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	:	**1432-20**
TITLE	:	**MONITORING RESEARCH STUDIES**
ORIGINATING DEPT.	:	**KING ABDULLAH INTERNATIONAL MEDICAL RESEARCH CENTER (417780)**
ORIGINAL DATE	:	**APRIL 2012**
REVISED DATE	:	**SEPTEMBER 2015**

1. PURPOSE

To provide a process for monitoring approved research studies to ensure they have been executed in compliance with the approved study proposal, International Conference of Harmonisation/Good Clinical Practice (ICH/GCP) guidelines, King Abdullah International Medical Research Center (KAIMRC) and other requirements from regulatory authorities.

2. APPLICABILITY

To all staff involved in clinical and non-clinical research studies conducted at MNG-HA facilities.

3. RELATED REFERENCES

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

3.2 APP 1432-04: Appeal process for Rejected Research Proposal or Suspended Ongoing Research Study.

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

3.4 APP 1433-37 Conducting Research Studies

3.5 APP 1429-19 Conflicts of Interest

3.6 APP 1435-10 Budget Approval for Intramural Research Grant

3.7 APP 1425-01: Central Archiving of Document Files

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المملكة العربية السعودية

3.8 Declaration of Helsinki

3.9 Saudi Food and Drug Authority (SFDA) rules and regulations

3.10 King Abdullah International Medical Research Center – Standard Operating Procedures (SOPs)

3.11 King Abdulaziz City for Science and Technology. National Committee of Bio Ethics (NCBE) - Implementing Regulations of the Law of Ethics of Research on Living Creatures

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

3.13 Joint Commission International Accreditation Standards for Hospitals, 5th Edition (2014) – HRP.4, ME.1-3,5 & 6

4. DEFINITIONS

4.1 **Adverse Event (AE)** refers to any untoward or unfavorable event detected from the baseline health of a study subject during the course of a clinical research study.

4.2 **Audit** 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 **Auditor** refers to a qualified staff with assigned responsibility for conducting audit in KAIMRC.

4.4 **Case Report Form** refers to a printed, optical, or electronic document designed to record all protocol required information to be reported to the sponsor on each trial subject.

4.5 **Chief Principal Investigator (Chief PI)** refers to an individual who has the responsibilities of the principal investigator and is responsible for submitting the research proposal for multi-center studies and overall conduct of the research in other sites.

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

4.7 **Clinical Trials** are 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)

4.8 **Compliance** refers to adherence to all study-related requirements, Good Clinical Practice (ICH/GCP) requirements, and the applicable regulatory requirements.

4.9 **Contract Research Organizations (CRO)** refers to a person or organization (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial-related duties and functions.

4.10 **External Multi-Centered Studies** refers to a study designed and written by any non-MNG-HA organization and or any non-MNG-HA Funding Agency, whether this agency was national e.g. King AbdulAziz City of Science & Technology (KACST) or international e.g. National Institute of Health (NIH).

4.11 **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.

4.12 **International Conference of Harmonisation/Good Clinical Practice (ICH/GCP)** refers to an international ethical and scientific quality standard for designing, conducting, recording, and reporting research involving the participation of human subjects.

4.13 **Investigator Initiated Study** refers to a study designed written and submitted by an MNG-HA staff member.

4.14 **Investigator's Brochure** refers to a compilation of clinical and non-clinical data on investigational product(s) relevant to the study of such product(s) in human subjects.

4.15 **Monitor** refers to the person who periodically oversees the progress of a research study, and ensures that it is conducted, recorded, and reported in accordance with research study protocol, SOPs, ICH/GCP and applicable regulatory requirement(s).

4.16 **Monitoring** refers to the act of overseeing the progress of a clinical trial, ensuring that it is conducted, recorded and reported in accordance with research study protocol, SOPs, ICH/GCP and the applicable regulatory requirement(s).

4.17 **Monitoring Plan** is a document that describes the key activities for monitoring an approved research study. This document describes the responsibilities of the monitor, frequency of visits and the documents which will be presented by the PI during monitoring visits.

4.18 **Monitoring Report** refers to a written report from the monitor to the Research Office after each site visit and/or other trial-related communication.

4.19 **Monitoring Unit** refers to a division of the Research Office section of KAIMRC, which deals with the monitoring of approved research studies.

4.20 **Non-Clinical Research** refers to type of studies that do not involve participation of human subjects, including but not limited to, in-vivo or in-vitro experiments and animal studies.

4.21 **Principal Investigator (PI)** refers to a person 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 team leader.

4.22 **Protocol Deviation** refers to any change or alteration from the procedures stated in the research study protocol, consent document, recruitment process, or study materials (such as questionnaires) originally approved by the IRB.

4.23 **Protocol Violation** refers to any planned or unintended major changes or major deviations from the IRB approved research study protocol, consent document, recruitment process or study materials that were not approved by the IRB, prior to the initiation of the changes.

