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	:	**1433-37**
TITLE	:	**CONDUCTING RESEARCH STUDIES**
ORIGINATING DEPT.	:	**KING ABDULLAH INTERNATIONAL MEDICAL RESEARCH CENTER (KAIMRC) (419801)**
ORIGINAL DATE	:	**DECEMBER 2012**
REVISED DATE	:	**FEBRUARY 2019**

1. PURPOSE

To provide a process for conducting all research studies in accordance with the approval of the Institutional Review Board (IRB).

2. APPLICABILITY

To all employees of Ministry of National Guard - Health Affairs (MNG-HA) and all its affiliated facilities.

3. RELATED REFERENCES

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

3.2 APP 1426-02: Institutional Review Board (IRB)

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

3.4 APP 1432-20: Monitoring Research Studies

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

3.6 International Conference of Harmonization (ICH): ICH Harmonized Tripartite Guideline - Guideline for Good Clinical Practice E6(R1)

3.7 Saudi Central Board for Accreditation of Healthcare Institutions (CBAHI), National Hospitals Standards, 3rd Edition (2015) – PFR.8, PFR.10 and PFR.16.

3.8 Joint Commission International Accreditation Standards for Hospitals, 6th Edition (2017) – HRP.3, HRP.6, HRP.7 ME 1-6 and HRP.7.1 ME 1-3 and PRF.5.1

4. DEFINITIONS

4.1 **Adverse Event (AE)** refers to any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product which does not necessarily have a causal relationship with this treatment. An adverse event (AE) 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) or Serious Adverse Drug Reaction (SADR)** refers to an untoward medical occurrence that at any dose: results in death, a life-threatening situation, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity or a congenital anomaly/birth defect.

4.1.2 **Suspected Unexpected Serious Adverse Reaction (SUSAR)** refers to a serious adverse event or serious adverse drug reaction considered **unexpected**. An event is considered unexpected if it is not listed in the investigator brochure or is not listed at the specificity or severity that has been observed; or, if an investigator brochure is not required or available, is not consistent with the risk information described in the general investigational plan or elsewhere as applicable.

4.2 **Audit**, for the purpose of this APP, refers to a systematic and independent examination of research study-related activities and documents to determine whether the evaluated study-related activities were conducted, and the data were recorded, analyzed, and accurately reported according to the protocol, sponsor's Standard Operating Procedures (SOP), Good Clinical Practice (GCP), and the applicable regulatory requirements.

4.3 **Clinical Research** refers to a branch of medical research that determines the safety and effectiveness of medications, medical devices, diagnostic products and/or treatment regiments intended for human use.

4.3.1 **Clinical Trials** refers to a set of tests in medical research and drug development that generate safety and efficacy data for health interventions, e.g., drugs, diagnostics, devices and protocols.

4.4 **Essential Documents** refers to documents that allow on individual and collective bases to evaluate the conduct of a study and the quality of the data produced.

4.4.1 **Source Documents** refers to original documents, data and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial).

4.5 **Informed Consent**, for the purpose of this APP, refers to the process by which a subject voluntarily confirms their willingness to participate in a particular study, after having been informed of all aspects of the study that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed and dated Informed Consent Form (ICF).

4.6 **Inspection** refers to act by a regulatory authority of conducting an official review of documents, facilities, records and any other resources that are deemed by the authority to be related to the clinical trial and that may be located at the site of the trial, at the sponsor's and/or contract research organizations' (CRO's) facilities or at other establishments deemed appropriate by the regulatory authority.

4.7 **Institutional Review Board (IRB)** refers to an independent body composed of medical, scientific and non-scientific members whose responsibility is to ensure the protection of the rights, safety and well-being of human subjects involved a research studies. It has the right to terminate or suspend research study based on ethical grounds, violation of patient rights or safety.

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

4.9 **Investigational Product** refers to a pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.

4.9.1 **Investigational Drug Services Unit** refers to a sub-unit of the Research Office composed of licensed pharmacists which provides support and guidance for the safe and efficient management of investigational products used in clinical trials. It provides services on dispensing, accountability, handling, storage and control of investigational drugs in compliance with the research study protocol, Program policies, external sponsor policies, ICH/GCP guidelines and applicable regulatory requirements.

