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III. POST-APPROVAL REVIEW

1. Objectives

This SOP describes how the UPMREB 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 from stakeholders, serious adverse event reports (SAEs) and suspected, unexpected serious adverse reactions (SUSARs), and site visit reports.

3. Responsibilities

It is the responsibility of the PI to comply with post-approval review requirements, including the registration in the Philippine Health Research Registry (PHRR) upon approval of the study protocol, and submission of required reports listed in **UPMREB FORM 4(B) 2019: CERTIFICATION OF APPROVAL** while study is in progress.

The Secretariat Staff is responsible for receiving and processing all submissions, including inquiries or complaints from research participants and other stakeholders. Original primary reviewers are responsible for reviewing these post-approval submissions.

In the event that a Site Visit becomes necessary, it is the responsibility of the Chair 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 panel 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 Report, and Queries, Notifications and Complaints Workflow

ACTIVITY	RESPONSIBILITY
Screen, receive and manage documents submission in iREB ↓	Secretariat Staff

Classify submission as expedited or full board (via iREB) ↓	UPMREB Coordinator/Chair
Review submissions (via iREB or manually depending on the reviewer) ↓	Panel Chair/Primary Reviewers
Review full board study protocols in panel 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 proposed change(s) to or formal clarification of a protocol and/or informed consent documents that is yet to be implemented. Favorable opinion or approval should be obtained from the UPMREB Panel 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 fully accomplished **UPMREB FORM 3(A) 2012: STUDY PROTOCOL AMENDMENT SUBMISSION FORM** with the amended study protocol or protocol-related documents by the principal investigator to the UPMREB Panel that issued the ethical clearance or approval to the study protocol. This comprises the study protocol amendment package.

4.1.1.3. The principal investigator registers amendment application in iREB and submits a complete amendment package once the submission has been accepted upon notification by the Secretariat Staff.

4.1.1.4. The Secretariat Staff checks the iREB submission for completeness and forwards the submission to the iREB account of UPMREB Coordinator for classification of review.

4.1.1.5. The Secretariat Staff stamps the receiving date on the submitted study protocol package and gives a receiving copy of **UPMREB FORM 3(A) 2012: STUDY PROTOCOL AMENDMENT SUBMISSION FORM** to the PI or his/her representative.

4.1.1.6. Upon receipt of the study protocol amendment package, the Secretariat Staff logs the date of submission on the **SUBMISSIONS LOG [UPMREB FORM 4(M)2012]**.

4.1.2. ***Classification of Review by the UPMREB Coordinator***

4.1.2.1. The Secretariat Staff forwards the iREB submission to the account of the UPMREB Chair/Coordinator 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 UPMREB Chair/Coordinator, 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

4.1.2.3. Study protocol amendments that do not change the risk profile of study participants are classified for expedited review.

4.1.3. ***Review by Panel Chair and Primary Reviewers***

4.1.3.1. All study protocol amendment submissions will be forwarded to the Primary Reviewers, via iREB and also by courier in exceptional circumstances, together with the originally approved protocol for the reviewer to determine whether the amendment will change the original risk-benefit assessment. The reviewers will be notified once the protocol submission has been forwarded.

4.1.3.2. For submissions under expedited review, action is finalized at the level of the Panel Chair within **ten** (**10**) calendar days.

4.1.3.3. Study protocol amendment packages subject to full board review received within the cut-off period of **seventeen** (**17**) days before the panel meeting are sent to Primary Reviewers **twelve** (**12**) to **fourteen** (**14**) calendar days before the panel meeting.

4.1.3.4. The Primary Reviewers accomplish the review and return the signed **UPMREB FORM 3(A)2012: STUDY PROTOCOL AMENDMENT SUBMISSION FORM** to the Secretariat Staff through iREB or hand deliver them with the study protocol amendment package seven (7) days upon receipt for expedited review and on or before the day of the Panel Meeting for full board review.