4.24 **Regular/Routine Monitoring Visit** is any visit that occurs after the site is initiated and up until the site is closed out. Sites will be periodically visited to ensure that they are compliant with all the regulations, subject safety is being adequately followed, data is being captured in a timely and reliable manner, the Investigational Product is being handled as per protocol and relevant regulations/guidelines, there are no significant deviations from the planned study protocol, all important study documentation is being generated and stored properly, and that the research site is adequately supplied in regards to lab kits and other pertinent study materials. The ultimate purpose of our job is to protect subject safety by monitoring the trial conduct for ICH/GCP compliance and regulatory requirements.

4.25 **Regulatory Authorities** refer to the bodies having the power to regulate. In the ICH/GCP guidelines, the expression 'regulatory authorities' includes the authorities that review submitted clinical data and those that conduct inspections. It includes the Saudi Food and Drug Administration (SFDA).

4.26 **Research Committee (RC)** refers to a body composed of medical practitioners/clinicians whose responsibility is to review research proposals for Ministry of National Guard - Health Affairs and make recommendations for amendments and/or approval/disapproval on a scientific basis.

4.27 **Research Quality Management Section (RQMS)** refers to a section of KAIMRC that deals with quality management within King Abdullah International Medical Research Centre.(KAIMRC).

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

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

4.30 **Research Office (RO)** is a section of KAIMRC which manages all research studies conducted by or within MNG-HA.

4.31 **Site Initiation Visit** refers to the procedures undertaken to review all pre-study start up essential documents, ensure that all research team members are familiar with the protocol, ICH/GCP requirements along with their duties toward conducting the protocol. This visit usually occurs after the site has completed all regulatory requirements and has obtained IRB approval for the research study at their site.

4.32 **Site Principal Investigator (Site PI)** refers to an individual who has the responsibilities of the principal investigator and is responsible for conducting the research study for a particular center of multi-center studies.

4.33 **Site/Study Close Out Visit** refers to the procedures undertaken to fulfill administrative, regulatory and human participant requirements, either after all participants have completed all study related requirements or when the study is prematurely terminated for any reason.

4.34 **Subject or Trial Subject** refers to an individual who participates in a clinical research study.

5. POLICY

5.1 All approved research studies (internal and external) must be monitored by the KAIMRC Monitoring Unit.

5.1.1 The purpose of monitoring the research study is to:

5.1.1.1 Ensure that appropriate measures are taken by the PI and research team to protect the rights, safety and well-being of research participants

5.1.1.2 Ensure that the external sponsors comply with the defined policy and procedures for assuring quality, safety, confidentiality and ethics of research

5.1.1.3 Ensure that, if the sponsor has delegated any responsibility to Contract Research Organizations (CROs), the contracted CRO complies with defined policy and procedures for assuring quality, safety, confidentiality and ethics of the research

5.1.1.4 Verify compliance to the research study protocol, all applicable KAIMRC, MNG-HA, ICH/GCP and other national and international regulatory requirements

5.1.1.5 Verify whether the PI has taken adequate steps to close the gaps/issues identified in the previous visits

5.1.1.6 Verify the progress of a research study at periodic intervals and to ensure that the study has met all requirements for moving from one stage to the next, as described in the timeframe of the research study protocol.

5.2 Monitoring of financial transactions of the funded research studies against the approved budget shall not be reviewed by the monitoring unit, however, these shall be reviewed by the financial affairs department of MNG-HA.

5.3 The type and scope of monitoring a research study varies with the status of each study. Monitoring Visits are classified as follows:

5.3.1 **Site Initiation Visit**: The monitor reviews whether all requirements for initiating a research study have been met. This review must be carried out after the IRB approval and before the initiation of the research study.

5.3.2 **Routine Monitoring Visit**: The monitor reviews the progress of a study as well as compliance to the research study protocol and all applicable regulatory requirements. This review must be carried out after initiation of the study and before final close out. Frequency of routine Monitoring Visits must be established by the Monitoring Unit.

5.3.2.1 Frequency of Routine Monitoring Visits must be based on research project size, timeframe, turning points, critical events in the study path, recruitment and logistics. The Monitoring Unit must determine the frequency of the visit for each research project.

5.3.3 **Closeout Monitoring Visit**: The monitor reviews whether all requirements for closing a study have been met. This review must be carried out either prior to the final close out of the study or when the research study is prematurely terminated for any reason.

