NAMA DOKUMEN:	**MEDICAL RESEARCH ETHICS COMMITTEE (MREC)** **STANDARD OPERATING PROCEDURE FOR POST APPROVAL REVIEW**	
NOMBOR DOKUMEN:	**KOSONGKAN**	**MUKA KULIT**
TARIKH KELULUSAN:	**KOSONGKAN**	
TARIKH BERKUATKUASA:	**KOSONGKAN**	
TARIKH KAJISEMULA:	**KOSONGKAN**	
PENULIS DOKUMEN:	**PROF. DR. NG CHIRK JENN**	
DISEMAK OLEH:	**MEDICAL RESEARCH ETHICS COMMITTEE**	
DILULUSKAN OLEH:	**KOSONGKAN**	
DISAHKAN OLEH WAKIL PENGURUSAN:	**KOSONGKAN**	

Tarikh Berkuatkuasa:	**KOSONGKAN**
No. Kajisemula:	

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ABBREVIATIONS

ABBREVIATION	FULL TEXT
GCP	Good Clinical Practice
IEC	Independent Ethics Committee
IRB	Institutional Review Board
MREC	Medical Research Ethics Committee
PI	Principal Investigator
UMMC	University of Malaya Medical Centre

1.0 INTRODUCTION

Post approval monitoring of studies is an important function of any Ethics Committee. The UMMC-MREC complies with requirements of the MGCP in post approval monitoring of studies to ensure studies are conducted in compliance with approved protocols and safety of subjects are continuously assured.

2.0 OBJECTIVES

This SOP aims to detail out how the MREC reviews post approval submissions by PIs, conduct of site visits, and how queries and complaints are handled. Submissions may undergo either expedited or full board review. The SOP describes the submission procedures, required forms, documentation of decision, communication of decision to the PI, and filing of related documents.

3.0 SCOPE

This SOP applies to all studies approved by UMMC-MREC. Post approval submissions that are reviewed include requests for amendments, progress reports (including annual study reports), study closure reports, non-compliance (deviation or violation) reports, early study termination applications, queries from stakeholders, serious adverse event reports (SAEs), and suspected unexpected serious drug reactions (SUSARs).

4.0 RESPONSIBILITIES

It is the responsibility of PIs to comply with post approval review requirements, including the submission of the following reports:

- Amendments
- Protocol deviations
- Protocol violations
- SAEs and SUSARs
- Annual and closure

The Secretariat Staff is responsible for receiving and processing all submissions, including inquiries or complaints from research participants and other stakeholders.

The MREC Chair/Deputy Chair is responsible for determining whether these post approval submissions undergo expedited or full board review. Expedited review will

be done by the Chair/Deputy Chair and endorsed by full board at the soonest meeting.

MREC members are responsible for discussing and deciding on the submissions forwarded for full board review.

5.0 GENERAL WORKFLOW OF REVIEW OF POST APPROVAL SUBMISSIONS

ACTIVITY	RESPONSIBILITY
Receive and manage document submission	Secretariat Staff
Submit documents to the MREC Chair/Deputy Chair to determine classification of review as expedited or full board	Secretariat Staff
Classifies submission for expedited review or full board meeting	MREC Chair/Deputy Chair
Review submissions via expedited review and arrive at decision. Presents review decision to full board for endorsement.	MREC Chair/Deputy Chair
Review submissions in full board meeting and decide on approval	MREC members
Communicates decisions to PIs	Secretariat Staff
Files submitted documents	Secretariat Staff

Flowchart for the processes is shown in Fig. 1 below.

Fig. 1. Flowchart of procedures for processing submissions of amendments, protocol non-compliances, progress reports, study closure reports, SAE and SUSAR reports.

