Standard Operating Procedures
III. POST-APPROVAL REVIEW

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1. Objectives

This SOP describes how the JEPeM-USM processes post approval submissions by the Principal Investigators. Depending on the nature of the submissions, they may be processed by either "expedited" or full board review. This chapter describes submission procedures, required forms, documentation of board action, communication of board action to the PI, and filing of results.

2. Scope

This SOP applies to all study protocol-related submissions after approval has been issued for the study protocol and study protocol-related documents. These submissions include requests for amendments, continuing review applications, final reports, non-compliance (deviation or violation) reports, early study termination, queries or complaints from stakeholders, serious adverse event reports (SAEs) and suspected unexpected serious drug reactions (SUSARs), and site visit reports.

3. Responsibilities

It is the responsibility of the PI to comply with post-approval review requirements, including the submission of required reports listed in **JEPeM-USM FORM 4(B): APPROVAL LETTER TO THE STUDY PROTOCOL.**

The Secretariat Staff is responsible for receiving and processing all submissions, including inquiries or complaints from research participants and other stakeholders. JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary will decide on type of review for post approval application into full board or expedited review. For full board decision, the primary reviewer(s) is/are requested to review relevant documents related to this.

In the event that a Site Visit becomes necessary as decided by JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary, it is the responsibility of the Chairperson of Site Visit Sub-Committee Team to form a Site Visit Team. The responsibility of the assigned members to conduct the Site Visit and issue a report for presentation in the JEPeM-USM full board meeting, and responsibility of the Secretariat Staff to organize the Site Visit.

4. Study Protocol Amendments, Continuing Review Applications, Final Reports Noncompliance Reports, Early Study Termination Application, and Participant Queries or Complaints Workflow

ACTIVITY	RESPONSIBILITY
Receive and manage documents submission ⍰	Secretariat Staff
Submit documents to the JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary to determine classification of review as expedited or full board ⍰	Secretariat Staff
JEPeM-USM Chairperson/ Deputy Chairperson/Panel Chair/Member Secretary reviews submissions classified as expedited review; Primary reviewers review submissions classified as full board review	JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary/Primary
Review full board study protocols in JEPeM-USM meeting ↓	Members
Communicate results to PI/Participant ↓	Secretariat Staff
Manage study protocol files	Secretariat Staff

DETAILED INSTRUCTIONS

4.1. Study Protocol Amendment

4.1.1. *Receipt and management of the Study Protocol Amendment package upon submission*

4.1.1.1. A study protocol amendment is a written description of a change(s) to or formal clarification of a protocol and/or informed consent documents. Favorable opinion or approval should be obtained from the JEPeM-USM that issued the ethical clearance or approval prior to the implementation of an amendment.

4.1.1.2. A study protocol amendment is facilitated through the submission of **JEPeM-USM FORM 3(A): STUDY PROTOCOL AMENDMENT SUBMISSION FORM** with the amended study protocol or protocol-related documents by the principal investigator to the JEPeM-USM that issued the ethical clearance or approval to the study protocol. This comprises the study protocol amendment package.

4.1.1.3. Upon receipt of the study protocol amendment package, the Secretariat Staff logs the date of submission on the database.

4.1.1.4. The Secretariat Staff checks the submission for completeness and gives an acknowledgement of receipt of **FORM JEPeM-USM FORM 3(A): STUDY PROTOCOL AMENDMENT SUBMISSION** to the PI or representative. If incomplete submission, the secretariat staff will request PI or representative to complete the submission

4.1.1.5. The Secretariat Staff ensures that sufficient copies (5 hardcopy/1 softcopy) relevant document related to protocol amendment including documents with track changes and clean version for the JEPeM-USM Members have been submitted by the PI or representative for submissions.

4.1.2. *Classification of Review by the JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary*

4.1.2.1. The Secretariat Staff sends the Study Protocol Submission Package to the JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary immediately for classification of review as expedited or full board.

4.1.2.2. A full board review is necessary if the proposed study protocol amendment increases risk to study participants, as assessed by the JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary, such as a change in study design, which may include but is not limited to:

- Additional treatments or the deletion of treatments
- Any changes in inclusion/exclusion criteria
- Change in method of dosage formulation, (e.g. oral changed to intravenous)
- Significant change in the number of subjects
- Significant decrease or increase in dosage amounts

4.1.3. *Review by JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary and Primary Reviewers*

4.1.3.1. For submissions under expedited review, action is taken at the level of the JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary within **ten (10) working days.** The decision will be endorsed in the next full board meeting.