5.4 The Monitoring Unit must be responsible for evaluating the compliance of research studies against national and international regulations. The specific responsibilities of the Monitoring Unit include:

5.4.1 Site selection procedures for Investigator initiated multi-center studies

5.4.2 Prepare a monitoring plan for each approved research study as applicable

5.4.3 Review all study related documentation, records and procedures for each research study

5.4.4 Ensure compliance to research study protocol, ICH/GCP guidelines KAIMRC/MNG-HA policy and procedures together with any other applicable national/international regulations

5.4.5 Schedule a Monitoring Visit fifteen (15) working days prior to the date of visit with the PI

5.4.6 Prepare a Monitoring Report upon completion of each visit and submit a response to the PI within fifteen (15) working days

5.4.7 Effectively communicate any significant findings from the Monitoring Visits to the Research Office (RO) Chairman

5.4.8 Retain records of site visits for a period of five (5) years.

5.5 The PI and all other research team members must comply with Monitoring Unit requirements for monitoring of research studies. The specific responsibilities of the PI include:

5.5.1 Conduct the research study in accordance with research study protocols, ICH/GCP guidelines, KAIMRC/MNG-HA policy and procedures, requirements of the external sponsor (if applicable), and all other applicable national/international requirements

5.5.2 Confirm the proposed date of the Monitoring Visit

5.5.2.1 The RO may communicate to IRB and request them to suspend the research study if the PI does not respond to the Monitoring Unit within the time specified in the Monitoring Visit request and without a valid reason.

5.5.2.2 The monitoring visits may be re-scheduled to a maximum of only two (2) times

5.5.3 Meet with the monitor at the end of each Monitoring Visit in order to discuss any findings and issues identified

5.5.4 Inform all research team members at least ten (10) working days prior to the scheduled date of visit

5.5.5 Ensure that all required documents are available for review

5.5.6 Act promptly on the recommendations proposed by the Monitoring Unit and ensure that non-compliance incidences identified are closed within the agreed timeline

5.5.6.1 RO may communicate to IRB and request them to suspend the research study if the PI does not comply with the timeline specified in the monitoring documents/reports.

5.5 Site visit monitoring must be carried out by monitors approved by the Monitoring Unit.

5.6 The role of the Monitoring Unit must not interfere with the IRB as stated in APP 1426-02.

5.7 The Monitoring Reports prepared by the Monitoring Unit may be reviewed by the following committees:

5.7.1 Institutional Review Board for reviewing and ensuring compliance to ethical policies and standards

5.7.2 Funding Committee for assessing compliance to protocol requirements for fund utilization.

5.8 All external multi-centered studies must be reviewed by the Monitoring Unit at least twice annually or more if necessary.

5.8.1 Site initiation visit must be carried out by the monitoring unit, on the following conditions:

5.8.1.1 Not conducted by the external sponsor

5.8.1.2 Initiation visit carried out over teleconference/telephone.

5.9 Any complaints against the Monitor/Monitoring Unit must be sent to the Research Office in writing or to kaimrclients@ngha.med.sa.

5.9.1 Any request for appeal must follow the APP 1432-04.

5.9.2 The RO must provide the response and the feedback to the PI within fifteen (15) working days.

5.10 Audits are carried out for both Investigator initiated and External multi-centered research studies as required as follows:

5.10.1 Periodic audits conducted by RQMS

5.10.2 Incident triggered audits conducted by RQMS as informed by the Monitoring Unit.

5.11 Regulatory inspections may carried out for Investigator initiated and External multi-centered research studies by the applicable regulatory authorities as follows:

5.11.1 Routine inspection

5.11.2 For cause inspection.

6. PROCEDURES

6.1 Monitoring Investigator Initiated Studies

6.1.1 Upon approval of the research study, the Monitoring Unit submits a Monitoring Plan (**Appendix A**) to the PI. For sites other than MNG-HA, it will be created after the site initiation visit.

6.1.1.1 The PI confirms receipt of the Monitoring Plan. Any suggestions for modifications will be submitted to the Monitoring Unit within twenty (20) working days of receipt.

6.1.1.2 The PI will distribute copies of the final Monitoring Plan to all sub-investigators, study sites and investigational teams and file it in the trial master file.

6.1.2 The Monitoring Unit conducts the Initiation Visit using the Study Initiation Monitoring Checklist and Report (**Appendix B**) in order to verify whether the study has met all the requirements for initiating the research study.

6.1.2.1 The monitor will:

6.1.2.1.1 Assess compliance to all KAIMRC and MNG-HA applicable policies and procedures to be met prior to initiating the study

6.1.2.1.2 Provide appropriate orientation for the PI regarding the rules and responsibilities for conducting the research study.

6.1.2.2 Monitoring Unit submits a report to the RO and PI, informing the outcome of the initiating visit. If the study meets all requirements for initiation, Monitoring Unit recommends initiation of the study. If the study does not meet the requirements for initiation, Monitoring Unit will not recommend the initiation for the study until all the queries are resolved as per the report. Revisits will be conducted until the PI meets the requirements for initiating the study.

6.1.3 Upon initiation of the study, the Monitoring Unit will conduct routine site visits at pre-defined intervals, as described in the Monitoring Plan. The PI will be informed fifteen (15) working days prior to each visit.

6.1.3.1 The Monitoring Unit submits the routine visit report (**Appendix C**) on recommendations for resolving the identified non-compliance and areas of improvement to the PI through research office, either onsite (i.e. during the Monitoring Visit) or within fifteen (15) working days of completion of the Monitoring Visit.

