APP 1429-19: Conflict of Interest

3.6 APP 1432-04: Appeal Process for Rejected Research Proposal or Suspended Ongoing Research Study

3.7 APP 1432-20: Monitoring Research Studies

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3.8 APP 1433-37: Conducting Research Studies

3.9 APP 1435-08: Safety Reporting System (SRS)

3.10 APP 1435-10: Budget Approval for Intramural Research Grant

3.11 APP 1439-02: Code of Ethics and Professional Conduct

3.12 Islamic General Rules and Guidelines

3.13 National Committee of BioEthics Implementing Regulations of the Law of Ethics of Research on Living Creatures, Second Edition, 2016

3.14 International Conference of Harmonisation (ICH): ICH Harmonised Tripartite Guideline - Guideline for Good Clinical Practice E6(R1)

3.15 The Belmont Report. Ethical Principles and Guidelines for the Protection of Human Subjects of Research published The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, April 1979.

3.16 The Nuremberg Code (1947)

3.17 United Nations Educational, Scientific and Cultural Organization UNESCO: Declaration on Bioethics and Human Rights, October 2005

3.18 WMA Declaration of Helsinki 1964 (revised in 2013). Ethical Principles of Medical Research Involving Human Subjects.

3.19 Saudi Central Board of Accreditation for Healthcare Institutions (CBAHI), National Hospital Standards, 3rd Edition (2015) – PFR.16, PFR.16.1 - PFR.16.5

3.20 Joint Commission International Accreditation Standards for Hospitals, 6th Edition (2017) – HRP.4 ME 1,2,4-6, HRP.1.1 ME 1, HRP.7 ME 1-6, HRP.7.1 ME 2.3 and GLD.12 ME 1-3

4. DEFINITIONS

4.1 **Adverse Event (AE)** refers to any untoward medical occurrence in a patient or unfavorable event detected from the baseline health of a study subject during the course of a clinical research study, which can be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product research studies.

4.1.1 **Serious Adverse Event (SAE)** refers to any untoward medical occurrence that at any dose results in any of the following outcomes: death, a life-threatening event, requires inpatient hospitalization, prolongation of existing hospitalization, a persistent or significant disability/incapacity or a congenital anomaly/birth defect.

4.2 **Clinical Monitoring Unit** refers to a unit under the Research Office of King Abdullah International Medical Research Center (KAIMRC) that is responsible for monitoring all approved clinical trial research studies (sponsored internally and externally) as well as evaluating the compliance of clinical trial studies against national and international regulations.

4.3 **Human Subject or Social/Behavioral Context Under Research** refers to a living individual(s) about whom an investigator will obtain data through intervention or interaction with the individual(s); private identifiable information, such as that obtained from confidential medical records or registries.

4.4 **Institutional Review Board (IRB)** refers to an independent body composed of medical, scientific and non-scientific members, whose responsibility is to ensure protection of the rights, safety and wellbeing of human subjects involved in research studies and acts according to the charges outlined in the committee formation order.

4.5 **International Conference on Harmonization-Good Clinical Practice (ICH-GCP)** refers to an international ethical and scientific quality standard for the design, conduct, performance, monitoring, auditing, recording, analysis and reporting researches/clinical trials involving the participation of human subjects that provides assurance that the date and reported results are credible and accurate and that the rights, integrity and confidentiality of trials subjects are protected.

4.6 **Minimal Risk** refers to the level of risk not greater than ordinarily encountered in daily life or a routine physical/physiological examination or a test.

4.7 **Principal Investigator (PI)** refers to an individual, or group of individuals, who prepares, develops and submits research proposals for review of relevant Research Committee and are responsible for conducting the research study according to the research proposal process, ICH/GCP guidelines and other applicable regulatory authority requirements.

4.7.1 **Sub-Investigator** refers to any individual member of the clinical trial team designated and supervised by the Investigator at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions (e.g., associates, residents, research fellows).

4.8 **Program** refers to the Ministry of National Guard - Health Affairs (MNG-HA) and all its affiliated facilities.

4.9 **Research Studies (internal and external)** refers to all approved research proposals conducted within MNG-HA facilities and sponsored by MNG-HA or by external sponsorship and funding.