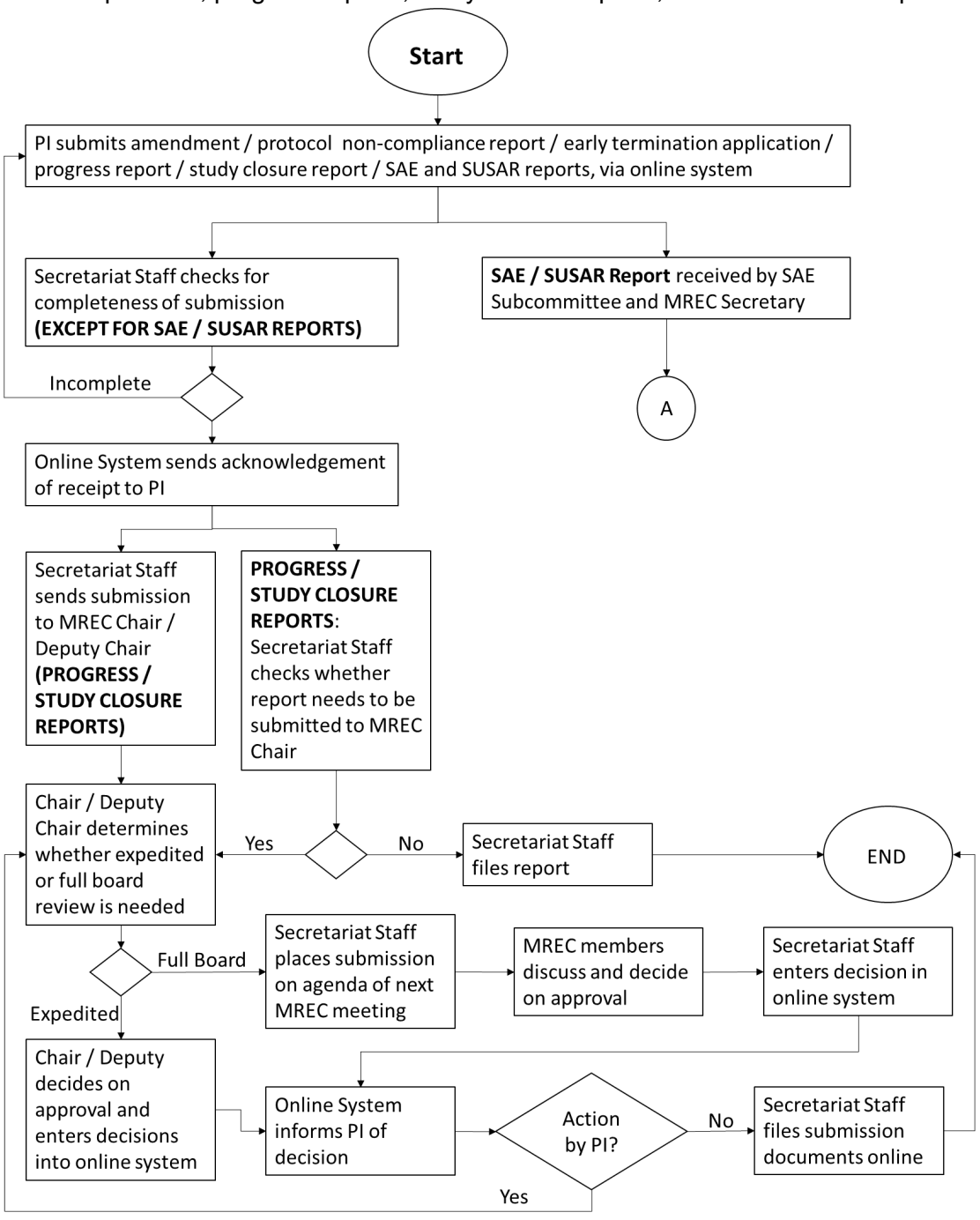
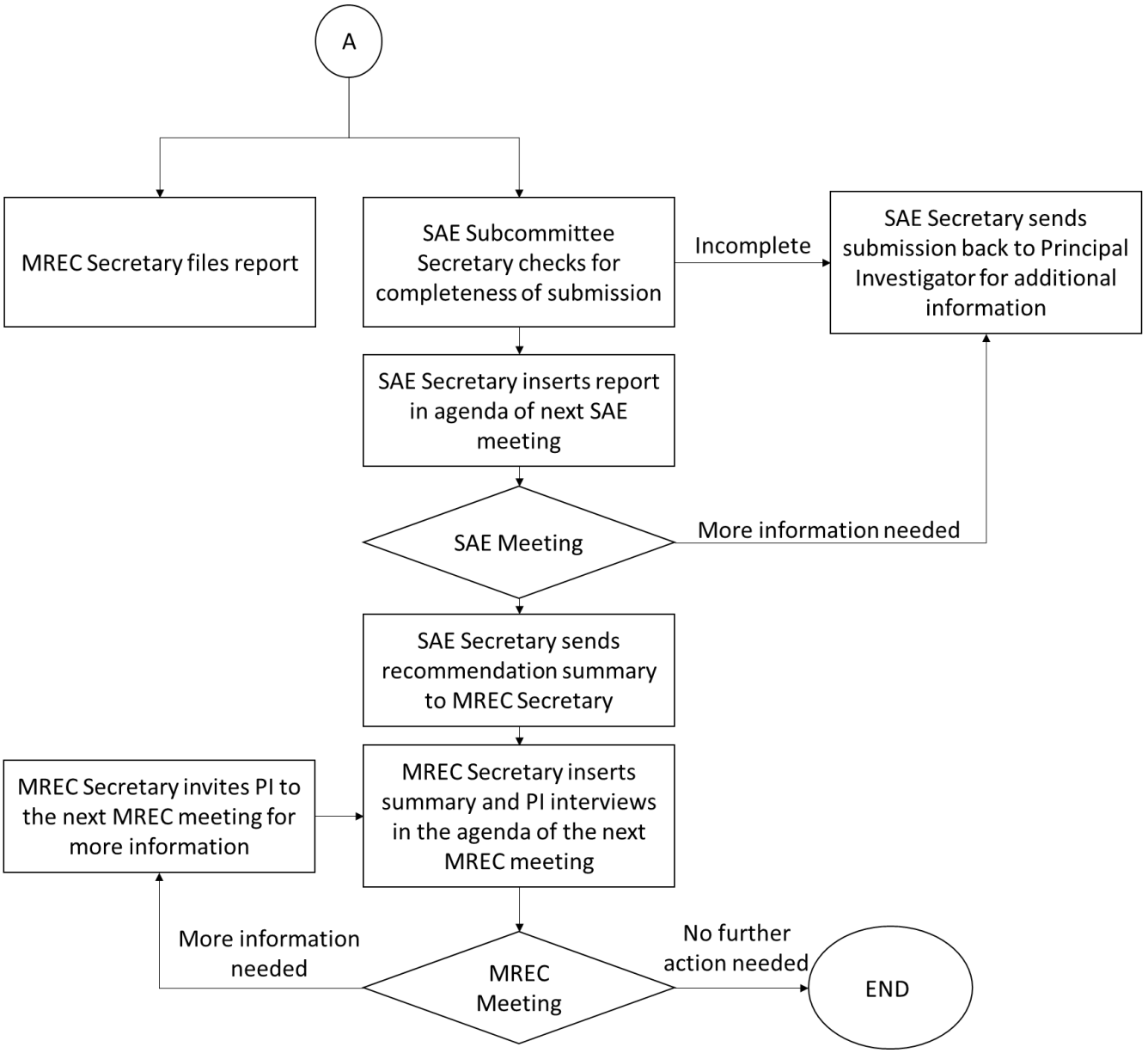


Fig. 1: Continued



5.1. Study Protocol Amendment

5.1.1. Management of the Study Protocol Amendment Documents

A study protocol amendment is a change to contents of approved study documents. Approval should be obtained from the MREC prior to the implementation of an amendment.

Amendments for studies that are approaching the original study completion date or nearing the expiry date of MREC approval, and requesting for extension of the completion date or ethics approval, should be submitted to MREC via the online system at least 30 days prior to the expiry date.

The online system logs the date of submission of any amendment submitted online.

The Secretariat Staff checks submissions for completeness and sends acknowledgement of receipt of the submission to the PI via the online system.

5.1.2. Classification of Review by the MREC Chair

The Secretariat Staff forwards all submitted amendments to Chair/Deputy Chair who decides within 14 working days of submission, whether the amendments are minor or major.

Amendments that satisfy the following criteria are considered minor and qualify expedited review:

- Involves administration changes that do not change the way the study is conducted
- Involve changes to the original study document that do not significantly increase risk to subjects

An amendment is considered major if the amendment increases risk to study participants, such as a change in study design, that may include but is not limited to:

- Additional treatments or omission of treatments
- Any changes in inclusion/exclusion criteria
- Change in drug formation, (e.g. oral changed to intravenous)
- Significant change in number of subjects

- Significant decrease or increase in dosage

Major amendments shall undergo full board review.

5.1.3. Review by MREC Chair/Deputy Chair

The MREC Chair/Deputy Chair shall determine within 14 working days whether an amendment will undergo expedited or full board review according to the above stated criteria.