4.10 **Monitoring** refers to the act of overseeing the progress of a clinical trial and ensuring that clinical trial is conducted, recorded and a written monitoring report is submitted from the monitor to the Research Office after each site visit and/or other trial-related communications in accordance with the research study protocol, Standard Operating Procedures (SOPs), Good Clinical Practice (GCP) and the applicable regulatory requirements.

4.11 **Principal Investigator (PI)** refers to a person or group of persons responsible for the conduct of a clinical trial at a trial site. If a trial is conducted by a team of individuals at the trial site, the PI is the responsible leader of the team.

4.11.1 **Clinical Research Associates** work closely with the PI to perform various responsibilities for conducting research studies as directed by the PI.

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

4.12 **Research Funding Committee (RFC)** refers to a committee responsible for review and approval of fund requests for conducting research projects per Committee Formation Order-KAIMRC-01-011.

4.13 **Research Office** refers to a section of KAIMRC which is responsible for processing, scientifically reviewing, and approval of all research studies conducted by or within MNG-HA.

4.14 **Research Study Protocol** refers to a document that describes the objective(s), design, methodology, statistical considerations and organization of a trial. The research study protocol usually gives the background and rationale for the trial, however, these may be provided in other protocol referenced documents.

4.14.1 **Protocol Amendment** refers to a written description of a change(s) or formal clarification of an approved protocol.

4.15 **Standard Operating Procedure (SOP)** refers to a document that specifies all operational steps, acceptance criteria, personnel responsibilities and materials required to accomplish a task.

4.16 **Sponsor** refers to an individual, company, institution or organization who takes responsibility for the initiation, management and/or financing of a research study.

4.16.1 **Externally Sponsored Research Studies** refer to studies sponsored and/or funded by any non-MNG-HA organization.

4.17 **Study Close Out** refers to the procedures undertaken to fulfill administrative, regulatory and human participant requirements either after completion of study related requirements or if the study is prematurely terminated for any reason.

4.18 **Subject/Trial Subject** refers to an individual who participates in a clinical trial, either as a recipient of the investigational product(s) or as a control.

5. POLICY

5.1 The Principal Investigator (PI) is primarily responsible for overall conduct of the research study, selecting and identifying their research team members and ensuring proper protection of research subject's rights, safety and well-being.

5.1.1 The PI must:

5.1.1.1 Conduct the research study in a systematic and orderly manner, and ensure compliance with all relevant policies, national laws and related international regulations

5.1.1.2 Not initiate any research study and/or recruit any research subjects without obtaining the approval of the Institutional Review Board (IRB) on the research protocol and other study documents, as applicable, unless the research proposal has been exempted from IRB approval.

5.1.1.2.1 The PI must:

5.1.1.2.1.1 Report any deviation from research protocol or changes to the approved protocol to the IRB and Research Office within five (5) working days

5.1.1.2.1.2 Obtain IRB approval prior to the implementation of any protocol amendments as per APP 1426-02.

5.1.2 The PI is responsible for reporting Serious Adverse Events (SAEs) and Suspected Unexpected Serious Adverse Reaction (SUSAR) to the IRB and Adverse Events (AEs) in the Case Report Form in a timely manner.

5.1.3 For all investigator-initiated clinical studies subject to Saudi Food and Drug Authority (SFDA) regulations, the PI must obtain SFDA approval for the conduct of the research study prior to the implementation of any research related activities as per **Appendix B**.

5.1.4 For all externally sponsored clinical studies subject to SFDA regulations, the PI is responsible for ensuring the sponsor has fulfilled and obtained all SFDA requirements and approval for the research study prior to implementation of any research related activities.

5.1.5 Other responsibilities of PIs in conducting research studies are outlined in **Appendix C**.

5.2 The research team must be responsible for protecting the confidentiality and privacy of all screened and enrolled research subjects.

5.3 King Abdullah International Medical Research Center (KAIMRC) must allow monitoring and auditing by the sponsor and inspection by the appropriate regulatory authority.

5.4 Patients and families must be identified and informed about how to gain access to clinical research, investigations or trials relevant to their treatment needs in accordance with KAIMRC Standard Operating Procedures (SOPs). The following measures must be adopted as applicable:

5.4.1 Publication of relevant information about all ongoing trials in the KAIMRC website, display of posters/screens containing relevant information about trials in the outpatient & inpatient clinics and/or distribution of leaflets in the outpatient clinics and inpatient areas.