4.1.3.2. Study protocol amendment packages subject to full board review

will be forwarded to the primary reviewers who will complete the review within **ten (10) working days**. In the event where primary reviewers are no longer available, new reviewers will be appointed by Chairperson/Deputy Chairperson/Panel Chair/Member Secretary.

4.1.3.3. The Primary Reviewers accomplish the review and return the signed JEPeM-USM FORM 3(A): STUDY PROTOCOL AMENDMENT SUBMISSION FORM to JEPeM-USM together with the Study Protocol Amendment Package.

4.1.3.4. The Secretariat Staff places the study protocol amendment request on the agenda for the next JEPeM-USM meeting.

4.1.4. ***Full board review of Study Protocol Amendment Submission Package***

4.1.4.1. The Secretariat Staff distributes the following Study Protocol Amendment Package to JEPeM-USM Members along with the meeting agenda:

- Amended study protocol or protocol-related document; with amended section clearly indicated
- Other documents that have been affected by the revision

4.1.4.2. The documents are presented to JEPeM-USM Members when amendments are deliberated on. For detailed information on the conduct of full board review of study protocol amendments, see **SOP II-8.8.1.**

4.1.5. ***Communication of Results***

4.1.5.1. The PI is notified of the JEPeM-USM decision noting which amended documents are approved for use through an action letter.

4.1.5.2. The PI may be required to modify the amendment, provide additional information, or submit additional documents.

4.1.5.3. If the amendment is approved, the PI is requested to submit an amended study protocol or protocol-related document with a new version number and date.

4.1.6. ***Files Management***

4.1.6.1. The Secretariat Staff receives the approved amended study

protocol or protocol- related document with a new version number and date and stamps it "APPROVED" with the approval date. For electronic version, it will be stamped electronically.

4.1.6.2. The newly approved documents will supersede previous versions of the study protocol or protocol-related document.

4.1.6.3. The Secretariat Staff files the signed and approved documents in the study protocol folder.

4.2. Continuing Review Application

4.2.1. *Receipt and management of the Continuing Review Application package upon submission*

4.2.1.1. Ethical clearance or approval is typically granted for a period of one year. After approval, continuing review is required to be done at least once a year, depending on the risk assessment of the study protocol. This is facilitated through the submission of **JEPeM-USM FORM 3(B): CONTINUING REVIEW APPLICATION FORM**.

4.2.1.2. The frequency of continuing review is indicated in **JEPeM-USM FORM 4(B): APPROVAL LETTER TO THE STUDY PROTOCOL,** which is provided to the PI upon approval of the study.

4.2.1.3. For ethical clearance or approval approaching one year expiry date and requiring a renewal or extension, it is advisable to submit **JEPeM-USM FORM 3(B): CONTINUING REVIEW APPLICATION FORM 60 calendar days** prior to expiry date.

4.2.1.4. The Secretariat Staff informs the respective PIs at least **90 calendar days** before expiry date of the approval by fax, e-mail, or post using **JEPeM- USM FORM 4(N): REMINDER LETTER FOR CONTINUING REVIEW OR FINAL REPORT** and keeps a copy of the communication.

4.2.1.5. The continuing review application is facilitated through the submission of
JEPeM-USM FORM 3(B): CONTINUING REVIEW APPLICATION FORM.

4.2.1.6. The Secretariat Staff checks the submission for completeness and

gives acknowledgment of **JEPeM-USM FORM 3(B): CONTINUING REVIEW APPLICATION FORM** to the PI or representative.

4.2.1.7. The Secretariat Staff logs the date of submission on the database.

4.2.1.8. The Secretariat Staff ensures that sufficient copies (5 hardcopy/1 softcopy) relevant document related to continuing review for the JEPeM-USM Members have been submitted by the PI or representative for submissions.

4.2.2. Classification of Review by the JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary

4.2.2.1. The JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary classifies the submission as either full board or expedited review.

4.2.2.2. Generally, classification of continuing review as expedited or full board is based on the initial review classification (i.e. continuing review of full board study protocols is done through full board review); unless otherwise indicated by the specificities of the submitted information. If the approval has expired for more than 1 year, the PI will be invited to full board meeting for further clarification.

