In Search Of Better Health

K E M R I

STANDARD OPERATING PROCEDURE FOR PROTOCOL DEVIATIONS, VIOLATIONS AND NON-COMPLIANCE

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1. PURPOSE

This SOP describes the procedures for recording and reporting protocol deviations, protocol violations and non-compliance in research studies to KEMRI SERU.

2. SCOPE

This SOP applies to all research investigators and research personnel involved in study conduct or oversight of study conduct. Non-compliance can be reported by other individuals (may be done anonymously) via telephone, email or letter to the SERU; this is covered under the SOP entitled *Research Complaints and Concerns*.

3. INTRODUCTION

Investigators are responsible for ensuring that their research is carried out as approved by SERU and in accordance with applicable scientific, ethical and regulatory requirements; but there are instances when the research does not follow this plan. Such occurrences can have a negative impact on research participants.

Protocol violations and non-compliances can alter the risk-benefit ratio for participants or may otherwise jeopardise in some way the safety, rights, and welfare of subjects. On the other hand, there are certain times when it is necessary to deviate from the approved protocol or continue aspects of the research during a lapse in approval in order to protect participants.

Regardless of the reason behind them, all protocol deviations, violations and non-compliances must be reported to and reviewed by the SERU. Such reports are considered possible non-compliances until a determination has been made by SERU. This guidance outlines the reporting responsibilities for protocol deviations, violations and non-compliances.

4. TERMS & DEFINITIONS

4.1 Protocol deviation - a departure from the approved study protocol or study procedure(s) that has not been approved by SERU, which **does not** increase risk or decrease benefit or; **does not** have a significant effect on the subject's rights, safety or welfare; and/or on the integrity of the data. Deviations may result from the action of the participant, researcher, or research staff.

4.2 Protocol violation- a departure from the approved study protocol or study procedure(s) that has not been approved by SERU, which **does** increase risk or decrease benefit or; **does** have a significant effect on the subject's rights, safety or welfare; and/or on the integrity of the data or the scientific conduct.

4.3 Non-compliance- failure to comply with applicable institutional/SERU policies and/or procedures, or applicable regulatory requirements relevant to the conduct of the research

4.4 Continuing non-compliance- a repeated pattern or unrectified instance of non-compliance Definition: Failure to comply with applicable institutional/SERU policies and/or procedures that does/does not affect the rights, safety, and/or welfare of participants, or the quality of research data in a repeated pattern or unrectified.

4.5 Minor non-compliance- non-compliance that does not affect the rights, safety, and/or welfare of participants, or the quality of research data

4.6 Major non-compliance- non-compliance that affects the rights, safety, and/or welfare or participants, or the quality of research data

4.7 Self-reporting- for non-compliances reported by the PI or designee

4.8 Hazard-a potential source of harm or adverse health effect

5. OBJECTIVES

To ensure protocol deviations, violations and non compliance are reported in a timely manner.

6. INPUTS/RESOURCES

6.1 Personnel
6.2 Stationery and office equipment
6.3 Email
6.4 Phone

7. EXPECTED OUTPUTS

7.1 Agenda

7.2 Record of received application

8. KEY PERFORMANCE INDICATORS

8.1 No. of protocol deviations received

9. RESPONSIBILITY AND AUTHORITY

9.1 Principal Investigator

Investigator: - to report protocol deviations, violations or non-compliances to SERU. The P.I, to the best of their ability, determines whether a departure from study protocol or procedures constitutes a deviation or a violation and whether non-compliance is major or minor.

SERU Secretariat: - The SERU Centre Compliance Officer receives, pre-reviews and records all protocol deviation applications submitted to SERU

10. DETAILS OF PROCEDURE

10.1 Protocol Deviations and Minor Non-compliance

Provide to the SERU a summary of protocol deviations and self-reported minor non-compliance that occurred during the prior SERU approval period at the time of continuing approval request.

10.2 Protocol Violations

10.2.1 Notify the SERU of any protocol violation(s) no later than 48 hours after becoming aware of the event by email (seru@kemri.org).

10.2.2 Complete the protocol violation form and submit to the SERU, in hard copy, no later than 10 working days after discovery of the event.

10.3 Changes to Remove a Hazard

10.3.1 Notify the SERU of any protocol violation(s) no later than 48 hours after becoming aware of the event by email (seru@kemri.org).

10.3.2 If a protocol change has been initiated to remove an apparent immediate hazard to one or more study participants, report this change as per the *KEMRI SERU APP SOP 2.0 Amendments to Research Studies* to the SERU prior to implementation.

10.3.3 Complete the protocol violation form and submit to the SERU, in hard copy, no later than 5working days after initiation of the change.

10.4 Major and Continuing Non-Compliance

10.4.1 Notify the SERU of any protocol violation(s) no later than 48 hours after becoming aware of the event by phone (+254717719477) or email (seru@kemri.org)

10.4.2 Complete a non-compliance reporting form and submit to SERU no later than 10 working days after discovery of the event.