For expedited review, a decision is made by the MREC Chair/Deputy Chair within 14 working days of receipt of the submission. The Chair/Deputy Chair enters the decision in the online system. The possible decisions are:

- Approve
- Decision deferred until further information is received
- Modifications required
- Disapprove

The Secretariat Staff shall place amendments that require full board review on the agenda for the next MREC meeting. Amendments shall be reviewed not later than 30 working days after classification by the Chair.

5.1.4. Full Board Review of Study Protocol Amendment Submission Documents

MREC members review submitted amendments documents online before the MREC meeting. The Chair will table amendments and members shall discuss and decide on approval. The possible decisions are:

- Approve
- Decision deferred until further information is received
- Modifications required
- Disapprove

The Secretary will record the decisions and enter them into the online system.

5.1.5. Communication of Decisions

The online system will issue a letter within 7 working days of the MREC meeting, to the PIs notifying them of the MREC decisions including which amended documents are approved.

5.1.6. File Management

Amended study documents with new version numbers and dates are archived in the online system with the approval date. Newly approved documents will supersede previous versions in the online system.

5.2. Study Protocol Noncompliance (Deviation/Violation) Report

5.2.1. Management of Submitted Noncompliance Reports

The investigator should document and report to the MREC any noncompliance from the approved protocol, whether minor or major, at the soonest possible time via the online system. Other supporting documents that helps to clarify the noncompliance should be submitted as well.

Investigators may implement a deviation to eliminate an immediate hazard(s) to study subjects without prior MREC approval, but must submit an online report as soon as possible.

The Secretariat Staff checks the submission for completeness and acknowledges the receipt of the submission to the PI via the online system. The online system logs the date of submission.

5.2.2. Classification of Review by the MREC Chair/Deputy Chair

The MREC Chair/Deputy Chair determines the submission for either expedited or full board review.
Minor or administrative deviations that do not affect the scientific soundness of the study protocol or compromise the rights, safety, or welfare of human participants in the study shall undergo expedited review.
Major deviations or protocol violations that are persistent protocol noncompliance with potentially serious consequences that could critically affect data analysis or put patients' safety at risk shall undergo full board review.

5.2.3. Review by MREC Chair/Deputy Chair

The MREC Chair/Deputy Chair reviews all study protocol noncompliance submission documents together with the originally approved protocol within 14 working days of forwarding by the Secretary, to determine the type of review required.

For submissions under expedited review, a decision is made at the level of the MREC Chair/Deputy Chair within 14 working days of submission of the amendment. The Chair/Deputy Chair will enter the decision in the online system.
The Chair/Deputy Chair can make any of the following decisions:

- No action needed
- Decision deferred until further information is received
- Table for full board meeting

For any report requiring full board review, the Secretariat Staff places the noncompliance report on the agenda for the next MREC meeting. The report will be reviewed within 30 working days of classification of the report by the Chair.

5.2.4. Full Board Review of Noncompliance Report

The Chair shall table noncompliance reports at the MREC meeting. Members shall review the noncompliance report and other supporting documents.
The MREC members shall deliberate and decide on appropriate action based on the type and severity of impact of the noncompliance.
The MREC can make any of the following decisions:

- No action needed
- Reprimand to PI to avoid similar noncompliance in the future
- Suspend ethics approval or recruitment of subjects until noncompliance issues are addressed
- Withdraw ethics approval for the following noncompliance: (a) fraud, and (b) unresolved serious safety issues

The Secretary shall record all discussions and decisions and enters the information in the online system.

5.2.5. Communication of Decisions

The online system will send within 7 working days of the MREC meeting, an email to PIs to notify them of the MREC decision.
The PI may be requested to provide additional information, submit additional documents, or implement a corrective and preventive action.

5.2.6. File Management

All noncompliance reports and supporting documents shall be archived in the online system.

5.3. Early Study Termination Application

5.3.1. Application for Early Study Termination

An application for early termination of an approved study is submitted when (a) it is recommended by MREC when safety of the study participant is doubtful or at risk, and (b) upon the request of the PI or the sponsor owing to the existence of unresolvable issues.

The application is submitted online together with documents deemed relevant by the investigator to support or clarify information stated in the application.

Secretariat Staff checks the submission for completeness and sends an online acknowledgement of receipt of the submission to the PI. The online system logs the date of submission.

5.3.2. Classification of Review by MREC Chair

The MREC Chair reviews all early study termination application documents together with the originally approved protocol within 14 working days of submission, to determine whether the early termination will change the original risk-benefit assessment. Termination that changes the assessment will undergo full board review, otherwise the application will undergo expedited review by the Chair.

5.3.3. Expedited Review by MREC Chair

For submissions under expedited review, a decision is reached by MREC Chair within 14 working days of selection for expedited review. The Chair/Deputy Chair will enter the decision in the online system. The possible decisions are:

- Approve
- Decision pending submission of more information
- Further action required
- Table for full board meeting

5.3.4. Full Board Review of Early Study Termination Application

Secretariat Staff will place the early study termination applications on the agenda for the next MREC meeting. The application will be reviewed within 30 working days of classification of the report by the Chair.

The MREC will deliberate on the implications of the application on the rights, safety, and welfare of the study participants. PIs may be required to adopt specific provisions for continued protection and dissemination of specific information to the study participants. The MREC may request more information from the PI or invite the PI for an interview. The MREC can make one of the following decisions:

- Approve
- Decision pending submission of more information
- Further action required
- Disapprove

The Secretary records the discussion and decision, and enters the information into the online system.

5.3.5. Communication of Decisions

The PI is notified of the committee's decision via email by the online system within 7 working days of the MREC meeting.
If the application is approved, the PI is requested to complete a study closure report (BK-QSU-025-E01).

5.3.6. File Management

The early study termination application documents will be stored in the online system.

5.4. Progress Reports (including Annual Study Reports)

5.4.1. Submission of Progress Reports (including Annual Study Reports)

Ethical approval is typically granted for the duration of the study. After approval, progress reports are required at least once a year, depending on the risk assessment of the study protocol, and determined during the initial review. Progress reports that are required to submitted once a year is referred to as Annual Reports. Submission of the progress/annual report using form BK-QSU-025-E01 **(Appendix 1)** is via the online system.

The frequency of reports is indicated in MREC approval letter. The online system will send reminders to PIs at 30 working days before the due date of a report.

The Secretariat Staff checks the submission for completeness and sends an acknowledgement of receipt of the report to the PI via the online system. The online system logs the dates of submission and acknowledgement.