4.2.3. *Review by JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary and Primary Reviewers*

4.2.3.1. The continuing review application package is sent together with a copy of the study protocol to the JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary for expedited review study protocols. For full board review study protocols, the review of the application is done by the the primary reviewers. In the event where primary reviewers are no longer available, new reviewers will be appointed by JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary.

4.2.3.2. For submissions under expedited review, action is finalized at the level of the JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary within **ten (10) working days**.

4.2.3.3. For submission under full board review, JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary /Primary Reviewers accomplish the review and return the signed **JEPeM-USM FORM 3(B): CONTINUING REVIEW APPLICATION SUBMISSION FORM** to JEPeM-USM together with relevant documents.

4.2.3.4. The Secretariat Staff places the continuing review application on the agenda for the next JEPeM-USM meeting.

4.2.4. *Full Board Review of Continuing Review Application*

4.2.4.1. The Secretariat Staff distributes the following continuing review application package to JEPeM-USM Members along with the meeting agenda:

- **JEPeM-USM FORM 3(B): CONTINUING REVIEW APPLICATION FORM**
- **Study protocol synopsis**
- Current informed consent documents

4.2.4.2. The documents are presented to JEPeM-USM Members when continuing review applications are deliberated on. For detailed information on the conduct of full board review of continuing review applications, see **SOP II-8.8.2.**

4.2.5. *Communication of Results*

4.2.5.1. The PI is notified of the decision noting board action on the continuing review application through a letter.

4.2.5.2. The PI may be requested to provide additional information or submit additional documents.

4.2.6. *Files Management*

4.2.6.1. The Secretariat Staff files the signed continuing review application documents in the study protocol file folder. For electronic version, it will be stamped electronically.

4.3. Final Report

4.3.1. *Management of the Final Report Package upon Submission*

4.3.1.1. Upon completion of the study, the investigator should provide the JEPEM-USM with a summary of the outcome of the study, especially of the human participants who were involved using **JEPeM-USM FORM 3(C[i] or C[ii]): FINAL REPORT FORM.**

4.3.1.2. The Secretariat Staff will remind the respective PIs 90 days before the study protocol is expired to submit a Final Report at least one month in advance of the due date of review by fax, e-mail, or post using **JEPeM-USM FORM 4(N): REMINDER LETTER FOR CONTINUING REVIEW OR FINAL REPORT** and keeps a copy of the communication.

4.3.1.3. The end of study reporting is facilitated through the submission of **JEPeM- USM FORM 3(C[i] or C[ii]): FINAL REPORT FORM,** together with documents deemed relevant by the investigator to clarify information

indicated in the final report. This comprises the final report package. For clinical trials form C[i] will be used and for other studies form C[ii].

4.3.2. *Classification of Review by the JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary*

4.3.2.1. The JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary classifies the submission as either full board or expedited review.

4.3.2.2. Generally, classification as expedited or full board is based on the initial review classification (i.e. final report review of full board study protocols is done through full board review); unless otherwise indicated by the specificities of the submitted information.

4.3.3. *Review by JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary and Primary Reviewers*

4.3.3.1. The final report package is sent together with a copy of the study

protocol to the JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary/Primary Reviewers. For full board review study protocols, the review of the final report package is done by the the primary reviewers. In the event where primary reviewers are no longer available, new reviewers will be appointed by JEPeM-USM chairperson/deputy chairperson/panel chair/member secretary.

4.3.3.2. For submissions under expedited review, action is finalized at the level of the JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary within **ten (10) working days**.

4.3.3.3. For submission under full board review, the JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary /Primary Reviewers accomplish the review and return the signed **JEPeM-USM FORM 3(C[i] or C[ii]) : FINAL REPORT FORM.**

4.3.3.4. The Secretariat Staff places the final report package on the agenda for the next JEPeM-USM meeting.

4.3.4. ***Full Board Review of Final Report***

4.3.4.1. The Secretariat Staff distributes the following final report package to JEPeM-USM Members along with the meeting agenda:

- **JEPeM-USM FORM 3(C[i] or C[ii]): FINAL REPORT FORM**
- Relevant documents

4.3.4.2. The documents are presented to JEPeM-USM Members when final reports are deliberated on. For detailed information on the conduct of full board review of final reports, see **SOP II-8.8.3.**

4.3.5. ***Communication of Results***

4.3.5.1. The PI is notified of the JEPeM-USM decision, noting JEPeM-USM action on the final report through a letter.

4.3.5.2. The PI may be requested to provide additional information or submit additional documents, in which case the final report may be accepted, but action regarding archiving may be deferred pending submission of results of the study.