6.1.3.2 The Monitoring Unit submits the routine visit report through the RO to the PI and IRB with the significant findings that require major attention with corrective actions to be implemented. Significant findings may include, but are not limited to the following:

6.1.3.2.1 If the study is not initiated within ninety (90) days of obtaining receipt of IRB approval.

6.1.3.2.2 Major protocol deviations/violations and/or adverse events, that affect the rights, safety and well being of research participants and/or research data integrity.

6.1.3.2.3 PI non-compliance with KAIMRC standards, regulations, contracts and agreements.

6.1.3.2.4 Any recommendation for termination/suspension of a research study as a result of ethical violations will be sent through RO to IRB to take appropriate actions for ensuring quality of research and compliance to ICH/GCP guidelines, KAIMRC and other regulatory requirements. (See APP 1426-02).

6.1.3.2.5 Any recommendations for termination/suspension of a research study as a result of scientific and administrative violations will be sent through Research Committee (RC) chairman to IRB to take appropriate actions for ensuring

quality of research and compliance to ICH/GCP guidelines, KAIMRC and other regulatory requirements.

6.1.4 The PI will take appropriate action to comply with the recommendations provided by the Monitoring Unit within ten (10) working days, in order to prevent study terminations and/or suspension.

6.1.5 The Monitoring Unit verifies compliance to the recommendations stated by the PI during the next scheduled visit or as requested by the Monitoring Unit through a response report.

6.1.6 Upon completion of the research project, the PI must request the Monitoring Unit to conduct the Closeout Monitoring Visit (**Appendix D**).

6.1.7 The Monitoring Unit verifies whether all requirements for closing out a study have been met.

6.1.7.1 If the study does not meet closeout requirements, the Monitoring Unit submits the recommendations through RO to the PI for closing identified gaps. Revisits will be conducted by the Monitoring Unit until the PI meets all requirements for closing out the study. See SOPs for conducting a research study, refer APP 1433-37 for details of the Closeout Visit.

6.1.7.2 If the study meets all of the closeout requirements, the Monitoring Unit recommends final closeout of the study through the RO to the PI, and to the IRB. The IRB will send acknowledgement memo for completion of the study based on the report.

6.1.8 The Monitoring Unit retains the site visit reports for five (5) years, and will be archived as described in APP 1425-01.

6.2 Monitoring External Multi-Centered Studies

6.2.1 Upon approval of the study by the IRB, the PI submits a copy of the sponsor's monitoring plan to the KAIMRC Monitoring Unit.

6.2.2 The PI informs the monitoring unit of the schedule of the site initiation visit conducted by the sponsor in advance.

6.2.3 The Monitoring Unit participates in the sponsor's initiation visit as necessary

6.2.4 The PI submits the copy of the Initiation Visit Report to the Monitoring Unit for review within five (5) working days from the receipt of the initiation visit report from the sponsor.

6.2.5 Upon receiving the report, the Monitoring Unit reviews the sponsor's initiation visit report to ensure the compliance with ICH/GCP and applicable regulations and makes recommendations and raises issues, if necessary.

6.2.6 The PI submits the routine monitoring visit follow-up letter of the external monitor to the Monitoring Unit within fifteen (15) working days of completion of each visit.

6.2.7 The Monitoring Unit directly conducts at least two (2) scheduled internal monitoring visits per annum for all external multi-centered studies.

6.2.7.1 The Monitoring Unit reviews the Monitoring Reports and determines if the study requires additional review by the Monitoring Unit. Additional reviews may be carried out in the following situations:

6.2.7.1.1 If the follow-up letter by the external monitor is unsatisfactory.

6.2.7.1.2 If significant adverse events are reported.

6.2.7.1.3 If major protocol deviations/violations are reported.

6.2.7.2 The PI will be asked to take immediate action if significant protocol deviations/violations/adverse events are reported.

6.2.8 The Monitoring Unit submits the copy of monitoring visit report through RO to the PI, IRB and if requested by the external sponsor.

6.2.9 Upon completion of the study activities, the PI informs the monitoring unit on the sponsor's close out visit.

6.2.9.1 The Monitoring Unit will be participating in the sponsor's closeout visit as necessary.

6.2.10 The Monitoring Unit reviews the sponsor's close out visit report to ensure compliance with ICH/GCP and applicable regulations and makes recommendations and raise issues, if necessary.

6.3 Quality Audits

6.3.1 The auditor will inform the PI and submit the audit plan two (2) weeks before the scheduled date with a copy to the Monitoring Unit.

6.3.2 PI makes the arrangements for the audit which will be facilitated by the Monitoring Unit.

6.3.3 The auditor conducts the audit on the schedule date and submits the audit report to the PI and Research Office. The PI will comply with the recommendations stated in the audit report.