5.4.2. Action on the Progress Report by the Secretariat Staff

The Secretariat Staff will screen the progress report within 14 working days of receipt, for the following matters on concern:

- 5 or more SAEs
- 5 or more protocol deviation/violation
- No subject was recruited

If a study reported any of the above, it will be forwarded to the MREC Chair/Deputy Chair for further action. If none of the above is reported, the progress report will be filed and no further action will be taken.

5.4.3. Review by the MREC Chair/Deputy Chair

The MREC Chair/Deputy Chair reviews the report within 14 working days from notification by the Secretariat Staff and enters decision in the online system. The MREC Chair/Deputy Chair will decide on the following action to be taken:

- No further action required
- Decision pending submission of more information
- Suspension of ethics approval for the study
- Table for full board review
- Forward to SAE subcommittee for action
- Forward to Site Visit committee for action
- Other action to be determined by the Chair/Deputy Chair

For progress reports requiring full board review, the Secretariat Staff places the progress report on the agenda for the next MREC meeting. Reports will be reviewed within 30 working days of receipt of the report.

If necessary, the PI will be interviewed at the meeting.

5.4.4. Full Board Review of Progress Reports (including Annual Study Reports)

The MREC members deliberate the progress report (including annual study report) at the meeting and decide on action to be taken.

The Secretary records all discussions and decisions, and enter the information in the online system.

5.4.5. Communication of Decisions

The online system will email the PI within 7 working days of the MREC meeting, stating the decision of the MREC and any actions to be taken.

5.4.6. File Management

The progress reports and related documents will be stored in the online system.

5.5. Study Closure Report

5.5.1. Submission of Study Closure Report

Upon completion of the study, the PI should provide the MREC with a summary of the outcome of the study, especially regarding human participants, in a study closure report. If no report is submitted, the online system will send a reminder to the PI within 30 working days of the planned date of completion of the study. The reminder will state that if no report is submitted, the study will be automatically closed by the system 6 months after the planned completion date, and no further action on the study will be taken by MREC.

The report will be submitted online using form BK-QSU-025-E01 together with documents deemed relevant by the investigator to clarify information indicated in the report.
The Secretariat Staff checks the submission for completeness and acknowledges the receipt of the submission to the PI via the online system. The online system logs the dates of submission and acknowledgement.

5.5.2. Actions on the Study Closure Report by the Secretariat Staff

Secretariat Staff will screen the reports for any of the following matters of concern:

- 5 or more SAEs
- 5 or more protocol deviations/violations
- No subject was recruited

If a study reported any of the above, it will be forwarded to the MREC Chair/Deputy Chair for further action. If there is none, the report will be filed and no further action will be taken.

5.5.3. Classification of Review by the MREC Chair/Deputy Chair

The MREC Chair/Deputy Chair reviews the report within 14 working days from notification by the Secretariat Staff and enters the decision in the online system. The MREC Chair/Deputy Chair may choose any of the following decisions:

- Approve, no further action required
- Decision pending submission of more information by PI
- Table for full board review
- Forward to SAE subcommittee for action
- Forward to Site Visit subcommittee for action
- Any other action as identified by the Chair/Deputy Chair

For reports requiring full board review, the Secretariat Staff places the reports on the agenda for the next MREC meeting.

The reports shall be reviewed within 30 working days of classification by the Chair.

If necessary, the PI will be interviewed at the meeting.

5.5.4. Full Board Review of Study Closure Report

The MREC members will deliberate and decide on the action to be taken at the full board meeting.
The Secretary will record and enter all discussions and decisions in the online system.

5.5.5. Communication of Decisions

The online system will notify the PI by email within 7 working days after the MREC meeting, of the MREC's decision, noting the action to be taken by the PI.

The PI will be informed of the following if the report is approved:

- The study account in the online system will be locked and no new information can be entered into the system.
- Ethics approval will expire effective from the date of the MREC approval.

Records of study documents will be made available for three (3) years in the archives after the expiration date of ethics approval.

5.5.6. File Management

Study closure reports and supporting documents shall be archived in the online system, upon approval of the final report, when no further action is expected from the PI. The study file will be labelled as “TUTUP”.

5.6. Serious Adverse Event (SAE) And Suspected Unexpected Serious Adverse Reaction (SUSAR) Reports Workflow

5.6.1. Definitions

The reporting of the SAE and SUSAR is based on the Malaysian Guideline for Safety Reporting of Investigational Products.

Adverse Events

Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment.

Adverse Drug Reactions (ADR)

All noxious and unintended responses to a medical product related to any dose should be considered adverse drug reactions. The phrase “responses to a medicinal product” means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e. the relationship cannot be ruled out.

Unexpected Adverse Drug Reaction

An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g. Investigator’s Brochure for an unapproved investigational medical product).

Serious Adverse Event or Serious Adverse Reaction

A serious adverse event (SAE) or serious adverse drug reaction (Serious ADR) is any untoward medical occurrence that at any dose that:

- Results in death
- Is life-threatening (places the subject at immediate risk of death from the event as it occurred)
- Requires inpatient hospitalization or prolongation of existing hospitalization
- Results in a persistent or significant disability/incapacity
- Results in a congenital anomaly/birth defect

- Based upon appropriate medical judgement, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition

Expectedness of the Adverse Drug Reaction
An "unexpected" adverse reaction is one, the nature or severity of which is not consistent with information in the relevant source document(s). Until source documents are amended, expedited reporting is required for additional occurrences of the reaction.

5.6.2. Submission of Reports

Investigators must report information that may influence the risk-benefit assessment of a medicinal product or that would be sufficient to consider changes in medicinal product administration or in the overall conduct of a clinical investigation. Examples include:

- Single cases of SUSAR
- For an "expected", serious ADR, an increase in the rate of occurrence which is judged to be clinically important
- A significant hazard to the patient population, such as lack of efficacy with a medicinal product used in treating life-threatening disease
- A major safety finding from a newly completed animal study (such as carcinogenicity)

SAE or SUSAR from the following do not need to be reported:

- Clinical Trial not conducted in UMMC site
- Suspected drug is known to be other than the investigational product (e.g. other study treatments, placebo or comparator drug)

The reporting will commence from the date of MREC approval and continue till all trial sites in UMMC are closed.

The reporting timeframe for the investigator for the MREC and type of report to be submitted are as follows:

- Serious Adverse Event (SAE) or Suspected Unexpected Serious Adverse Reaction (SUSAR) that is fatal/life threatening: As soon as possible but not later than 7 calendar days from awareness of event by investigator, followed by a complete report within 8 additional calendar days.