4.3.5.3. If the final report is approved, the PI is informed of the following:

- The protocol is classified as inactive
- Study protocol records will be made available for **three (3) years** in the archives after the expiration date.

4.3.5.4 PI or his/her representative will be notified after 6 months after the expiry date and the second reminder will be made and copied to HOD/PTJ. If there is no submission from the PI or representative, JEPeM-USM will classify the protocol as INACTIVE.

4.3.6. ***Files Management***

4.3.6.1. The Secretariat Staff files the signed final report documents in the study protocol file folder, upon approval of the final report, when no further action is expected from the PI. For electronic version, it will be stamped electronically.

4.3.6.2. The Secretariat Staff enters relevant study protocol data into the Study Protocol Database to signify the end of study.

4.3.6.3. The Secretariat Staff transfers the study protocol folder to the inactive files. See **SOP IV-8: Archived (Inactive/Completed/Terminated) Files** for management of inactive files.

4.4. Study Protocol Noncompliance (Deviation/Violation) Report

4.4.1. ***Management of the Study Protocol Noncompliance Reports upon Submission***

4.4.1.1. The investigator should document, explain, and report to the JEPeM-USM any noncompliance from the approved protocol, whether minor or major, at the soonest possible time.

4.4.1.2. The investigator may implement a deviation from the protocol to eliminate an immediate hazard(s) to study subjects without prior JEPeM-USM approval, but must submit as soon as possible, a report of deviation or change, the reasons for it, and, if appropriate, an appropriate study protocol amendment(s).

4.4.1.3. Reporting of study protocol noncompliance is facilitated through the submission of **JEPeM-USM FORM 3(D): STUDY PROTOCOL NONCOMPLIANCE (DEVIATION OR VIOLATION) REPORT,** together with documents deemed relevant by the investigator to clarify information indicated in the report. This comprises the study protocol

noncompliance report package.

4.4.1.4. The Secretariat Staff checks the submission for completeness and gives an acknowledgment of receipt of **JEPeM-USM FORM 3(D): STUDY PROTOCOL NONCOMPLIANCE (DEVIATION OR VIOLATION) REPORT** to the PI or representative. If incomplete submission, the secretariat staff will request PI or representative to complete the submission.

4.4.1.5. The Secretariat Staff logs the date of submission on the database.

4.4.2. ***Classification of Review by the JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary***

4.4.2.1. The JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary classifies the submission as either full board or expedited review.

4.4.2.2. Minor or administrative deviations which do not affect the scientific soundness of the study protocol or compromise the rights, safety, or welfare of human participants in the study are classified under expedited review.

4.4.2.3. Major deviations or protocol violations that consist of persistent protocol noncompliance with potentially serious consequences that could critically affect data analysis or put patients' safety at risk are classified under full board review.

4.4.3. ***Review by JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary/Primary Reviewer***

4.4.3.1. For submissions under expedited review, action is finalized at the level of the JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary within **ten (10) working days**.

4.4.3.2. Submissions subject to full board review will be forwarded to the primary reviewers who will complete the review within **ten (10) working days**. In the event where primary reviewers are no longer available, new reviewers will be appointed by JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary.

4.4.3.3. The Primary Reviewers accomplishes the review and returns the signed **JEPeM-USM FORM 3(D): STUDY PROTOCOL NONCOMPLIANCE (DEVIATION OR VIOLATION) REPORT.**

4.4.3.4. The Secretariat Staff places the study protocol noncompliance report on the agenda for the next JEPeM-USM meeting.

4.4.4. ***Full Board Review of Study Protocol Noncompliance Report***

4.4.4.1. The Secretariat Staff distributes the following Study Protocol Noncompliance Report Package to JEPeM-USM Members along with the meeting agenda:

- **JEPeM-USM FORM 3(D): STUDY PROTOCOL NONCOMPLIANCE (DEVIATION OR VIOLATION) REPORT**
- Documents related to the deviation

4.4.4.2. The documents are presented to JEPeM-USM members when study protocol noncompliance reports are deliberated on. The JEPeM-USM deliberates on both the type and degree of noncompliance and takes the appropriate action.