6.3.4 The auditor conducts re-audit as required.

6.4 Regulatory Inspections

6.4.1 The regulatory authority(s) will inform the PI on the communication for inspection.

6.4 Regulatory Inspections

6.4.1 The regulatory authority(s) will inform the PI on the communication for inspection.

6.4.2 PI informs the Monitoring Unit of the schedule of regulatory inspection and the Monitoring Unit will facilitate the process and prepare the site along with the PI for the inspection by conducting a monitoring visit

6.4.3 The visit report will be communicated to PI and a copy to the RO and make action items/recommendations, if necessary before the inspection visit.

6.4.4 PI has to comply with the action items/recommendations as stated in the report.

7. RESPONSIBILITY

7.1 KAIMRC Research Quality Management Section, Research Office, Monitoring Unit and any other relevant sections and other departments of MNG-HA will be responsible for implementation of the provisions of this APP.

7.2 Internal Audit and Organizational Development will randomly monitor compliance to the provisions within this APP.

8. APPROVAL

PREPARED BY:

05 OCT 2015

DR. AHMED AL ASKAR
Executive Director, KAIMRC

DATE

REVIEWED BY:

11-oct-2015

SAAD AL OTAIBI
Executive Director
Internal Audit & Organizational Development, MNG-HA

DATE

APPROVED BY:

26 OCT 2015

H.E. DR. BANDAR AL KNAWY
Chief Executive Officer, MNG-HA
President, KSAU-HS

EFFECTIVE DATE

Appendix A

Monitoring Plan

This Monitoring Plan will be used in conjunction with Departmental Policy and Procedures for monitoring research studies established by the Monitoring Unit, King Abdullah International Medical Research Center (KAIMRC).

Investigator: _____

Protocol #: _____ **Title:** _____

_____

Locations

(Specify the location in which the study will be conducted)

Example:

MNG-HA - Central Region - ICU department.

Purpose

The purpose of the Monitoring Plan is to facilitate compliance with GCP guidelines, KAIMRC requirements and other applicable authorities' regulations, which require the Monitor to verify that:

- The rights and well-being of human subjects are protected
- Reported trial data are accurate, complete, and verifiable from source documents
- The conduct of the trial is in compliance with currently approved protocol, GCP guidelines and applicable regulatory requirements.

This document identifies key monitoring activities, the type and nature of data to be reviewed over the course of the research study.

Site Visit Confirmation

The Monitor will contact the Principal Investigator (PI) two (2) weeks in advance, in order to confirm a date and time for the monitoring visit.

After scheduling a visit with the PI, the following will occur:

- The Monitor will review previous monitoring reports in order to identify any unresolved issues.

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Study Staff Responsibilities and Training

(Specify any protocol specific training and delegation of responsibilities for study staff based on their role)

Frequency of Visits and Monitoring Activities

The Monitoring Unit will provide monitoring before, during and at the end of research studies.

In general, monitoring visits will be scheduled:

- Prior to enrolling the first subject and after IRB approval
- As soon as possible after the first subject is enrolled
- Every six to eight (6-8) weeks during the study data collection phase
- After the last subject has completed their participation in the study.

(Specify the frequency of monitoring visits for this research study)

The monitoring schedules for any specific research study may be revised, based on and not limited to the following reasons:

- History of serious adverse events/reports generated from the study
- History of protocol deviations/violations, and/or protocol non-compliance
- Complexity of the research study
- Subject enrollment rate
- IRB and/or research office request.

(Indicate who will be responsible for conducting monitoring visits)

Extent of Data Monitoring

(Indicate the extent of data monitoring for this research study)

For example:

- Review 100% of all informed consent forms.
- Review 100% of subject eligibility.

Scope of Monitoring (Monitors Responsibilities)

The Monitor's primary responsibilities (GCP 5.18.4), when relevant to the clinical trial/research study, are to:

1- Verify that the Investigator has adequate qualifications and resources (see 4.1, 4.2, 5.6) and remain adequate throughout the trial period, i.e., facilities including laboratories, equipment and staff are adequate to safely and properly conduct the trial and remain adequate throughout the trial period.

2- Verify that investigational product(s):

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i) Storage times and conditions are acceptable, and that supplies are sufficient throughout the trial.
ii) Are supplied only to subjects eligible to receive investigational product(s) and at the protocol-specified dose(s).
iii) Are provided with necessary instruction on proper usage, handling, storage, and returns process.
iv) Receipts, use and return at he trial sites are controlled and documented adequately.
v) Disposition (if unused) at the trial sites complies with applicable regulatory requirement(s), and in accordance with the sponsor.

3- Verify that the Investigator follows the approved protocol and all approved amendment(s), if any.

4- Verify that written informed consent has been obtained before each subject's trial participation.

5- Ensure that the Investigator receives the current Investigator's Brochure, all documents, and all trial supplies required to conduct the trial properly and to comply with applicable regulatory requirement(s).

6- Ensure that the Investigator and their trial staff are adequately informed about the trial.

7- Verify that the Investigator and their trial staff are performing the specified trial functions in accordance with protocol and any other written agreement between the sponsor and the Investigator/institution and have not delegated these functions to unauthorized individuals.