- All other SUSARs: As soon as possible but no later than 15 calendar days from awareness of event by investigator. Follow up information should be actively sought and submitted as it becomes available.

PIs must report online using form BK-MIS-1118-E01 **(Appendix 2)**, all SAEs and SUSARs, together with other documents deemed relevant by the investigator to clarify information indicated in the report.

The SAE Subcommittee Secretary will check the submission for completeness and acknowledges receipt of the submission to the PI via the online system. The online system logs the dates of submission and acknowledgement.

5.6.3. Review of SAE and SUSAR Reports

The SAE Subcommittee Chair will screen the reports and table them for the next SAE Subcommittee meeting, which are held the week before an MREC meeting. All SAE Subcommittee members will have access to the study protocol and relevant documents via the online system.

The SAE Subcommittee Secretary will fix the date for the SAE Subcommittee meeting and notify all Subcommittee members at least 7 working days before the meeting.

The SAE Subcommittee meets to make recommendations which will be present at the MREC meeting by the SAE Subcommittee Chair or a representative of the subcommittee. The SAE Subcommittee Secretary will email the recommendations to the MREC Secretary then the MREC Secretary will table them for the next MREC meeting. SAE reports shall be discussed at the MREC meeting within 30 days of the Secretariat receiving the recommendations from the SAE Subcommittee meeting.

During the meeting, the MREC Chair calls for a decision on the SAE report(s) with respect to the recommendation(s) of the SAE Subcommittee as presented by the SAE Subcommittee Chair. The MREC may take any of the following actions:

- No further action
- Recommend further action

- Decision pending submission of more information or major clarifications
- Suspension of ethics approval or recruitment of subjects until issues are resolved.

The Secretary records all discussions and decisions and enters the information in the online system.

5.6.4. Communication of Decisions

The PI is notified online by an email, within 7 working days of the MREC meeting, of the MREC decision, noting actions to be taken on the Serious Adverse Event(s) Report.

The PI may be requested to provide additional information, submit additional documents, or implement corrective action.

5.6.5. File Management

The SAE reports and related documents will be archived in the online system.

6.0 SITE VISIT WORKFLOW

ACTIVITY	PERSON REPONSIBLE
Select study sites to visit	Site Visit Subcommittee Chair
Notify PI of date of site visit	Secretariat Staff
Create Site Visit Team	Site Visit Subcommittee Chair
Conduct Site Visit	Site Visit Team
Present findings during MREC meeting	Site Visit Subcommittee Chair
Communicate results of Site Visit and subsequent MREC action to PI	Secretariat Staff
Manage Site Visit documents	Secretariat Staff

See flowchart in Fig. 2 on the following page.

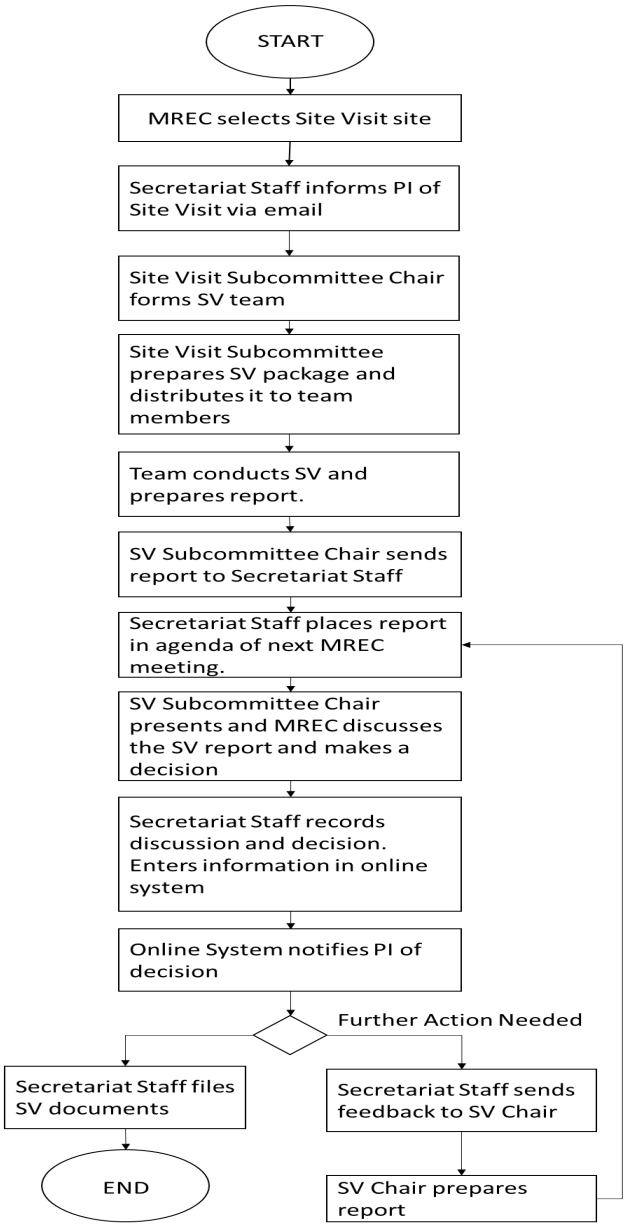


Fig. 2: Flowchart of Site Visit

6.1. Selection of Study Sites

Study sites may be selected for Site Visits based on the following criteria:

- The nature of the study being conducted (i.e. high-risk studies)
- Frequent failure to submit progress reports
- Reports of major protocol noncompliance
- Significant number of serious adverse events
- Reports of complaints from study participants and other stakeholders

Site Visits may be conducted upon the recommendation of the MREC.
Study sites may also be selected for a Site Visit upon the recommendation of the SAE Subcommittee.

6.2. Notification of PI of the Date of Site Visit

The Site Visit Subcommittee Chair, through the Secretariat, will inform the PI at least 10 working days before the scheduled visit through an email. A copy of the MREC Site Visit Form **(Appendix 3)** is attached to the email.
The email will provide Site Visit schedule details and instructions on what the PI needs to prepare such as documents and files that will be reviewed during the Site Visit, as well as orderly preparation of the site.

6.3. Creation of a Site Visit Team

A Site Visit (SV) team is organized for each site visit. The members of this team are assigned (and appointed for non-Subcommittee members) by the SV Subcommittee Chair. The term of appointment of non-Subcommittee members will end when the site visit is closed.