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 Panel Members along with the meeting agenda:

- **UPMREB FORM 3(A)2012: STUDY PROTOCOL AMENDMENT SUBMISSION FORM**
- 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 Panel Members when amendments are deliberated on. For detailed information on the conduct of full board review of study protocol amendments, see **SOP II-5.7.1.**

4.1.5. ***Communication of results***

4.1.5.1. The PI is notified of the UPMREB Panel decision noting which amended documents are approved for use through a notice of action. The notice of action is sent to the PI via e-mail and can also be claimed at the UPMREB office.

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 amended study protocol or protocol-related document with a new version number and date and stamps it "APPROVED" with the approval date.

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 stores 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 granted for a period of one year or less. After approval, continuing review is required to be done at least once a year, depending on the risk assessment of the study protocol, which is determined during initial review. This is facilitated through the submission of **UPMREB FORM 3(B) 2012: CONTINUING REVIEW APPLICATION FORM**.

4.2.1.2. The frequency of continuing review is indicated in **UPMREB FORM 4(B) 2019: CERTIFICATION OF APPROVAL,** which is provided to the PI upon approval of the study.

4.2.1.3. For ethical clearance or approval approaching the one-year expiry date and requiring a renewal or extension, submit **UPMREB FORM 3(B) 2012: CONTINUING REVIEW APPLICATION FORM 30 days** prior to expiry date.

4.2.1.4. For clinical research and clinical trials, the PI and study team are required to submit evidence of a valid Good Clinical Practice (GCP) Training together with the **UPMREB FORM 3(B) 2012: CONTINUING**

REVIEW APPLICATION FORM for further extension of ethical clearance.

4.2.1.5. The Secretariat Staff looks through the Study Protocol Database for the titles of study protocols that are due for continuing review at the end of the month.

4.2.1.6. The Secretariat Staff informs the respective PIs at least **60 days** in advance of the expiration of review by fax, e-mail, or post using **UPMREB FORM 4(N) 2012: REMINDER LETTER FOR CONTINUING REVIEW OR FINAL REPORT** and keeps a receiving copy of the communication.

4.2.1.7. The continuing review application is facilitated through the submission of accomplished **UPMREB FORM 3(B) 2012: CONTINUING REVIEW APPLICATION FORM**, together with the synopsis of the study protocol and current informed consent documents. This comprises the continuing review application package.

4.2.1.8. The principal investigator registers the continuing review application in iREB and submit a complete application package once the submission has been accepted and the PI has been notified by the Secretariat Staff.

4.2.1.9. The Secretariat Staff screens the iREB submission for completeness and forwards the submission to the iREB account of the UPMREB Coordinator for classification of review.

4.2.1.10. The Secretariat Staff stamps the receiving date on the submitted study protocol package and gives a receiving copy of **UPMREB FORM 3(B) 2012: CONTINUING REVIEW APPLICATION FORM** to the PI or his/her representative.

4.2.1.11. The Secretariat Staff logs the date of submission on the **SUBMISSIONS LOG [UPMREB FORM 4(M) 2012]**.

4.2.2. ***Classification of Review by the UPMREB Chair or Coordinator***

4.2.2.1. The UPMREB Chair/Coordinator 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.

4.2.3. *Review by Panel Chair and Primary Reviewers*

4.2.3.1. All continuing review application submissions will be forwarded to the Primary Reviewers, via iREB and also by courier in exceptional circumstances, together with a copy of the originally approved protocol for the reviewer to determine if there is any change in the original risk-benefit assessment. The reviewers will be notified once the protocol submission has been forwarded.

4.2.3.2. For submissions under expedited review, action is finalized at the level of the Panel Chair within **ten** (**10**) calendar days.

4.2.3.3. Continuing review application packages subject to full board review received within the cut-off period of **seventeen** (**17**) days before the panel meeting are sent to Primary Reviewers **twelve** (**12**) to **fourteen** (**14**) calendar days before the meeting.

4.2.3.4. The Secretariat Staff places the continuing review application on the agenda for the next panel meeting.

4.2.3.5. The Primary Reviewers accomplish the review and return the signed **UPMREB FORM 3(B) 2012: CONTINUING REVIEW APPLICATION FORM** to the Secretariat Staff through iREB or hand deliver them with the continuing review application package seven (7) days upon receipt for expedited review and on or before the day of the Panel 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 Panel Members along with the meeting agenda:

- **UPMREB FORM 3(B)2012: CONTINUING REVIEW APPLICATION FORM**
- Study protocol synopsis
- Current informed consent documents

4.2.4.2. The documents are presented to Panel 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-5.7.2.**

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 e-mail. The notice of action can be claimed at the UPMREB office while the certificate of approval is endorsed to the Research Grants and Administration Office to be claimed by the PI.

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 stores the signed continuing review application documents in the study protocol file folder.

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 UPMREB with a summary of the outcome of the study, especially of the human participants who were involved, in a form of an end of study report.

4.3.1.2. The Secretariat Staff looks through the Study Protocol Database for the titles of study protocols that are due for final report at the end of the month.

4.3.1.3. The Secretariat Staff informs the respective PIs of study protocols whose ethical clearances have expired to submit a Final Report at least **60 days** in advance of the due date of review by fax, e-mail, or post using **UPMREB FORM 4(N) 2012: REMINDER LETTER FOR CONTINUING REVIEW OR FINAL REPORT** and keeps a receiving copy of the communication.

4.3.1.4. The end of study reporting is facilitated through the submission of **UPMREB FORM 3(C) 2012: 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.

4.3.1.5. The principal investigator registers final report in iREB and submit a complete package once the submission has been accepted and the PI has been notified by the Secretariat Staff.

4.3.1.6. The Secretariat Staff screens the iREB submission for completeness and forwards the submission to the iREB account of the UPMREB Coordinator for classification of review.

4.3.1.7. The Secretariat Staff stamps the receiving date to the submitted printed package and gives a receiving copy of **UPMREB FORM 3(C) 2012: FINAL REPORT FORM** to the PI or his/her representative.

4.3.1.8. The Secretariat Staff logs the date of submission on the **SUBMISSIONS LOG [UPMREB FORM 4(M) 2012]**.

4.3.2. ***Classification of Review by the UPMREB Chair or Coordinator***

4.3.2.1. Generally, final reports are classified for expedited review, unless otherwise indicated by the specificities of the submitted information.

4.3.3. ***Review by Primary Reviewers***

4.3.3.1. The final report submission is forwarded to the Primary Reviewers, via iREB and also by courier, in exceptional circumstances. The reviewers will be notified once the submission has been forwarded.

4.3.3.2. Under expedited review, action is finalized at the level of the Primary Reviewers within **ten** (**10**) calendar days.

4.3.3.3. The Primary Reviewers accomplish the review and return the signed **UPMREB FORM 3(C) 2012: FINAL REPORT FORM** to the Secretariat Staff through iREB or hand deliver them with the final report package seven (7) days upon receipt.

4.3.4. ***Communication of results***

4.3.4.1. The PI is notified of the panel decision, noting panel action on the final report through a notice of decision. The certificate of decision of final reports are claimed at RGAO.

4.3.4.2. 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.

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

- The study protocol is classified as inactive.
- Ethical clearance is expired effective on the day of the notice of decision.
- Study protocol records will be made available for three (3) years in the archives after the expiration date.

4.3.5. ***Files management***

4.3.5.1. The Secretariat Staff stores 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.

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

4.3.5.3. 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. A study protocol noncompliance is any deviation from, or changes of the protocol without agreement by the sponsor and prior review and documented approval or favorable opinion from the IRB/IEC of an amendment, except where necessary to eliminate an immediate hazard(s) to trial subjects, or when the changes involves only logistical

or administrative aspects of the trial (e.g., change in monitor/s, change of telephone number/s) (ICH-GCP).

4.4.1.2. The investigator should document, explain, and report to the UPMREB any noncompliance from the approved protocol, whether minor or major, at the soonest possible time up to six (6) months after the event.

4.4.1.3. The investigator may implement a deviation from the protocol to eliminate an immediate hazard(s) to study subjects without prior UMPREB 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).

4.4.1.4. Reporting of study protocol noncompliance is facilitated through the submission of **UPMREB FORM 3(D) 2012: 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.

4.4.1.5. The principal investigator registers the noncompliance report in iREB and submit a complete noncompliance report package once the submission has been accepted and the PI has been notified by the Secretariat Staff.

4.4.1.6. The Secretariat Staff screens the iREB submission for completeness and forwards the submission to the iREB account of the UPMREB Coordinator for classification of review.

4.4.1.7. The Secretariat Staff stamps the receiving date on the submitted noncompliance report package and gives a receiving copy of **UPMREB FORM 3(D) 2012: STUDY PROTOCOL NONCOMPLIANCE (DEVIATION OR VIOLATION) REPORT** to the PI or his/her representative.

4.4.1.8. The Secretariat Staff logs the date of submission on the **SUBMISSIONS LOG [UPMREB FORM 4(M) 2012]**.

4.4.2. *Classification of Review by the UPMREB Coordinator*

4.4.2.1. Generally, study protocol noncompliance reports are classified as full board review; unless otherwise indicated by the specificities of the submitted information.

4.4.3. *Review by Panel Chair and Primary Reviewers*

4.4.3.1. The noncompliance report submission is forwarded to the Primary Reviewers after review classification by the Panel Chair via iREB and also through courier, in exceptional circumstances. The reviewers will be notified once the protocol submission has been forwarded.

4.4.3.2. Study protocol noncompliance reports are assessed whether noncompliance have potentially serious consequences that could critically affect data integrity or put patients' safety at risk.

4.4.3.3. Study protocol noncompliance report packages subject to full board review received within the cut-off period of **seventeen** (**17**) days before the panel meeting are sent to Primary Reviewers **twelve** (**12**) to **fourteen** (**14**) calendar days before the panel meeting.

4.4.3.4. For submissions under expedited review, action is finalized at the level of the Primary Reviewers within **ten** (**10**) calendar days.

4.4.3.5. The Secretariat Staff places the study protocol noncompliance report on the agenda for the next panel meeting.

4.4.3.6. The Primary Reviewers accomplish the review and return the signed **UPMREB FORM 3(D) 2012: STUDY PROTOCOL NONCOMPLIANCE (DEVIATION OR VIOLATION) REPORT** to the Secretariat through iREB or hand deliver them together with the study protocol noncompliance report package on or before the day of the Panel Meeting together.

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 Panel Members along with the meeting agenda:

- **UPMREB FORM 3(D)2012: STUDY PROTOCOL NONCOMPLIANCE (DEVIATION OR VIOLATION) REPORT**
- Documents related to the deviation

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

4.4.4.3. The UPMREB Panel can suspend ethical clearance or subject recruitment until noncompliance issues are addressed.

4.4.4.4. The UPMREB Panel 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 noncompliance report, **see SOP II-5.7.5**.

4.4.5. ***Communication of results***

4.4.5.1. The PI is notified of the panel decision, noting panel action on the study protocol noncompliance report through e-mail. The notice of action for noncompliance reports are claimed at the UPMREB office.

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 stores the signed study protocol noncompliance report documents in the study protocol file folder.

4.5. EARLY STUDY TERMINATION REPORT

4.5.1. ***Management of the early study termination report upon submission***

4.5.1.1. A report for early study termination is submitted when a study approved by the UPMREB 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 unresolvable valid complaints.

4.5.1.2. Early study termination is facilitated through the submission of **UPMREB FORM 3(E) 2012: EARLY STUDY TERMINATION REPORT 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 principal investigator registers the report in iREB and submit complete early study termination report package once the submission has been accepted and the PI has been notified by the Secretariat Staff.

4.5.1.4. The Secretariat Staff screens the iREB submission for completeness and forwards the submission to the iREB account of the UPMREB Coordinator for classification of review.

4.5.1.5. The Secretariat Staff stamps the receiving data on the submitted printed copies and gives a receiving copy of **UPMREB FORM 3(E) 2012: EARLY STUDY TERMINATION REPORT FORM** to the PI or his/her representative.

4.5.1.6. The Secretariat Staff logs the date of submission on the **SUBMISSIONS LOG [UPMREB FORM 4(M) 2012]**.

4.5.2. ***Classification of Review by UPMREB Chair or Coordinator***

4.5.2.1. Generally, review of early study termination reports are classified as full board.

4.5.3. ***Review by Panel Chair and Primary Reviewers***

4.5.3.1. The early termination report is forwarded to the Primary Reviewers through iREB, and courier in exceptional circumstances. The reviewers will be notified once the protocol submission has been forwarded.

4.5.3.2. Early study termination report packages subject to full board review received within the cut-off period of **seventeen** (**17**) days before the panel meeting are sent to Primary Reviewers **twelve** (**12**) to **fourteen** (**14**) calendar days before the panel meeting.

4.5.3.3. The Secretariat Staff places the early study termination report on the agenda for the next panel meeting.

4.5.3.4. The Primary Reviewers accomplish the review and return the signed **UPMREB FORM 3(E) 2012: EARLY STUDY TERMINATION REPORT FORM** to the Secretariat through iREB or hand deliver them together with the early study termination report package on or before the day of the Panel Meeting.

4.5.4. ***Full board review of early study termination report***

4.5.4.1. The Secretariat Staff distributes the following early study termination report package to Panel Members along with the meeting agenda:

- **UPMREB FORM 3(E)2012: EARLY STUDY TERMINATION REPORT FORM**
- Documents related to the early study termination

4.5.4.2. The UPMREB Panel deliberates on the implications of the report 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 panel may request information from the PI or invite the PI for clarificatory interview.

4.5.4.4. For detailed information on full board review of early study termination report, **see SOP II-5.7.6**.

4.5.5. ***Communication of results***

4.5.5.1. The PI is notified of the panel decision, noting panel action on the early study termination report through an action letter. Notice of action for early termination report is claimed at the office of the UPMREB.

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

4.5.6. *Files management*

4.5.6.1. The Secretariat Staff stores the early study termination report and related documents in the study protocol file folder.

4.6. Queries, Notification, and Complaints

4.6.1. *Management of submitted queries or complaints*

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

4.6.1.2. UPMREB can also accept communications of queries, notifications, and complaints from other parties provided these communications are relevant to UPMREB oversight.

4.6.1.3. Any UPMREB personnel can receive a query or complaint. Action on queries and complaints is managed through the use of **UPMREB FORM 3(I) 2014: QUERIES, NOTIFICATIONS AND COMPLAINTS.** This form should be accomplished by any party communicating queries, notifications, and complaints or grievances for information or action by the UPMREB.

4.6.1.4. In case of communication from research subjects or participants, UPMREB personnel can encode the information on their behalf if needed.

4.6.1.5. Information reported in this form is processed either as a study-protocol-related or non-study-protocol-related communication, as the case may be.

4.6.1.6. If necessary, a letter may be attached to this form by the sending party, but a summary of the nature of communication should still be encoded in this form to allow proper filing of communication.

4.6.1.7. The Secretariat Staff logs the communication into the **SUBMISSIONS LOG [UPMREB FORM 4(M) 2012]** for proper filing and action by relevant UPMREB personnel.

4.6.2. ***Classification of Review by UPMREB Coordinator***

4.6.2.1. The sending party must indicate in UPMREB FORM 3(I) 2014: QUERIES, NOTIFICATIONS AND COMPLAINTS whether or not the communication is study-protocol-related or non-study-protocol-related.

4.6.2.2. The UPMREB Coordinator classifies communication for either full board or expedited review depending on the nature of the communication and response needed from UPMREB.

4.6.2.3. Complaints are classified under full board review.

4.6.2.4. For non-study-protocol-related queries, review and recommendations can be finalized at the level of the UPMREB Coordinator.

4.6.3. ***Review by Panel Chair and Primary Reviewers of Study-Protocol-Related Communications***

4.6.3.1. For communications under expedited review, action is finalized at the level of the Panel Chair within **ten** (**10**) calendar days.

4.6.3.2. Communications subject to full board review received within the cut-off period of **seventeen** (**17**) days before the panel meeting are sent to Primary Reviewers **twelve** (**12**) to **fourteen** (**14**) calendar days before the panel meeting.

4.6.3.3. The Secretariat Staff places the query/notification/complaint in the agenda of the next panel meeting.

4.6.3.4. The Panel Chair or Primary Reviewers review the information entered in **UPMREB FORM 3(I) 2014: QUERIES, NOTIFICATIONS AND COMPLAINTS**.

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

4.6.4. ***Full board review of study-protocol-related participant query or complaint***

4.6.4.1. The Secretariat Staff distributes the completed **UPMREB FORM 3(I) 2014: QUERIES, NOTIFICATIONS AND COMPLAINTS** to Panel Members along with the meeting agenda.

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

4.6.4.3. The panel may request information from the PI, invite the PI for clarificatory interview, or require corrective action.

4.6.4.4. For detailed information on full board review of queries or complaints, **see SOP II-5.7.7**.

4.6.5. ***Communication of results***

4.6.5.1. The UPMREB responds to queries, notification, and complaints in writing after a course of action of appropriate response is identified whether through expedited or full board review.

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

4.6.6. ***Files Management***

4.6.6.1. The Secretariat Staff stores the signed documents in the study protocol file folder.

5. Serious Adverse Event (SAE) and Suspected Unexpected Serious Adverse Reaction (SUSAR) Reports Workflow

ACTIVITY	RESPONSIBILITY
Screen and receive serious adverse event (SAE)) and suspected unexpected serious adverse reaction (SUSAR)report/s submitted in iREB ↓	Secretariat Staff
Log SAE submission to Submissions Log ↓	Secretariat Staff
Assign primary reviewers ↓	SAE Committee Chair
Forward UPMREB SAE reports to assigned SAE Committee primary reviewer of the month together with previously submitted offsite and onsite SAE protocol-specific reports, latest Investigator's Brochure, and protocol summary ↓	Panel Secretariat Staff

III. POST-APPROVAL REVIEW

ONSITE (SAE and SUSAR)	OFFSITE (SAE and SUSAR)	
Assess and determine causality of SAE reports ↓		SAE Committee Primary Reviewer
Receives reviews of SAE Primary reviewers and forwards a summary of reviews to the assigned SAE panel representative of the month ↓		Panel Secretariat Staff
Includes SAE reports in the monthly panel meeting ↓		Panel Secretariat Staff
Discuss the SAE reports and review during the monthly panel meeting ↓		SAE Panel Representative of the month
Communicate results to principal investigator ↓		Panel Secretariat Staff
If no further action: Send notification of decision to PI **If recommend further action:** Send notification with recommendations to PI; process response by full board review **If request information**: Send notification of requested information to PI; process response by full board review **If pending:** Send notification of decision with major clarifications to PI; process response by full board review		
File in the respective protocol folder		Panel Secretariat Staff
Conduct of SAE Committee Meeting		
Prepare agenda including list of protocol SAE reports and summary of reviews ↓		SAE Secretariat Staff
Present SAE reports including assessment of possible signals if common event/reactions are found ↓		SAE Committee Primary Reviewer
Communicate results to principal investigator for any additional action necessary		Secretariat Staff

↓	
Prepare a summary report of the meeting ↓	Secretariat Staff
Present meeting summary report during the monthly panel meeting ↓	SAE Committee Panel Representative
Manage study protocol files	Secretariat Staff

DETAILED INSTRUCTIONS

5.1. Screening and receipt of the SAE/SUSAR report upon submission

5.1.1. Suspected, unexpected serious adverse reactions (SUSARs) are events that are unexpected and not consistent with the applicable product information that are temporally associated with the subject's 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

5.1.2. The PI must report serious adverse advents to the UPMREB panel in accordance with the **UPMREB GL 01: Guideline on Reporting Adverse Events.**

5.1.3. The PI must report suspected, unexpected, serious adverse reactions (SUSAR), and other documents deemed relevant by the investigator to clarify information indicated in the report. This comprises the study protocol SUSAR report package and are submitted via iREB.

5.1.4. The Secretariat Staff screens the iREB submission for completeness and notifies PI to submit two (2) sets of hard copies of **UPMREB FORM 3(G)2012:**

SUSPECTED UNEXPECTED SERIOUS ADVERSE EVENT/REACTION/S REPORT and other relevant documents.

5.1.5. The Secretariat Staff stamps the hard copies and receiving copy 'received' and date of submission and returns the receiving copy to the PI or his/her representatives.

5.1.6. The Secretariat Staff logs the date of submission on the **SUBMISSIONS LOG [UPMREB FORM 4(M)2012]**.

5.1.7. The SAE Committee Chair assigns SAE primary reviewers who will assess the report packages.

5.2. Processing of Serious Adverse Events (SAE) and Suspected Unexpected Serious Adverse Reactions (SUSARs) Reports

5.2.1. *Onsite Serious Adverse Event/s and Suspected, Unexpected, Serious Adverse Reactions (SUSAR) Reports*

5.2.1.1. The secretariat staff forwards the iREB application of onsite SAE Report Package comprised of the following documents to the iREB account of the respective SAE Committee Primary Reviewer within three working days of receipt:

- **UPMREB FORM 3(G) 2012: SUSPECTED UNEXPECTED, SERIOUS ADVERSE EVENT/REACTION/S REPORTS**
- **UPMREB FORM 3(J)2016: SAE AND SUSAR REPORTS SUMMARY**
- Latest Investigator's Brochure
- Protocol Summary
- Previously submitted offsite and onsite SAE protocol-specific reports
- Other supporting documents, if any

5.2.1.2. The SAE Committee Primary Reviewer accomplishes the review and returns the signed **UPMREB FORM 3(G) 2012**: **SUSPECTED UNEXPECTED, SERIOUS ADVERSE EVENT/REACTION/S REPORTS** and **UPMREB FORM 3(J)2012: SAE AND SUSAR REPORTS SUMMARY** to the Secretariat seven (7) days after his/her receipt of the SAE/SUSAR report package.

5.2.1.3. If the SAE Committee Chair assesses the report/s to be needing immediate action, he/she will forward the report/s and his/her recommendation to the Panel Chair for immediate action.

5.2.1.4. The secretariat staff includes the SAE and SUSAR report/s on the agenda of the next panel meeting, provided that cut-off period for panel meeting inclusion is **seventeen (17)** days prior, in which an SAE Committee Member is required to attend and presents the SAE reports. If the member is not available on the said meeting, the Panel Chair will present the review to the board in the panel meeting.

5.2.1.5. The Secretariat Staff generates a summary of review using **UPMREB FORM 3(K)2018: SAE AND SUSAR PROTOCOL-SPECIFIC SUMMARY OF REVIEWS** to be included in the panel meeting agenda and forwards the review summary to the panel for action.

5.2.1.6. The following documents are included in the panel meeting file to be distributed to each panel member together with the agenda:

- **UPMREB FORM 3(J)2012: SAE AND SUSAR REPORT SUMMARY**
- **UPMREB FORM 3(K)2018: SAE AND SUSAR PROTOCOL-SPECIFIC SUMMARY OF REVIEWS**

5.2.1.7. During the meeting, the Panel Chair calls for a decision on the SAE/SUSAR report/s with respect to the recommendation/s of the SAE Primary Reviewer. For detailed information on full board review of SAE/SUSAR reports, **see SOP II-5.7.3.**

5.2.2. ***Offsite Serious Adverse Event/s and Suspected, Unexpected, Serious Adverse Reactions (SUSARs) Reports***

5.2.2.1. Summary listing of offsite SAE and SUSAR reports are filed in the study protocol and serve as reference when reviewing onsite SAE/SUSAR reports.

5.3 Conduct of Meeting

5.3.1 The meeting is conducted to identify trends and patterns and assess causality and signals of SAE and SUSAR reports.

5.3.2 The SAE Secretariat staff encodes and collates onsite SAE and SUSAR reports submitted since the quarter prior to the meeting using the **UPMREB FORM 3(J)2012: SAE AND SUSAR REPORTS SUMMARY.**

5.3.3 The SAE secretariat staff forwards the list of protocol SAE reports and summary of reviews to the assigned reviewers.

5.3.4 Copies of the **UPMREB FORM 3(J)2012: SAE AND SUSAR REPORTS SUMMARY** are distributed to each panel member together with the agenda.

5.3.5 The primary reviewer presents his/her assessment of SAE reports and checks for possible signals if common event/reactions are found.

5.3.6 During the meeting, the SAE Committee Chair calls for a decision on the SAE/SUSAR report with respect to the assessment of causality and signals. The panel may require any of the following actions:

- *No further action*
- *Recommend further action*
- *Request information*
- *Pending, if major clarifications are required before decision can be made*

5.3.7 The SAE secretariat staff prepares a summary report of the quarterly meeting to be presented to the panel by the SAE member representative during the nearest monthly panel meeting.

5.4 Communication of results

5.4.1 The PI is notified of the panel decision, noting panel action on the Serious Adverse Event/Suspected, Unexpected, Serious Adverse Reaction/s Report through an action letter.

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

5.5 Files management

5.5.1 The Secretariat Staff stores the signed SAE/SUSAR report/s in the study protocol file folder.

5.5.2 Files are managed in accordance with **SOP IV-7: Active Files.**

III. POST-APPROVAL REVIEW

6. Site Visit Workflow

ACTIVITY	RESPONSIBLE PERSON
Select study sites to visit ↓	UPMREB Chair, Panel Chairs, Panel Secretaries, and Members
Notify PI of date of "site visit" ↓	Panel Chair and Panel Secretary
Create Site Visit Team ↓	Panel Chair and Panel Members
Conduct Site Visit ↓	Site Visit Team
Present findings during panel meeting ↓	Panel Chair
Communicate results of Site Visit and subsequent panel action 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 Panel

6.1.2. Study sites may also be selected for Site Visit upon recommendation of the UPMREB Serious Adverse Event Committee.

6.1.3. A decision for Site Visit is deliberated on during a full board meeting of the UPMREB Panel that issued the ethical clearance or approval to a study.

6.2. Notification of PI of date of site visit

6.2.1. The Panel Chair, through the Secretariat, informs the PI at least two **(2)** weeks before the scheduled visit through a letter. A copy of **UPMREB FORM 3(F)2012: SITE VISIT REPORT FORM** is attached to this letter.

6.2.2. 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 Panel Chair.

6.3.3. The Site Visit Team should be composed of at least three (**3**) people: one (**1**) of the primary reviewers of the protocol, one (**1**) SAE Subcommittee member, and one (**1**) Panel Member.

6.3.4. The Site Visit Team members are informed of their assignment through the issuance of **UPMREB FORM 3(H)2012: NOTICE OF SITE VISIT.**

6.3.5. The Secretariat Staff prepares a Study Visit Package for each members of the Site Visit Team, inclusive of the **UPMREB FORM 3(F)2012: SITE VISIT REPORT FORM** and a copy of the approved study protocol and related documents**.**

6.3.6. The Site Visit Team prepares by reviewing the contents of the study file and the requirements of **UPMREB FORM 3(F)2012: SITE VISIT REPORT FORM.**

6.4. Conduct of Site Visit

6.4.1. Upon arrival in the study site, the Site Visit Team uses **UPMREB FORM (F)2012: SITE VISIT REPORT FORM** to do the following:

- Review the study protocol
- Review the informed consent documents and verify if the site is using the most recently 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. Upon arrival in the study site, the Site Visit Team uses **UPMREB FORM** 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 UPMREB Panel Meeting

6.5.1. The Site Visit Team completes **UPMREB FORM 3(F) 2012: 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 seven (7) calendar days after the Site Visit.

6.5.2. The Secretariat Staff logs the date of submission on the **SUBMISSIONS LOG [UPMREB FORM 4(M) 2012].**

6.5.3. The Secretariat Staff places the Site Visit Report in the agenda of the next panel meeting.

6.5.4. During the meeting, the Secretariat Staff distributes the completed **UPMREB FORM 3(F) 2012: SITE VISIT REPORT FORM** to Panel Members along with the meeting agenda.

6.5.5. The UPMREB Panel deliberates on the implications of results of the Site Visit on the rights, safety, and welfare of the study participants; and makes an overall determination of protocol compliance in the study site.

6.5.6. For detailed information on full board review of Site Visit Reports, **see SOP II-5.7.4**.

6.6. Communication of results

6.6.1. The PI is notified of the panel action or recommendations through an action 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 Primary Reviewers, Panel Secretary, and Panel Chair sign the **UPMREB FORM 3(F) 2012: SITE VISIT REPORT FORM.**

6.7.2. The Secretariat Staff stores the Site Visit documents in the study protocol file folder.