4.4.4.3. The JEPeM-USM can suspend ethical clearance or subject recruitment until noncompliance issues are addressed.

4.4.4.4. The JEPeM-USM may opt to withdraw ethical approval under the following circumstances:

- Fraud
- Unresolved serious safety issues

4.4.4.5. For detailed information on full board review of study protocol noncomplicance report, **see SOP II-8.8.6**

4.4.5. ***Communication of Results***

4.4.5.1. The PI is notified of the JEPeM-USM decision, noting JEPeM-USM action on the study protocol noncompliance report through a letter.

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

4.4.6. ***Files Management***

4.4.6.1. The Secretariat Staff files the signed study protocol noncompliance

report documents in the study protocol file folder. For electronic version, it will be stamped electronically.

4.5. Early Study Termination Application

4.5.1. *Management of the Early Study Termination Application upon Submission*

4.5.1.1. An application for early study termination is submitted when a study approved by the JEPEM-USM is being recommended for termination before its scheduled completion. This is done when the safety of the study participant is doubtful or at risk and also upon the request of the PI or the sponsor owing to the existence of irresolvable valid complaints.

4.5.1.2. Early study termination is facilitated through the submission of **JEPeM-USM FORM 3(E): EARLY STUDY TERMINATION APPLICATION FORM,** together with documents deemed relevant by the investigator to support or clarify information indicated in the application. This comprises the early study termination application package.

4.5.1.3. The Secretariat Staff checks the submission for completeness and gives an acknowledgement of receipt of **JEPeM-USM FORM 3(E): EARLY STUDY TERMINATION APPLICATION FORM** to the PI or representative. If incomplete submission, the secretariat staff will request PI or representative to complete the submission.

4.5.1.4. The Secretariat Staff logs the date of submission on the database.

4.5.2. *Classification of Review by JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary*

4.5.2.1. The JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary classifies the submission as either full board or expedited review.

4.5.2.2. Generally, classification of review of early study termination applications as expedited or full board is based on the initial review classification (i.e. early study termination application of full board study protocols is done through full board review); unless otherwise indicated by the specificities of the submitted information.

4.5.3. ***Review by JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary and Primary Reviewers***

4.5.3.1. For submissions under expedited review, action is finalized at the level of the JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary within **ten (10) working days**.

4.5.3.2. Submissions subject to full board review will be forwarded to the primary reviewers who will complete the review within **ten (10) working days.** In the event where primary reviewers are no longer available, new reviewers will be appointed by JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary.

4.5.3.3. The Primary Reviewer accomplishes the review and returns the signed **JEPeM-USM FORM 3(E): EARLY STUDY TERMINATION APPLICATION FORM**

4.5.3.4. The Secretariat Staff places the early study termination application on the agenda for the next JEPeM-USM meeting or if there are urgent issues, a special meeting can be called by the JEPeM-USM Chairperson.

4.5.4 ***Full Board Review of Early Study Termination Application***

4.5.4.1 The Secretariat Staff distributes the following early study termination application package to JEPeM-USM Members along with the meeting agenda:

- **JEPeM-USM FORM 3(E): EARLY STUDY TERMINATION APPLICATION FORM**
- Documents related to the early study termination

4.5.4.2 The JEPeM-USM deliberates on the implications of the application on the rights, safety, and welfare of the study participants, including adapting specific provisions for continued protection and dissemination of specific information to the study participants.

4.5.4.3 The JEPeM-USM may request information for clarification by email or interview from the PI or representative

4.5.4.4 For detailed information on full board review of early study termination application, **see SOP II-8.8.7**

4.5.4. *Communication of Results*

4.5.4.1. The PI is notified of the JEPeM-USM decision, noting JEPeM-USM action on the early study termination application through a letter.

4.5.5. *Files Management*

4.5.5.1. The Secretariat Staff files the early study termination application documents in the study protocol file folder. For electronic version, it will be stamped electronically.

4.6. Queries or Complaints

4.6.1. *Management of Submitted Queries or Complaints*

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

4.6.1.2. Any JEPeM-USM personnel can receive a query or complaint. Action on queries and complaints is managed through the use of **JEPeM-USM FORM 3(I): QUERIES OR COMPLAINTS.** Each query or complaint received will be individually entered into this form by respective JEPEM-USM personnel, and then forwarded to the Secretariat for processing.

4.6.1.3. The Secretariat Staff logs the query or complaint into the **database.**

4.6.2. *Classification of Review by JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary*

4.6.2.1. The JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary classifies queries as either full board or expedited review depending on the nature of the query and response needed.

4.6.2.2. Complaints are classified under full board review or expedited review.

4.6.3. ***Review by JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary and Primary Reviewers***

4.6.3.1. For submissions under expedited review, action is finalized at the level of the JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary within **ten (10) working days**.

4.6.3.2 Submissions subject to full board review will be forwarded to the primary reviewers who will complete the review within **ten (10) working days**. In the event where primary reviewers are no longer available, new reviewers will be appointed by JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary.

4.6.3.3 The Primary Reviewers accomplishes the review and returns the signed **JEPeM-USM FORM 3(I); QUERIES OR COMPLAINTS**

4.6.3.4 The Secretariat Staff places the query or complaint in the agenda of the next JEPeM-USM meeting.

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

4.6.4 ***Full Board Review of Study Participant Query or Complaint***

4.6.4.2 The Secretariat Staff distributes the completed **JEPeM-USM FORM 3(I): QUERIES OR COMPLAINTS** to JEPeM-USM Members along with the meeting agenda:

4.6.4.3 The JEPeM-USM deliberates on how best to address the concerns relevant to the query or complaint, and recommends a course of action.

4.6.4.4 The JEPeM-USM may request for clarification by email or interview from the PI.

4.6.4.5 For detailed information on full board review of queries or complaints, **see SOP II-8.8.8**

4.6.5 ***Communication of Results***

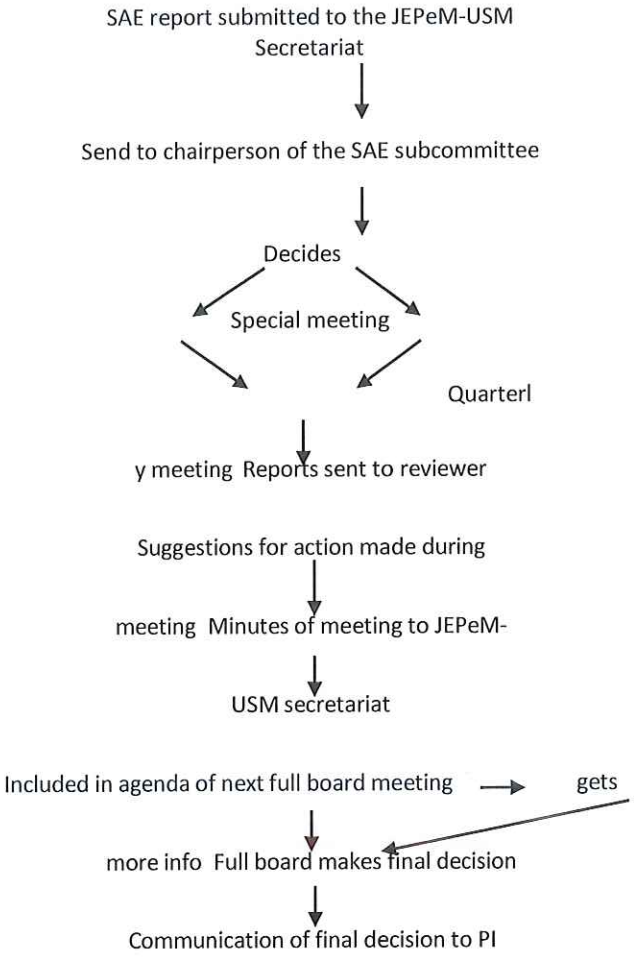
4.6.5.2 The JEPEM-USM responds to queries and complaints in writing after a course of action of appropriate response is identified whether through expedited or full board review.

4.6.5.3 The PI may be requested to provide additional information or submit additional documents.

4.6.6 *Files Management*

4.6.6.2 The Secretariat Staff files the signed documents in the study protocol file folder. For electronic version, it will be stamped electronically.

5. Serious Adverse Event Reports Workflow



DETAILED INSTRUCTIONS

5.1. *Management of the SAE Report upon Submission*

5.1.1. Serious adverse events are events temporally associated with the subject' participation in research that meets any of the following criteria:

- 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
- Any other adverse event that, based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition

Serious adverse events that are reported to the JEPeM-USM secretariat will be initially dealt with by a dedicated SAE subcommittee. The SAE subcommittee will meet on a quarterly basis (every three months) or when deemed necessary (special meeting).

5.1.2. The PI must report serious adverse advents to the JEPeM-USM in accordance with the **JEPeM-USM Guideline on Reporting Adverse Events (JEPeM-USM, GL01).**

5.1.3. Reporting of SAEs is facilitated through the submission of **JEPeM-USM FORM 3(G): SERIOUS ADVERSE EVENT/S REPORT**, together with the documents deemed relevant by the investigator to clarify information indicated in the report. This comprises the study protocol serious adverse event/s report package. If the PI submits a form similar to the FORM 3(G) (e.g. CIOMS form) this will be accepted as well and the PI does not have to transfer the data into FORM 3(G).

5.1.4. The Secretariat Staff assigned to the SAE Subcommittee checks the submission for completeness and gives acknowledgment of receipt of the received form to the PI or his/her representative.

5.1.5. The Secretariat Staff logs the date of submission on the database.

5.2. *Submission of SAE Package to SAE Subcommittee Chair*

5.2.1 Serious adverse event/s report packages received by the JEPeM-USM secretariat will be forwarded within **seven (7)** calendar days to the chair of the SAE subcommittee. The following documents will be submitted to the chair:

- The submitted form
- List of known ADRs as written in the Investigators' Brochure (latest version)
- Protocol Summary
- Investigators' Brochure (latest version)
- Other supporting documents, if necessary

5.2.2 The Chair of the SAE subcommittee classifies whether the SAE report will need urgent attention and requires a special SAE subcommittee meeting or whether it will be brought to the next quarterly SAE subcommittee meeting.

5.3 *SAE Subcommittee Meeting*

5.3.1 The SAE subcommittee will meet on a quarterly basis (every three months). SAE reports needing urgent action as decided by the Chair of the SAE subcommittee are brought to a special SAE Subcommittee Meeting.

5.3.2 The National Poison Management and Control Center may be requested to make further investigations if the SAE involves overdose or poisoning. A site visit may be conducted, in coordination with the PI, at the expense of the PI or sponsor.

5.3.3 Conduct of AE Subcommittee Meeting

5.3.3.1. The SAE report package comprising of the following documents is distributed to the respective AE Subcommittee Primary Reviewer(s) (1 or 2 based on the judgement of the chair of the SAE sub-committee) at least **ten (10) working days** before the panel meeting:

- The report form
- List of known ADRs as written in the Investigators' Brochure
- Protocol Summary
- Investigators' Brochure
- Other supporting documents, if necessary

5.3.3.2 The chair of the subcommittee places the SAE report on the agenda of the AE Subcommittee meeting.

5.3.3.3 The AE Subcommittee Primary Reviewers accomplish the review and bring their comments to the SAE subcommittee meeting.

5.3.3.4 The AE Subcommittee may recommend any of the following actions:

- *Uphold original approval with no further action required*
- *Request further information*
- *Recommendation for further action:*

→ Modification of participant inclusion or exclusion criteria to mitigate the newly identified risks or informed consent documents to include a description of newly recognized risks;

→ Recommend implementation of additional procedures for protecting/safeguarding participants;

→ Suspension of enrollment of new participants or research procedures among participants who are currently enrolled (check consistency)

→Recommend suspension of the entire study

5.3.4 Presentation of AE Subcommittee Recommendations to full board

5.3.4.1 The AE Subcommittee Chair submits the minutes of the meeting that contain the recommendations of the AE Subcommittee to the JEPeM-USM secretariat and these will be included in the agenda of the next meeting of the full board of the JEPeM-USM.

5.3.4.2 The following documents are distributed to each full board member together with the agenda:

5.3.4.2.1 SAE REPORT forms i.e **JEPeM-USM FORM 3(G) SERIOUS ADVERSE EVENT/S REPORT**

5.3.4.2.2 AE Subcommittee recommendations as outlined in the minutes of the meeting(s) of the SAE subcommittee

5.3.5 Deliberation on Full Board Action:

During the meeting, the JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary calls for a decision on the SAE report with respect to the recommendations of the SAE Subcommittee. The JEPeM-USM may require any of the following actions:

- *Uphold original approval with no further action*
- *Request information*
- *Recommendation for further action according to recommendations of SAE subcommittee*

5.4 *Communication of Results*

5.4.1 The PI is notified of the Full Board decision, noting required action on the Serious Adverse Event/s Report through a letter. A copy of this letter will be sent to the chair of the SAE subcommittee.

5.5 *Files management*

5.5.1 After the SAE meeting all documents are returned the JEPeM-USM secretariat where they will be filed in the study protocol file folder. For electronic version, it will be stamped electronically.

6. Site Visit Workflow

The site visits will be performed by a specifically appointed subcommittee. The process will proceed according the following table.