5.4.2 Any advertisement that can be used for the recruitment of research subjects, whether in the form of posters, emails, telephone calls and/or other materials must receive IRB approval prior to their application.

5.5 The research study must be conducted within the specified duration stated in the research protocol as approved by IRB.

5.5.1 The PI must:

5.5.1.1 Initiate study procedures no later than ninety (90) days from IRB approval or ninety (90) days from the release of funds, if applicable.

5.5.1.2 Ascertain the validity of the IRB approval which is typically valid for one (1) year

5.5.1.3 Submit request for extension, if necessary, in accordance with APP 1426-02

5.5.2 In the event of failure to conduct the research study within the specified duration, the PI must inform the Research Office, IRB and Research Funding Committee (RFC).

5.6 All research studies are subject to monitoring and evaluation by Research Outcome Evaluation Unit (ROEU) (except clinical trials) and clinical trials are monitored by the Clinical Monitoring Unit, KAIMRC.

5.6.1 The PI must comply with the monitoring process stipulated in APP 1432-20.

5.7 All investigational drugs must be dispensed, handled and managed by the KAIMRC Investigational Drug Services Unit.

5.8 The PI must comply with the retention period of the research study related documents after study closure.

5.8.1 Research study related documents, files and/or records must be retained at the investigational site for at least three (3) years after completion of the study; after which these documentations must be retained in a secure archival facility for at least five (5) years.

5.9 In the event of any conflict of interest arising during the conduct of a research study, action must be taken according to SOP RA 204 Conflict of Interest (**Appendix A**).

5.10 The PI can delegate some or all of their responsibilities to one (1) or more Sub-Investigators and/or other research team members (such as during temporary absences) provided the following conditions are met:

5.10.1 The delegated Sub-Investigators must be part of the research team previously approved by the IRB, qualified by training/education and experience to perform the delegated task

5.10.2 Delegation of responsibilities are documented in writing and signed by both the PI and the delegated Sub-Investigator

5.10.3 The start and end dates of delegation must also be documented.

5.11 If the PI is resigning/separating from MNG-HA or withdrawing from the project, the IRB must be notified and withhold the project until a new PI is assigned and resume responsibilities. The resigned/withdrawn PI can still continue in the project as Sub-Investigator.

5.12 The IRB, Research Office and/or RFC have the final authority to terminate or suspend any research study in case of non-compliance with policies, procedures and SOPs.

5.12.1 The PI has the right to appeal against any decision taken by the IRB and/or RFC to terminate or suspend a research study as per APP 1432-04.

6. PROCEDURES

6.1 Once the research proposal is IRB approved, the following preliminary activities will be carried out:

6.1.1 The IRB, Research Office and RFC (as applicable) will send a request to the PI for submitting the documents as described in SOP RA 202 Initial and On-going Submissions and SOP RA 203 Reporting Requirements (**Appendix A**).

6.1.2 The PI will compile all essential documents generated prior to and at the completion of the study as required by SOP RA 201 Essential Documents (**Appendix A**) and as directed by SOP GA 105 Records Management, Accountability and Retention/Documentation of Communication (**Appendix A**).

6.1.3 For all clinical trials and for some non-clinical trials as applicable, the Clinical Monitoring Unit will conduct an initial monitoring visit once the Clinical Monitoring Unit is notified that the research protocol has been approved by the IRB, RFC and/or the research grant fund is being released by MNG-HA, to ensure readiness of the PI and research team to carry out the research study procedures as per APP 1432-20.

6.1.4 The ROEU team will send a request to the PI for submitting a final scientific report and/or progress report for research study and/or relevant publication on regular base.

6.2 For all clinical trials and for various non-clinical trials as applicable, the PI initiates the study upon obtaining the recommendation for study initiation from the Clinical Monitoring Unit, or after conducting and completing the initiation visit by the sponsor's Clinical Research Associate for externally sponsored studies.

6.2.1 The PI will refer to SOP PM 302 Study Start Up (**Appendix A**) for general information and guidelines on study start up activities.