The SV team shall be composed of at least three people, including the SV Subcommittee Chair and one SV Subcommittee member. Additional team members could include staff from UMMC Clinical Investigation Centre (CIC) or a UMMC clinician. Non-subcommittee members of the team will sign the Confidentiality Agreement and Declaration of Conflict of Interest forms if they accept the appointment and before they are given access to study documents to be reviewed in preparation for the site visit.

The Secretariat Staff prepares an SV Package for each member of the SV team, that will include the MREC Site Visit Report Form **(Appendix 4)**, a copy of the approved study protocol and related documents. The SV team prepares for a visit by reviewing the contents of the SV Package.

6.4. Conduct of Site Visit

Upon arrival at the site, the Site Visit team will use the MREC Site Visit Report Form to perform the following tasks:

- Review the copy of study protocol kept at site
- Review the on-site informed consent documents and verify if the site is using the most recently approved versions
- Ask the PI or staff to explain the inform consent process
- Review the post-approval documents and verify if the site is using the most recently approved versions, or that these have been approved
- Verify security, privacy, and confidentiality of the documents at the study site
- Observe facilities in the study site
- Make an overall determination of the protection of the rights, safety, and welfare of human participants in the study
- Assess compliance to the approved protocol

At the end of the visit, the Site Visit team will discuss the findings with the study team and solicit their feedback.

6.5. Presentation of Findings at MREC Meeting

The Site Visit Subcommittee Chair complete the MREC Site Visit Report which shall reflect the consensus opinion of the Site Visit team members, and submits it to the Secretariat via email not later than 10 working days after the Site Visit.

The Secretariat Staff acknowledges the receipt of the report. The Secretariat Staff places the report in the agenda of the next MREC meeting. The report will be discussed at the MREC meeting within 30 working days of the receipt of the report.

The Secretariat Staff distributes the Site Visit Report to MREC members along with the meeting agenda via email at least 7 working days before the meeting.

The MREC deliberates on the implications of the findings of the Site Visit on the rights safety, and welfare of the study participants; and makes an overall determination of the protocol compliance in the study site. The possible decisions are:

- Full compliance; study can continue.
- PI is reprimanded and warned to be compliant with approved protocol. Study can continue.
- Suspension of ethics approval pending submission of corrective and preventive action plan by PI; study not allowed to recruit new subjects.
- Study is terminated.

The MREC Secretary records discussions and decisions and enters the information in the online system.

6.6. Communication of Decisions

The PI is notified of the MREC decision via online email within 7 working days of the MREC meeting.

6.7. File Management

The Secretariat Staff stores Site Visit documents in the designated MREC Secretariat computer.

7.0 QUERIES AND COMPLAINTS

7.1. Submission of Queries or Complaints

Communication of queries and complaints, especially from research participants, are major considerations because they provide mechanisms that contribute both to maintaining transparency of MREC decision-making processes, as well as empowerment of study participants.

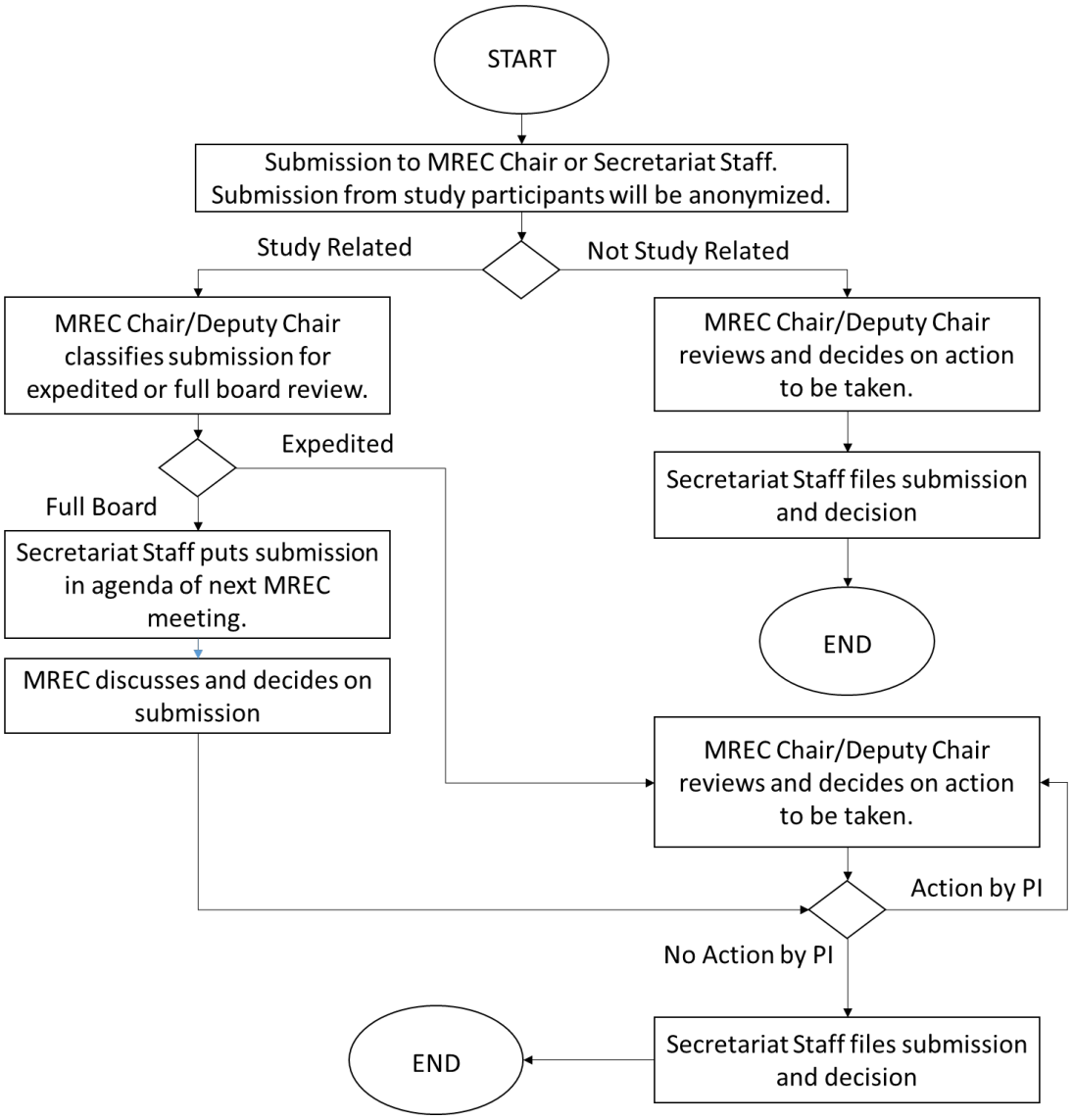
MREC also accept queries, notifications, and complaints from other parties provided they are relevant to MREC oversight.