ACTIVITY	RESPONSIBLE PERSON
Select study sites to visit ↓	JEPeM-USM Chairperson, Deputy Chairperson, Panel Chair, Member Secretary and Members
Chair of Site visit subcommittee will be informed ↓	Secretariat Staff
Notify PI of date of site visit ↓	Secretariat Staff
Create Site Visit Team ↓	Subcommittee Chair
Conduct Site Visit ↓	Site Visit Team
Present findings during full board meeting ↓	Site Visit Team

Communicate results of Site Visit and subsequent full board decision to PI ↓	Secretariat Staff
Manage Site Visit documents	Secretariat Staff

DETAILED INSTRUCTIONS

6.1 Selection of Study Sites

6.1.1 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 non-submission or failure to submit continuing review requirements
- Reports of major protocol noncompliance
- Significant number of serious adverse events
- Reports of complaints from study participants
- Site visits may be conducted upon recommendation of the JEPeM-USM

6.1.2 Study sites may also be suggested for site visit upon recommendation of the JEPeM-USMAdverse Event Subcommittee.

6.1.3 A decision for Site Visit is deliberated on during a full board meeting of the JEPeM-USM.

6.2 Communication JEPEeM-USM– subcommittee - PI

6.2.1 The Secretariat Staff prepares a Study Visit Package for each member of the site visit team, inclusive of the **JEPeM-USM FORM 3(F): SITE VISIT REPORT FORM** and a copy of the approved study protocol and related documents. A letter of notification that includes the reason for the site visit is forwarded together with these packages to the chair of the subcommittee for site visits.

6.2.2 Secretariat of JEPeM-USM informs the PI at least **ten (10) working days** before the scheduled visit through a letter. A copy of **JEPeM-USM FORM 3(F): SITE VISIT REPORT FORM** is attached to this letter.

6.2.3 The letter provides site visit schedule details and instructions on what the PI needs to prepare, such as documents and files that will be used for the site visit, as

well as orderly preparation of the site.

6.3 Creation of a Site Visit Team

6.3.1 A site visit team is organized for each site visit.

6.3.2 The members of this team are assigned by the Site Visit Sub-Committee Chair.

6.3.3 The site visit team should be composed of **at least two (2) members** of the committee for site visits.

6.3.4 The site visit team members are informed of their assignment through the issuance of **JEPeM-USM FORM 3(H): NOTICE OF SITE VISIT.**

6.3.5 The site visit team prepares by reviewing the contents of the study file and the requirements of **JEPeM-USM FORM 3(F): SITE VISIT REPORT FORM.** A pre-site visit meeting may be called by the chair of the subcommittee before the actual visit. The JEPeM-USM Chairperson/Deputy Chairperson/Panel Chair/Member Secretary may invite members of the JEPeM-USM to this meeting if it is deemed necessary.

6.4 Conduct of Site Visit

6.4.1 Upon arrival in the study site, the site visit team uses **JEPeM-USM FORM 3(F): SITE VISIT REPORT FORM** to do the following:

- Review the study protocol
- Review the informed consent documents and verify its approved version.
- Ask the PI or staff to explain the informed consent process
- Review the post-approval documents and verify if the site is using the most recently approved version, 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

6.4.2 At the end of the visit, the site visit team will:

- Discuss the findings with the research team
- Solicit feedback

6.5 Presentation of findings at JEPeM-USM Meeting

6.5.1 The site visit team completes **JEPeM-USM FORM 3(F): SITE VISIT REPORT FORM** which should reflect the consensus opinion of the site visit team members, and submits it to the Secretariat not later than **ten (10) working** days after the site visit.

6.5.2 The Secretariat Staff logs the date of submission on the **SUBMISSIONS LOG [JEPeM- USM FORM 4(M)].**

6.5.3 During the meeting, the Secretariat Staff distributes the completed **JEPeM-USM FORM 3(F): SITE VISIT REPORT FORM** to JEPeM-USM Members along with the meeting agenda

6.5.4 The JEPeM-USM members deliberate on the implications of results of the site visit on the rights, safety, and welfare of the study participants; and make an overall determination of protocol compliance in the study site.

6.6 Communication of results

6.6.1 The PI is notified of the full board recommendations through a letter.

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

6.7 Site Visit files management

6.7.1 The Secretariat Staff includes the discussions in the minutes of the meeting and files the site visit documents in the study protocol file folder