6.2.2 For all clinical trials and for some non-clinical trials as applicable, once the monitoring unit has recommended initiation of the study, the PI will start subject screening and enrollment. The PI will refer to SOP SM 401 Subject Recruitment and Screening for information and guidance.

6.2.3 The PI will obtain informed consent and document the process in the medical chart for each subject recruited by following SOP "SM 402: Informed Consent (**Appendix A**). The template of informed consent is available in the Appendices C, G-J of APP 1419-05.

6.2.4 If the PI decides to amend the protocol, Informed Consent form (ICF) and any other document pertaining to the research study, then the PI will change them according to the IRB policies and procedures.

6.2.4.1 Once the Protocol is re-approved, the PI will train the study team members on the amended protocol and this will be documented in the training log.

6.2.4.2 For ICF amendments, all research subjects and/or their legally acceptable representatives/Impartial Witness who are actively enrolled in the research study will be re-consented by reading and signing the modified ICF and the process will be documented in the medical charts of the subjects.

6.2.5 The PI will strictly comply with the eligibility and enrollment criteria for each enrolled and consented research subject as per the policy and procedures on subject eligibility and enrollment stipulated in SOP SM 403: Eligibility and Enrollment (**Appendix A**).

6.2.6 The PI will make all possible efforts to protect confidential information in research studies as per SOP SM 404 Protecting Confidential Information (**Appendix A**).

6.2.7 Deviations from research protocol will be as per SOP PM 307 Protocol Compliance - Waivers, Deviations, Memos to File (**Appendix A**).

6.2.8 All research subject visits and assessments will be organized as per SOP SM 405 Subject Visits and Assessment (**Appendix A**).

6.2.9 The PI will ensure that source documents, such as patient charts (hard and/or electronic format), are in compliance with the policy and procedures of SOP PM 304 Source Documentation (**Appendix A**).

6.2.10 Where applicable, the Investigational Drug Services Unit will follow the guidelines of SOP PM 303 Investigational Product Management (**Appendix A**).

6.2.11 Adverse Events (AEs) and Serious Adverse Events (SAEs) can be experienced by research subjects as a result of their direct or indirect participation in the study will be managed in accordance with SOP SM 406 AE Management (**Appendix A**).

6.2.12 Collection of research data will follow the policy and procedures as per SOP DM 501 Clinical Data Management (**Appendix A**).

6.2.13 In cases where an electronic data management system is utilized for research data collection, the PI will comply with the policy and procedures as per SOP DM 502 Use of Electronic Data Management Systems (**Appendix A**).

6.2.14 The PI is expected to comply with all routine monitoring activities performed by the KAIMRC Monitoring Unit during the course of the study. The PI will utilize SOP PM 305 Monitoring Visits (**Appendix A**) for the preparation of monitoring visits.

6.2.15 The research study can also be audited by the following bodies:

6.2.15.1 KAIMRC for assuring compliance to quality standards. The PI will refer to the SOP QA 601 Quality Assurance Audits (**Appendix A**) for details

6.2.15.2 Applicable regulatory authorities such as SFDA can conduct inspections for assuring compliance to the regulatory requirements. Refer to SOP QA 602 Inspections and Regulatory Authorities (**Appendix A**) for details.

6.2.16 During the temporary absence of the PI, a memorandum will be submitted to the Research Office stating the period of absence and the identity of the delegated Sub-Investigator.

6.2.17 The PI can request an extension of approval by submitting a memorandum, together with the annual progress report of the research study, to the IRB and Research Office.

6.3 Upon completion or premature termination of the research study, the PI notify the IRB and Clinical Monitoring Unit and closes out the study.

6.3.1 The PI submits the final study report to the IRB and Research Office.

6.3.2 The Monitoring Unit conducts the close out visit as per APP 1432-20.

6.3.3 If the Monitoring Unit recommends study closeout, the PI will follow SOP PM 306: Study Completion (**Appendix A**).

6.3.4 For management of records during and on completion of the research study, the PI will refer to SOP GA 105: Record Management, Accountability and Retention and Documentation of Communication (**Appendix A**).

6.4 The PI will submit a copy of the publication to the Research Office.

7. RESPONSIBILITY

7.1 It is the responsibility of the KAIMRC and all other relevant departments to ensure the implementation of and adherence to the provisions stipulated herein.

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

8. APPROVALS

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27 FEB 2019

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