8- Verify that the Investigator is enrolling eligible subjects only.

9- Report the subject recruitment rate.

10- Verify that source documents and other trial records are accurate, complete and maintained.

11- Verify that the Investigator provides all required reports, notifications, applications and submissions, and that these documents are accurate, complete, timely, legible, dated, and identify the trial.

12- Check the accuracy and completeness of CRF entries, source documents and other trial-related records against each other. The Monitor should specifically verify that:

i) Data required by protocol is reported accurately on the CRFs and is consistent with source documents.
ii) Any dose and/or therapy modifications are well documented for each trial subject.
iii) Adverse events, concomitant medications and intercurrent illnesses are reported in accordance with protocol on the CRFs.
iv) Visits that subjects fail to attend, tests not conducted, and examinations not performed, are clearly reported as such on the CRFs.
v) All withdrawals and dropouts of enrolled subjects from the trial are reported and explained on the CRFs.

13- Determine whether all adverse events (AEs) are appropriately reported within the time periods required by GCP guidelines, protocol, the IRB/IEC, the sponsor and applicable regulatory requirement(s).

14- Determine whether the Investigator is maintaining essential documents (see 8. Essential Documents for the Conduct of a Clinical Trial).

15- Inform the Investigator of any CRF entry error, omission, or illegibility. The Monitor should ensure that appropriate corrections, additions, or deletions are made, dated, explained (if necessary), and

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initialed by the Investigator or a member of their trial staff authorized to initial CRF changes on behalf of the Investigator. This authorization should be documented.

16- Communicate deviations from protocol, SOPs, GCP guidelines, and applicable regulatory requirements to the Investigator, taking any appropriate action designed to prevent recurrence.

Study Files

(Indicate who will be responsible for monitoring the contents of study files and how often this will occur in order to ensure they are up to date)

Specify the type and nature of study files to be monitored, for example:

Protocol:

- Signed protocol
- Protocol amendments.

IRB:

- IRB protocol, CRF, Informed consent….etc approvals.
- Serious Adverse Event reports to the IRB.

Study Documentation

Verify all applicable documents are completed and maintained by the PI. The following are examples of essential documents that must be reviewed by the Monitoring Unit:

- IRB, FDA, and other regulatory documents (e.g. reports, correspondence)
- Signed Protocol
- Investigator Brochure
- Consent Form and IRB-approved information for subjects
- Randomization Procedure
- CRF's
- Investigator and Sub-Investigators CV or documentation of qualifications and training
- Site Signature Log/Delegation of Responsibility Log
- Lab Normal Ranges
- Lab Certifications
- Screening Log
- Enrollment Log
- Adverse Event Reports
- Adverse Event Log
- Correspondence
- Subject Code List
- Product Accountability Log (IDS Registry)
- Product Handling and Storage Instructions
- Product Shipping Records and Certificates of Analysis
- Record of Retained Samples
- Decoding Procedures for Blinded Trials
- Record Retention Plan.

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Monitor-Investigator Meeting

At the end of each monitoring visit, the Monitor will meet with the PI or Research Coordinator to discuss any findings.

Documentation of Findings

The Monitoring Unit will send a copy of the Monitoring Report to the Head of the Research Office, KAIMRC and may send the same report to the PI.

The Monitoring Report will describe the progress of the research study, the findings identified during monitoring visits, unresolved items and follow up requirements. The Monitor conducting the visit will sign and date each Monitoring Report. If major findings are identified during the visit, the signature of the Head of the Research Office is also required on the report.

The Monitoring Report usually contains, but is not limited to the following:

- A list of documents and records reviewed
- Subject accrual rate
- Number of Case Report Forms (CRFs) reviewed
- Assessment of Investigational Product (IP) accountability
- Protocol Compliance Assessment.

(Describe how data queries will be generated and processed by the PI)

Queries examples:

- Missing data
- Incomplete source documents
- Out of window subject visits.

Study Completion

(Describe how study close out procedures will occur)

For example:

- All remaining investigational products to be returned to the sponsor.
- Study files and data will be retained by the PI for a period of not less than three (3) years after the marketing approval of the investigational product.

Completed by:

Name (print) & Signature _____ Date _____

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Appendix B

Study Initiation Monitoring Checklist and Report

MONITORING UNIT,
KING ABDULLAH INTERNATIONAL MEDICAL RESEARCH CENTRE

Investigator _____

Site Name _____

Site location _____

Protocol # _____ Title _____

_____

STUDY PERSONNEL PRESENT DURING VISIT

Name	Title
Name	Title
Name	Title

	Study Initiation checklist	Yes	No	NA	Comments
	A. Personnel, Protocol, Administrative				
a.	CVs of the PI and all other research team members				
b.	Licenses, Certifications & Training Investigators, CRCs, others, as applicable and update as applicable				
c.	Original Signed Protocol				
d.	Original Investigator Brochure (IB)				
e.	Original Case Report Forms (CRFs)				
f.	Original Informed Consent (IC)				
g.	Information given to subjects, other than IC and CRF-related items, e.g. advertisements, study information brochures, etc				
h.	Original Clinical Trial Agreement (CTA)				
i.	Any Financial Aspect of the trial not covered in the CTA				
J.	Any conflict of interest observed both financially and non-financially				
k.	Insurance Statements, if applicable				
l.	Medical/Laboratory/Technical Information Location: Department/Address + Key Personnel Contacts Certification Accreditation Quality Control Assessment				

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	Other validations, as necessary				
m.	Normal Values, Ranges for tests, procedures in protocol - update annually				
n.	Others:				
	B. Sponsor, IRB, Regulatory				
a.	IRB/EC Identifying/Contact Information + Composition				
b.	IRB/EC Correspondence (approvals/disapprovals) before 1st subject screened: (a) Protocol (b) Informed Consent (c) Case Report Forms (d) Advertisements/Brochures/Other Information given to Subjects (e) Compensation Correspondence (f) Other Correspondence (g) Other Documents				
c.	Others:				
	C. Sponsor Information (Clinical, Legal and Financial)				
a.	Sample Labeling for investigational product container(s)				
b.	Instructions for handling product(s) and other trial-related materials				
c.	Shipping Records/Documentation for products and trial-related materials				
d.	Certificates of Analysis for products shipped				
e.	Others:				
	D. Regulatory Authority Documentations				
a.	Regulatory Approvals - Original				
b.	Correspondences with regulatory authorities				
c.	Others:				
	E. Protocol Requirements, procedures, processes & Documentations				
a.	Protocol Compliance				
b.	Study-Related Procedures				
c.	Informed Consent Process				
d.	Study Timelines				
e.	Subject Coding and Randomization				
f.	Eligibility criteria				
g.	Subject Enrollment				
h.	Source Documents Requirements				
i.	Laboratory Procedures				
j.	CRF completion & Guidelines				
k.	Specimen Management				
l.	Recording Adverse Events				
m.	Other Worksheets				
n.	Data Management Process				
o.	Inventory Control Records				
p.	Document Retention Requirements				
q.	Others:				

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	F. Study Team Roles Defined				
a.	Investigator				
b.	Sub-investigators				
c.	Research Coordinator				
d.	Research Pharmacist				
e.	Other study team members				
f.	Others:				
	G. Subjects				
a.	Inclusion/Exclusion Criteria				
b.	Master Schedule of Study Visits / Study Matrix				
c.	Blank, Current CRFs (see also under personal, protocol, administrative)				
d.	Instructions for Reporting Serious Adverse Events / Adverse Events, plus AE/SAE forms				
e.	Others:				
	H. Investigational Product				
a.	Storage and Dispensing				
b.	Required Records				
c.	Investigational Product Accountability				
d.	Inventory Disposition/Return/Destruction				
e.	Others:				
	I. Reporting Requirements				
a.	Data Reporting to IRB, KAIMRC, Sponsor				
b.	Protocol Reporting Requirements				
c.	Reporting Unexpected Events				
d.	Reporting AEs				
e.	IRB Reporting Requirements				
f.	Regulatory Reporting Requirements				
g.	Others:				
	J. Other Administrative				
a.	Any Legal Agreements with other Institutions, Departments, Individuals (sub-contractors, consultants, etc.), Companies (vendors)				
b.	Project Plan/Milestones				
c.	Payments Received from KAIMRC, Sponsor …etc				
e.	Others:				
	K. Monitoring				
a.	Monitoring Plan prepared				
b.	Monitoring procedures/Expectations				
c.	Access to source Documents				
d.	Access to CRF and Worksheets				
e.	CRF Queries & Corrections				

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f.	Monitoring compliance				
g.	Corrective Actions procedures				
h.	Investigator/Monitor Meetings				
i.	Others:				

Action Item/Issue	*Reviewed on*	*Monitor*

Recommendations for study Initiation:

- ☐ **I recommend initiating the study.**
- ☐ **I do not recommend study initiation at this time.**

Reason(s):

_____

_____

_____

Completed by:

_____ _____

Reviewed by (if applicable):

_____ _____

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APPENDIX-C REGULAR MONITORING VISIT REPORT

MONITORING UNIT

KING ABDULLAH INTERNATIONAL MEDICAL RESEARCH CENTER

Investigator _____

Site Name _____

Site location _____

Protocol # _____ Title _____

_____

_____

Date:

A. Since the enrollment started there was _____ subjects enrolled out of _____ subjects screened with _____ active subjects in follow-up. During this visit I have done _____ % SDV for _____ subjects.

B. Enrollment Rate is currently at _____%

C. **TRIAL MASTER FILE:**

S.NO.	*Issue Description*	*Action*

D. **INFORMED CONSENT FORM (ICF) ISSUES:**

S.NO.	*SUBNO.*	*Issue Description*	*Action*	*Monitor*

E. **CASE REPORT FORM(CRF) ISSUES:**

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S.No.	Sub.No.	Issue Description	Action	Status(Open/ Closed) If open mention the expected date of resolution

F. **SERIOUS ADVERSE EVENT(SAE) ISSUES(if applicable):**

S.No.	Sub.No.	Issue Description	Action	Status(Open/ Closed) If open mention the expected date of resolution

G. **SOURCE DOCUMENTS REQUIREMENTS:**

S.No.	Sub.No.	Issue Description	Action	Status(Open/ Closed) If open mention the expected date of resolution

H. **INVESTIGATIONAL PRODUCT(IP) ACCOUNTABILITY ISSUES:**

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S.No.	*Sub.No.*	*Issue Description*	*Action*	*Status(Open/Closed) If open mention the expected date of resolution*

I. **Protocol Deviations/Violations:**

S.NO.	*SUBNO.*	*Issue Description*	*Action*	*Monitor*

J. **Study Progress:**

_____

_____

K. **Investigators/Study Team member Meeting:**

_____

_____

L. **Next Expected monitoring visit Date:** _____/_____/_____

Though there are few pending activities for your study team, we are confident that you will guide your team to ensure all the activities are completed and corrective actions taken in a timely manner. We would very much appreciate your corrective actions; response/clarifications on those issues within _____weeks from the date of the original routine monitoring report form, **PI's response expected Date:** _____/____/____

We would like to thank you once again for your valuable time and support.

Should you require any clarifications and support from our side, I will be happy to revert back to you immediately. Please contact me at **Ext_____, Email: _____@ngha.med.sa**
Best Regards,

_____ _____

Name & Signature of Research Monitor **Date**

_____ _____

Name & Signature of Co-Monitor **Date**

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Appendix D

Study Closeout Monitoring Report

MONITORING UNIT

KING ABDULLAH INTERNATIONAL MEDICAL RESEARCH CENTRE

Part A: Study details:		
Name of investigator:		
Site name:		
Site location:		
Protocol Number:		
Study Title:		
Study personnel present during the visit:	Name	Designation
	1.	
	2.	
	3.	
	4.	
	5.	
	6.	
	7.	

Part B:Study Close out Documentation Checklist:

SRN	Criteria	Yes	No	N/A	Comments
a.	Resolve all outstanding data queries.	☐	☐	☐	
b.	Resolve any pending monitoring findings/action items.	☐	☐	☐	
c.	Pending biological specimens to the designated lab are shipped.	☐	☐	☐	
d.	After all protocol-specified laboratory testing is completed, archive or destroy all remaining stored specimens (specimens obtained from participants who did not provide informed consent for post-study specimen storage and possible future research testing must be destroyed).	☐	☐	☐	
e.	In accordance with instructions provided by the Protocol, return or dispose of all investigational drug/product supplies.	☐	☐	☐	

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f.	Review and assemble for long-term storage all required essential documents, including:	☐	☐	☐	
g.	Administrative and regulatory documentation are finalized	☐	☐	☐	
h.	Log linking participant names and ID numbers (which also serves as the completed participant identification code list required by ICH GCP guidelines)	☐	☐	☐	
i.	All study documents bearing participant names	☐	☐	☐	
j.	All study documents bearing participant ID numbers	☐	☐	☐	
k.	All study drug/product receipt, dispensing, accountability, and final disposition documentation	☐	☐	☐	
l.	Updated financial disclosure if any relevant changes occur in the course of the study or for one year following completion of the study, if applicable	☐	☐	☐	
m.	Final report by investigator to IRB/EC as required and as applicable to regulatory authorities.	☐	☐	☐	
n.	Clinical study report finalized.	☐	☐	☐	
o.	Prepare for and take part in a study close-out visit; resolve all visit findings/queries; and file all visit documentation with other study documentation.	☐	☐	☐	
p.	To the extent possible, organize and categorize all study documentation according to ICH GCP guidelines (ICH E6, Section 8.4). Prepare a written inventory of all documentation and storage locations. Documents must be stored securely and with adequate protection of participant confidentiality according to ICH E6, 4.9.5 for IND studies. Documents must be stored securely and with adequate protection of participant confidentiality a period of 3 years (on site) after publication (or	☐	☐	☐	

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	decision not to publish) for non-IND studies.				
q.	Discuss data entry and analysis plans/procedures with the PI.	☐	☐	☐	
r.	Discuss data lock with the PI.	☐	☐	☐	
s.	Discuss the PI's obligations for publications.	☐	☐	☐	
t.	Complete, sign and date this checklist. File original with other study documentation	☐	☐	☐	
u.	Other observations:				

Part C: Recommendations:	
Recommendations:	☐ **Recommend study close out**
	☐ **Close out not recommended**
Comments:	
Prepared by:	
Date of submission to RO	Click here to enter a date.
Approved by:	
Date of dispatch:	Click here to enter a date.

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