In case of communication from research subjects, MREC Secretariat Staff can anonymize personal information to protect confidentiality of research subjects, if requested. The communication will be documented and stored in the online system.

7.2. Classification of Review by MREC Chair/Deputy Chair

The MREC Chair /Deputy Chair classifies communication for either expedited or full board review depending on the nature of the communication and response needed from MREC.

Fig. 3: Flowchart of processing queries and complaints



For non-study-protocol-related queries, review and recommendations can be finalized at the level of the MREC Chair/Deputy Chair.

7.3. Review by MREC Chair/Deputy Chair of Study-Related Communications

The MREC Chair/Deputy Chair reviews all study-related communications within 14 working days of receipt, to determine whether the information will change the original risk-benefit assessment.

For submissions under expedited review, action is finalized at the level of the MREC Chair/Deputy Chair within 14 working days.

For study-protocol-related communications requiring full board review, the Secretariat Staff places the study-related communications on the agenda for the next MREC meeting. The communication will be reviewed within 30 working days.

If necessary, the PI will be contacted to provide clarification.

7.4. Full Board Review of Study-Protocol-related Participant Query or Complaint

The MREC deliberates on how best to address the concerns relevant to the query or complaint and recommends a course of action.

The committee may request for more information from the PI, an interview with the PI, or require the PI to take corrective action(s). Feedback from the PI will be sent to the MREC Chair/Deputy Chair for a decision.

The Secretary records the discussion and decision of the meeting and enters the information in the online system.

7.5. Communication of Decisions

The online system will send an email to the PI notifying them of the MREC's decision.

7.6. File Management

All relevant documents will be stored in the designated MREC Secretariat computer.

APPENDIX 1

UNIVERSITI MALAYA
PUSAT PERUBATAN UM

JAWATANKUASA ETIKA PENYELIDIKAN PERUBATAN
PUSAT PERUBATAN UNIVERSITI MALAYA
ALAMAT: LEMBAH PANTAI, 59100 KUALA LUMPUR, MALAYSIA
TELEFON: 03-79493209 FAKSIMILI: 03-79492030

Date: _____

Chairman
Medical Ethics Committee
University Malaya Medical Centre

ANNUAL STUDY REPORT / STUDY CLOSURE REPORT
as of _____/_____/_____ (Date)
Applicable to studies that have commenced
Form to be completed and signed by principal investigator only

TITLE OF STUDY:

_____

_____

_____

_____

_____

MEC Ref. No : _____

PROTOCOL NO : _____

SPONSOR : _____

DATE ACTUAL RANDOMIZATION/RECRUITMENT BEGAN
_____/_____/_____
(Not screening)

STUDY STATUS:
(Please tick one)

- ☐ Randomization/Recruitment Phase
- ☐ Recruitment completed, on-going follow-up
  Expected completion date: _____/_____/_____
- ☐ Last Patient Last Visit reached
- ☐ All data clarified, study formally closed
- ☐ Early termination of study

Comments (if any):

_____

_____

_____

No. of subjects recruited/randomized to date: _____
(Exclude screen failures, include drop-outs)

No. of active study subjects: _____

No. of subject drop-out: _____
(Exclude death)

No. of deaths: _____

No. of local Serious Adverse Event (SAE) ie. Death, admissions, life-threatening conditions etc in the previous 12 months: _____

Has every SAE been reported to MEC in accordance to GCP?

- ☐ Yes
- ☐ No
- ☐ N.A.

Comments (if any):

_____

_____

No. of protocol deviation/violations in the previous 12 months: _____

Has sponsor and MEC has been notified:

☐ Yes
☐ No
☐ N.A.

Comments (if any):

Additional Remarks (general):

Status of the study: Close ( )
Ongoing ( )

Name of Principal Investigator: Date:

APPENDIX 2

SERIOUS ADVERSE EVENT REPORT

Study Name :

Protocol No. : Protocol Version Date : Principal Investigator :

Ethics Ref. No. :

Serious Adverse Event Report(s)

SAE Description	Expected Yes / No	UMMC Yes / No	Relationship to study drug	Event date	Report No.	Country

Subject ID :	Patient Age :	Patient Gender (M/F) :

Comment by Investigator (pertaining to the risk of our research subjects) :

Is there any ethical concern or other matter to be highlighted to MEC?

_____

_____

Signature : Date :

APPENDIX 3

Site Visit Form

Site:	Date:
Auditor:	**Site Personnel:**

No.	Pharmacy Documents	Comments
1	Protocol number Ethics approval number Product name/number Pharmacist blinded/unblinded Y/N	
2	Investigational brochure available Latest version	Y/N
3	Study contact information Site delegation log	Y/N/NA
4	Protocol and amendments Site Blinding Plan (if applicable) Standard Operating Procedures (SOP)?	Y/N/NA
5	Investigational product manual	Y/N
6	Documents pertaining IP Shipping and receipt Packing lists	Y/N

	IWRS (Interactive Web Response System) Instructions Randomization Dispensing Procedures (logs?)	
7	Drug accountability Patient logs, inventor logs	Y/N
8	Investigational product storage Temperature logs	Y/N
9	Drug destruction records At site/off site Destruction procedures Unblinding procedures	Y/N
10	Training logs	Y/N
11	Pharmacy agreement, payment, invoices	Y/N/NA

No.	**Storage of Investigational Products at site**	**Comments**
1	Room temperature storage Cupboard/locker available Locked? Who has access? Temperature monitoring? Thermometer calibrated?	Y/N
2	Refrigerator available? Locked? Who has access?	Y/N

	Temperature Monitoring? Calibration certificate?	
3	Management of temperature excursions Process, to explain	Y/N
4	Drug receipt process Temperature logger? How does it work? Damaged or lost Products. What happens?	Y/N

Additional comments:

Signature and date:

APPENDIX 4

MEDICAL RESEARCH ETHICS COMMITTEE
SITE VISIT SUBCOMMITTEE

SITE VISIT REPORT FORM

Adapted from Source:
http://www.cardiffandvaleuhb.wales.nhs.uk/sitesplus/documents/1143/SR-RG-012%20%20RESEARCH%20AUDIT%20V1.pdf