10.4.3 Promptly respond to all SERU communications, including request for action, information, or instructions.

11. RISKS AND OPPORTUNITIES

11.1 Risks

Process	Risk	Risk source	Mitigation
Protocol deviations, violation and compliance	Endangering lives of research participants	Delay in informing the Review board	Submit the notification as soon as they are noted in the field

11.2 Opportunities

Process	Opportunities	Action plan to maximise the opportunities
Protocol deviations, violation and compliance	Electronic notification	Have an electronic notification system to be used by the field officer

12. REFERENCE DOCUMENTS

1.1. External References

ICH GCP guidelines Sections 4.5, 5.20:
https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R1_Guideline.pdf

13. ANNEXES

13.1 Examples of protocol deviations, violations and non-compliance

13.2 Protocol deviation form

13.3 Protocol violation form

13.4 Process Flow Chart

Annex 1: EXAMPLES OF PROTOCOL DEVIATIONS, VIOLATIONS, NON COMPLIANCE FOR GUIDANCE

(The following are just examples for guidance but are not limited to these)

1) PROTOCOL DEVIATIONS

Examples:

a) Trial visit conducted outside of required timeframe

b) Failure of participant to return trial medication

c) Missed study visits

2) PROTOCOL VIOLATIONS

Examples:

a) Failure to perform a required safety assessment

b) Inclusion/exclusion criteria not met

c) Improper breaking of the blind

d) Incorrect or missing tests

e) Mishandled samples

f) Multiple visits missed or outside permissible windows

g) Accidental distribution of incorrect study medication or dose

3) MINOR NON COMPLIACE

Examples:

a) single instance of failure to submit a continuing review progress report to the IRB in time to prevent the lapse of approval

b) Administrative errors

4) MAJOR NON COMPLIANCE

Examples:

a) Conducting of Continuing a Non exempt human research activity without IRB approval

b) Written informed consent not appropriately obtained before initiation of trial-related procedures).

c) Failure to submit serious adverse events, unanticipated problems in line with IRB regulations

d) Initiating changes to the research protocol without prior IRB approval unless the change is necessary to eliminate apparent immediate hazards to the subject

e) Failing to take IRB or institutionally required human subjects protection training;

f) Enrolling more subjects than approved by an IRB

g) Failing to have research participants sign a new consent form when new and relevant risks are discovered or failing to provide this new information to participants

h) Altering an IRB-approved consent process or an IRB-approved recruitment process without prior IRB approval

i) Loss of laptop computer that contained identifiable, private information about subjects

5) CONTINUING NON COMPLIANCE

Examples

a) Repeated failures to provide Continuing or progress reports

b) Inadequate oversight of ongoing research

c) Failures to resolve previous non compliances.

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ANNEX 2 AND 3: SAMPLE PROTOCOL DEVIATION OR VIOLATION REPORTING FORM

APPENDIX 2: SAMPLE PROTOCOL DEVIATION OR VIOLATION REPORTING FORM

Version Number 4.0
Effective Date: 3 September 2009
Supersedes

Title of Proposal:
Principal Investigator(s)
SSC/NON-SSC No.:

1. Date of Deviation/Violation:

2. Study Participant number (where applicable):

3. Name of treating physician (where applicable):

4. Provide a description of the deviation/violation: State whether the study participants were adversely affected by the deviation/violation; whether the deviation/violation placed the study participants at greater risk and whether the study participants were informed of the deviation/violation, where applicable.

5. Provide an explanation as to why the deviation/violation occurred.

6. Describe the measures taken to address the deviation/violation.

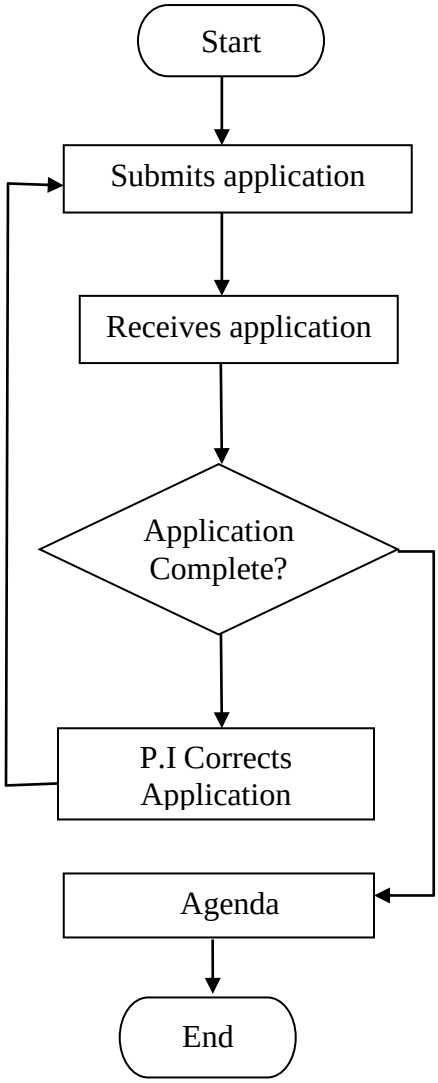
7. Describe the measures taken to preclude future recurrence of the deviation/violation.

8. Indicate whether the study sponsor has been notified.

_____ _____

Typed name and signature of the PI Date:

ANNEX 4: PROCESS FLOW CHART

Players	**Activity**	**Flow Chart**
Principal Investigator	Submitting protocol deviations, violations and non compliance applications to SERU	
Centre Compliance Officer	Receives, pre-reviews and records all protocol deviations, violations and non compliance applications submitted to SERU	