4.10 **Research Outcome Evaluation Unit (ROEU)** refers to a unit at KAIMRC that is responsible for monitoring and evaluating the progress and outcome of all approved research studies, excluding clinical trials.

4.11 **Vulnerable Groups** refers to groups of individuals in need of additional protection and it includes but not limited to children, prisoners, pregnant women, fetuses, persons who are either mentally disabled or cognitively impaired and staff or students.

5. POLICY

5.1 All research proposals involving human subjects must be submitted for approval by the Institutional Review Board (IRB) in accordance with APP 1419-05 and satisfactorily meet the established standards of all the following criteria before approval is granted:

5.1.1 Sharia rules or applicable laws and legislations within the Kingdom

5.1.2 Acceptable qualifications of the PI and all Sub-Investigators as human studies investigators

5.1.3 Acceptable risk/anticipated benefit analysis

5.1.4 Adequate and appropriate informed consent document

5.1.5 Scientifically justified selection of subjects

5.1.6 Adequate safeguards for privacy and confidentiality

5.1.7 Sound plan for collection, storage and analysis of data.

5.2 The IRB must review and oversee all researches or studies involving human subjects and/or social/behavioral research to ensure:

5.2.1 It meets ethical principles (**Appendix B**) and complies with local and international laws

5.2.2 To protect the rights and welfare of human participants. Specific responsibilities, composition and members of IRB are outlined in **Appendix C**.

5.3 Research Conduction

5.3.1 The Principal Investigator (PI) is responsible for ensuring that the research activity complies with the approved study protocol. Other responsibilities of PI are outlined in **Appendix D**.

5.3.2 Continuing Review of Ongoing Research Projects

5.3.2.1 IRB must publish a semi-annual tentative summary of the status of all submitted proposals, including status of application (under review, approved, rejected), progress of approved project (including date of next periodic review) and date of completion.

5.3.2.1.1 Monthly report must be submitted to the Executive Director, King Abdullah International Medical Research Center (KAIMRC) based on confidential aspects of information.

5.3.2.2 All on-going approved research projects must be monitored by report presentation or site visit.

5.3.2.2.1 Clinical Monitoring Unit team must ensure that all their activities are according to APP 1432-20 and/or IRB staff can proceed accordingly to carry out their functions.

5.3.2.2.2 Clinical Monitoring Unit report or IRB visit must be discussed with the PI for corrective action and compliance.

5.3.2.3 The PI must submit more than a report per year if requested by the IRB. If the PI fails to submit the report within set period, the IRB can suspend the research project until the report is submitted and must notify the PI thereof.

5.3.2.4 In the situation of requesting an extension of approval period, the PI must submit an Annual Extension Status Report for Studies Involving Human Participants (**Appendix A**) two (2) months before expiration of current approval period.

5.3.2.4.1 All extension requests for research study must be evaluated first by Research Outcome Evaluation Unit (ROEU) prior to IRB final decision.

5.3.2.4.1.1 If the IRB disapproves the extension of the study, the research study must be suspended.

5.3.2.5 Any drafted publication must be submitted to IRB for review prior to scientific publication.

5.3.2.6 Authorship rights and publication conduct must be maintained.

5.3.3 Amendments/Proposed Changes in Research Activity which was Previously Approved by IRB

5.3.3.1 No changes or amendments in the study protocol must be initiated before approval from the IRB, excluding:

5.3.3.1.1 Where necessary for eliminating an immediate hazard to a subject, or

5.3.3.1.2 Minor amendments which include administrative or logistical changes such as:

5.3.3.1.2.1 Addition of procedures that do not significantly increase risk to subjects, considering the original purpose and study design of the approved study

5.3.3.1.2.2 Addition of non-sensitive questions to a survey or interview and procedures

5.3.3.1.2.3 The addition of or revision to minor wording changes in the consent form(s), recruitment materials or measures which do not materially alter the research activities

5.3.3.1.2.4 Change to improve the clarity of statements or to correct typographical errors, provided that such changes do not alter the content or intent of the statement

5.3.3.1.2.5 Changes in the phone numbers of the IRB, PI, Medical Monitor, etc.

5.3.3.1.2.6 Addition of Sub-Invetigator/ research coordinator or any other personnel in the research team and their qualifications excluding PI.

5.3.3.2 Both cases must be reported to IRB as a notice of deviation.

5.3.3.3 If the change represents more than a minimal risk to subjects, it must be reviewed and approved by the IRB before being applied.

5.3.3.4 All major amendments, which include but not limited to the following, must be reported to the IRB and must not be implemented before approval by the IRB:

5.3.3.4.1 Changes in the the research aims or methodology, nature of subject participation, level of risk, proposed benefits, participant population, sample size, or the facilities available to support the safe conduct of research

5.3.3.4.2 Adding procedures that are not eligible for expedited review or addition to the consent form of a description of an unexpected event or serious risk

5.3.3.4.3 Procedures involving increased risk or discomfort or changes that increase the risk to study participants or might adversely affect the willingness of current participants to remain in the study

5.3.3.4.4 Major extensions of the duration of exposure to the test material or intervention

5.3.3.4.5 Major alteration in the human research participation payment.

5.4 Adverse Events (AE)/Serious Adverse Event (SAE)

5.4.1 All SAEs must be reported to the IRB immediately and within twenty-four (24) hours of discovering the event through the electronic Safety Reporting System (SRS) as per APP 1435-08 followed by a detailed report within seven (7) calendar days.

5.4.2 The PI, any member of the research team or any healthcare provider must report any adverse event that occurred at the site.

5.4.3 IRB must act on information or reports received from any source that indicate any adverse event.

5.4.3.1 IRB must investigate if the AE/SAE is related to the clinical research study or not.

5.4.3.2 If SAE related, IRB must participate with Quality and Patient Safety Department in conducting a thorough Root Cause Analysis (RCA) as per APP 1423-05.

5.4.4 The PI is responsible for providing the details of all AEs in the annual status reports.

5.4.5 IRB has the authority to take appropriate actions which include suspension/termination of the study or modifying approval condition as required to ensure patient safety.

5.4.6 Any conflict of interest that occurs during the conduction of the study must be reported to the IRB.

5.4.7 After completing the study and issuing the close-out report, a patient complaint can be received by the IRB office, reviewed for its relation to the study and proper action will be taken for compensation.

5.5 Noncompliance

5.5.1 For any noncompliance that is either reported to the IRB or identified by the IRB, the IRB Chairman must notify the PI in writing, detailing the corrective actions that need to be implemented by the PI. When the noncompliance continue, appropriate action must be determined at a convened meeting. Action by the IRB includes, but not limited to, the following:

5.5.1.1 Suspending the research until the PI is in compliance

5.5.1.1.1 If the research is halted, sponsor must be notified if the research is externally sponsored, and Saudi Food and Drug Authority (SFDA) must be notified if the research involves an SFDA regulated product or drug.

5.5.1.2 Requiring the Investigator to complete a training program

5.5.1.3 Barring the Investigator from conducting further research

5.5.1.4 Any other action deemed appropriate by the IRB.

6. PROCEDURES

6.1 Upon approval by the Chairman, Research Office, the research proposal will be forwarded to the IRB for their ethical review and approval.

6.2 Initially, IRB will determine the type of review according to the level of risk.

6.2.1 **Exempt review**. Research can be exempted from IRB review when no risk is expected from research and/or there is no human intervention.

6.2.2 **Expedited review**. The IRB can approve certain research by using the expedited review procedure in the following cases:

6.2.2.1 If the risk that the human subject can be exposed to does not exceed the minimal risk level

6.2.2.2 If the research does not reveal the identity of the human subject

6.2.2.3 If the research deals with clinical studies on drugs or medical equipment, provided that:

6.2.2.3.1 The drug is used in accordance with its licensing and dosages approved by the concerned party, and does not entail any increase in potential risk for the human subject

6.2.2.3.2 The medical equipment in use has originally been licensed by the concerned party and has already been utilized accordingly.

6.2.2.4 If taking biological samples for research purposes is carried out via non-invasive methods such as analysis of urine, saliva, nail or hair clippings, etc.

6.2.2.5 If research data is to be collected by using medical equipment approved persons to participate as subjects of the research will include the following data:

6.2.2.5.1 Research title and objective

6.2.2.5.2 Attributes qualifying persons targeted to be the research subjects (participants or volunteers)

6.2.2.5.3 Indication of all facilities to be provided to human subject

6.2.2.5.4 Number of research project in the local committee and expected date of completion

6.2.2.5.5 Expected risks of the research, if any

6.2.2.5.6 Name and address of PI or their representative, his contact numbers and electronic mail address so that individuals aiming to join the research group can call them for further information.

6.2.3 **Full board review**. Any research does not meet the conditions of exempt or expedited reviews, can be approved through full review procedure.

6.3 The IRB will recommend one (1) of the following:

6.3.1 Approval of submission

6.3.2 Approved pending receipt of required minor revisions to study procedures, informed consent documents, or other written materials by the PI or Sub-Investigators

6.3.3 Approved pending opinion from related experts

6.3.4 Disapproval. In such cases, the PI has the right to file an appeal in writing and subsequently appear in person before the IRB to challenge the decision as per APP 1432-04.

6.4 The IRB Chairman will inform the PI of the decision and a copy will be provided to the Research Office.

6.5 Continuing Review of Ongoing Research Projects

6.5.1 The PI will submit an annual report to the IRB summarizing the status of the project and requesting approval extension by completing **Appendix A**.

6.5.2 IRB will review the report and determine the risks to subjects continue to be minimized and reasonable in relation to the anticipated benefits as well as the following:

6.5.2.1 The selection of subjects continues to be reasonable in relation to anticipated benefits

6.5.2.2 Informed consent continues to be appropriately documented and the information is still accurate and complete.

6.5.3 If the original approval is through the full IRB review pathway:

6.5.3.1 The IRB with a quorum will meet to conduct the periodic review

6.5.3.2 At the time of approval, IRB will determine the exact date of the mandatory periodic review, as well as the information that needs to be provided by the PI in this report

6.5.3.3 IRB can request information from the PI, as necessary, to properly conduct this review

6.5.3.4 If the PI does not provide the requested information by the deadline, the IRB Chairman will send a letter informing the PI the project is temporarily suspended until such documentation is received and reviewed

6.5.3.5 If necessary and indicated by information that has arisen since the initiation of the study, IRB can request from the PI any and all information required to ensure continued safe conduct of the investigation.

6.5.4 If the original approval is through the expedited review pathway

6.5.4.1 The IRB Chairman or a designated reviewer appointed by the Chairman can conduct the periodic review

6.5.4.2 At the time of approval, the IRB Chairman will determine the exact date of the mandatory periodic review, as well as the information that needs to be provided by the PI in this report

6.5.4.3 IRB can request information from the PI, as necessary, to properly conduct this review

6.5.4.4 If the PI does not provide the requested information by the deadline, the IRB Chairman will send a letter informing the PI that the project is temporarily suspended until such documentation is received and reviewed

6.5.4.5 If necessary and indicated by information that has arisen since the initiation of the study, the IRB Chairman can request from the PI any and all information required to ensure continued safe conduct of the investigation.

6.5.5 IRB can request from Clinical Monitoring Unit an additional on-site monitoring of approved projects in order to determine from a source other than the investigator's report that no material changes have occurred in the project since the previous review.

7. RESPONSIBILITY

7.1 King Abdullah International Medical Research Center and all other relevant departments are responsible for ensuring full implementation of this APP.

7.2 Internal Audit will randomly monitor the implementation of the provisions within this APP.

8. APPROVALS

PREPARED BY:

13 MAR 2019

DR. ABDALLAH ADLAN — **DATE**
Chairman, Institutional Review Board
King Abdullah International Medical Research Center, MNG-HA

14 MAR 2019

DR. AHMED AL ASKAR — **DATE**
Executive Director
King Abdullah International Medical Research Center, MNG-HA

REVIEWED BY:

18/3/19

DR. MOHANAD AL EEBAN — **DATE**
General Director
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APPROVED BY:

19 MAR 2019

H.E. DR. BANDAR AL KNAWY — **EFFECTIVE DATE**
Chief Executive Officer
Ministry of National Guard – Health Affairs *and*
President
King Saud bin Abdulaziz University for Health Sciences