PROJECT DETAILS				
MREC ID No.: Study title: Protocol No. (if applicable): Sponsor (if any):				
Principal Investigator:	Co-Investigator (if any):			
Date of audit:				
Trial personnel present:	Auditor:			
Section 1: APPROVALS		**Yes**	**No**	**Comment**

a. Is there a record of full approval from MREC?			
b. If the study has been amended, has MREC approval been granted for any substantial amendments?			
Findings:			

Section 2: DATA PROTECTION **To fill as applicable. If not applicable, tick N/A**	**Yes**	**No**	**N/A**
a. If the study involves transfer of data to 3rd party, is there specific consent?			
b. Are the paper records stored in a locked filing cabinet?			
c. Are electronic files stored on a password protected computer?			
Findings:			

Section 3: CONSENT **To fill as applicable. If not applicable, tick N/A**	**Yes**	**No**	**N/A**
a. Are all persons taking informed consent recorded on the delegation/signature log?			
b. Is there a full record of all participants' written informed consent and/or where appropriate written carer assent?			

Tarikh Berkuatkuasa:	KOSONGKAN
No. Kajisemula:	

c. Is informed consent always taken prior to patient enrolment and any study specific procedures?			
d. Is a copy of the PIS always filed with the ICF for each subject? Copy in the medical notes for each subject? Original filed in the ISF for each subject?			
e. Has the consenting process been documented in the patient notes for each subject?			
f. Have the medical records been labelled to indicate the patient is participating in a clinical trial and the retention time?			
g. Is there evidence that the GP has been informed of the patients' participation in the study?			
h. Has a protocol amendment necessitated a re-consenting process?			
i. If re-consenting was required, was this done in a timely manner (for example at the next visit as defined in the protocol)			
j. Is there a sub-study in the clinical trial (for example pharmacokinetic or genetic studies)? If so, is there a process which tracks which subjects have consented to the sub-study?			
Findings:			

Section 4: TRIAL RECRUITMENT STATUS **To fill as applicable. If not applicable, tick N/A**	**Yes**	**No**	**N/A**

	Total
Planned	
Screened	
Excluded	

	Total
Enrolled	
Completed	
Ongoing	

Findings:

Section 5: SAFETY **To fill as applicable. If not applicable, tick N/A**	**Yes**	**No**	**N/A**
a. Have any SAEs/SUSARs been recorded?			
b. Are all reported SAEs/SUSARs verifiable against source documents?			
c. Is there evidence that SAEs/SUSARs have been reported within the expected timelines as required to the following:			
d. If there have been any serious breaches of GCP or the study protocol and have these been reported to the Sponsor in the required timelines?			

Findings:

Section 6: INVESTIGATOR SITE FILE CONTENTS

No.	Item	Findings
	Personnel	
	• Contact details • Delegation log and specimen signatures	
	• CVs (signed and dated) • Training Certificates (GCP, consent, others)	
	Sponsorship documents	
	Letter of acceptance of sponsorship	
	• Delegation of sponsorship roles • Sponsor's agreement	
	Insurance statement	
	Protocol	
	• Signed protocol • Protocol amendments	
	Patient Information Sheet / Consent and other written Information	
	• Participant Information Sheet (all versions) • Informed Consent Form (all versions)	
	• Additional information sheet/consent • GP letter (all versions)	
	• Patient Summary • Study invitation letter (if applicable)	
	Other(s)	
	Investigational Medicinal Product (IMP)	
	Investigator's Brochure (IB) or Summary of Product Characteristics (SmPC)	

	IB or SmPC updates	
Ethics		
	• Medical Research Ethics Committee favourable opinion • MREC composition	
	• Ethics application form • Ethics correspondence	
	Annual reports	
Safety		
	• Notification by investigator to sponsor of SAE and related reports • Notification by sponsor and/or investigator where applicable to MREC of SUSARs and of other safety information	
	• Notification by sponsor to investigator of safety information • SAE form	
	• SAE log • Interim or annual report	
Randomization		
	• Procedure of randomization • Procedure for un-blinding	
Case Report Form		
	Sample case report form	
Data Management Procedures		
	Data entry, checking, cleaning, edit trails, etc.	
	Data locking	
Logs and Completed Consent Forms		

	• File notes • Subject identification code list	
	• Subject screening log • Subject enrolment log	
	Signed informed consent forms	
Monitoring		
	Monitoring plan	
	• Monitoring visit log • Trial initiation monitoring report	
	• Routine monitoring report • Close-down visit report	
Equipment		
	Calibration schedule and certificates instruction for use/User Manual	
Audit		
	Audit report/correspondence/certificate	
Pharmacy File		
	Protocol number Ethics approval	
	Product name/number • Pharmacist blinded /unblinded • Study contact information • Site Delegation log • Protocol and amendments • Site Blinding Plan if applicable • Standard operating procedures (SOP)	
	• Investigation product manual • Instruction for handling IMP and trial-related materials • Shipping records for IMP and trial-related materials • Certificates of analysis of IMPs shipped Packing lists • IWRS (interactive web response system) instructions • Randomization	

	• Prescription cards/information • Drug supply procedures	
	• Dispensing procedure • Code-breaking envelopes	
	• Drug accountability • Inventory logs • Patient logs • Investigational product storage • Temperature logs • Documentation of IMP destruction (if destroyed at site/ off site) • Destruction procedures • Unblinding procedures • Training logs • Pharmacy correspondence • Others	
	Storage of Investigational Products at site (Y/N/ N/A) 1) Room temperature storage • Cupboard/locker available • Locked? • Details-Who has access • Temperature monitoring • Thermometer calibration 2) Refrigeration • Locked? • Details- Who has access? • Temperature Monitoring • Calibration certificate • Management of temperature excursions- Process, to explain 3) Drug receipt process • Temperature logger • Work process • SOP for Damaged or lost Products • Other issues and additional comments	

Laboratory		
	• Normal values/ranges for procedures and/or tests • Laboratory Accreditation Certificates	
	• Medical/lab/technical procedures/tests e.g. SOPs • Laboratory correspondence	
Other Local Providers (Specify)		
	• Contracts • Correspondence	
Correspondence		
	• Relevant letters, emails, meeting note and telephone calls	
Study report or publication		
	Study report or publication	
Findings:		

SECTION 7: SUMMARY OF FINDINGS AND CLASSIFICATION

Summary of observation and findings:

The most noteworthy finding(s) was/were as follows:

Author of report:

Name:

Signature:

Date: